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Electronic product information (ePI) in MRP and national procedures

Guide for applicants in the ePI pilot

1. Purpose and context

1.1. Purpose of this guide

This guide is for applicants participating in the ePI pilot. The pilot will involve regulatory procedures in real-time for a limited number of applications for centralised, European and purely national procedures. Participating authorities are the European Medicines Agency, the Danish Medicines Agency, the Dutch Medicines Evaluation Board, the Spanish Agency for Medicines and Health Products and the Swedish Medical Products Agency. It presents the electronic product information (ePI) process within MRP and national variation procedures and provides details on its practical implementation. Other guidance documents regarding procedures and creation of product information should be read in conjunction.

1.2. Preliminary requirements

For ePI creation in the Product Lifecycle Management (PLM) Portal, you will need an active EMA account and ePI user access role(s) assigned to that account.

Important note: ePI roles are currently only available to participants in the ePI pilot.

- EMA Account Management is the online platform to request and manage your EMA account
- The ePI guide to registration describes the steps to request ePI roles in the PLM portal
- The ePI guide to navigation shows users how to create and manage ePI in the PLM portal

2. ePI creation prior to submitting application

In case the variation affects any of the product information annexes, i.e. summary of product characteristics (SmPC), labelling and/or package leaflet:

- **If no ePI exists for the medicine**:
  prior to submitting the application, the applicant should create an ePI (including SmPC, labelling and package leaflet) in the Product Lifecycle Management Portal.
- **If an ePI already exists for the medicine**:
  prior to submitting the application, the applicant should update the ePI in the Product Lifecycle Management Portal.

- For creation and update, please follow the ePI user guide for applicants.
- The content of the ePI should be identical to the content of the PI in PDF (clean) format included in the eCTD of the variation submission. That means that the ePI entered in the PLM-portal consists of PL, SmPC and labelling, even though a change in the text might only involve e.g. the SmPC.

For MRP, common ePI texts and translations (or pure national texts for National procedures) should be submitted as per procedure i.e. only the English-language version of the ePI is required at submission unless the procedure requires translations at the beginning of the procedure. Regarding translations, these should be included at submission as part of the procedure, i.e. for variations type I, translations of the ePI is only required in the RMS language. For example, when SE as

participating agency in the ePI pilot is acting RMS, only the Swedish translation version of the ePI is required. All other translations (including the translated ePI) follow normal procedure, i.e. submitted in Microsoft Word versions according to procedural timeframes. ePI does not replace Word documents in this pilot.

While the ePI is being created, the ePI has the status '*Draft*'. At the time of submitting the application, the applicant must change the ePI status to '*Submission*'.

Changing the ePI status from '*Draft*' to *'Submission'* or *'Update'* requires that a declaration is completed and signed by a Signatory who is an authorised contact for the product.

The procedure number field of the ePI can be completed when available and can be edited when the ePI is in '*Draft*' to *'Submission'* status.

3. ePI submission and validation

In the cover letter accompanying the variation notification/application, the applicant should provide the related ePI ID obtained from the PLM portal by including the following sentences:

"An electronic version of the product information (ePI) has been created to accompany this submission with the ePI ID: <EPI/YY/XXX ID to be copied from PLM portal>.

<In case the ePI is an update of an existing ePI, include the sentence:><On publication, this ePI should replace the existing ePI with the ePI ID: <EPI/YY/XXX ID of existing ePI to be copied from PLM portal>."

During validation before the start of the procedure, the NCA will check that the ePI with the ePI ID provided is present in the PLM portal with the status *'Submission'*. Issues identified with ePI during validation will be notified to the applicant via e-mail. The applicant will be requested to provide responses to the issues raised within the validation phase. Delayed or insufficient responses may lead to the application proceeding without inclusion of ePI.

Provision of ePI does not negate the requirement to submit product information annexes in eCTD. The relevant complete set of product information annexes must be submitted in Word and PDF formats in the eCTD sequence and working documents folder as described in the post-authorisation guidance and the CMDh guidance documents.

The ePI format is not assessed, however the ePI drafts might be updated during the procedure at the discretion of the Applicant. It is the responsibility of the applicant to ensure that, at the end of the procedure, the ePI is identical in content to the final PI in Word and PDF formats.

Please note: The PLM portal includes a functionality to export ePI to Word, which applicants may wish to utilise for generation of Word files for eCTD submission.

4. ePI update

The NCA will notify the applicant about the outcome of the review, both at the end of each round and/or at the EoP.

Where the outcome is favourable and no additional changes are needed to the product information, no action is required from the applicant and the ePI remains in '*Submission*' status until publication.

Where the final outcome is unfavourable and/or the applicant decides to withdraw, when being notified of the unfavourable outcome, the applicant must change the status of the ePI for the procedure to '*Deactivated*' in the PLM portal.

5. ePI publication

In the case of a favourable outcome, after EoP the NCA will mark the ePI as approved in the PLM portal. This is not visible to the applicant in the PLM portal.

By 4-5 weeks after a favourable outcome, the NCA will publish the ePI to the FHIR repository, from where it will be publicly available via the ePI application programming interface. The status of the ePI in the PLM portal will change to '*Published*'.

6. Requirements per procedure

Type IA

Type IA is a variation that should not require any assessment, however there is a need for validation. The validation phase is 30 days from the date for submission, no clock stop allowed. Variations type IA may affect all parts of the product information.

Timetable for type IA procedures in general

Days	**Activity**	**ePI Activity**
Day 0	Procedure start	Create/Update ePI - common as well as translated. Change status from ´*Draft*´ to ´*Submission*´ in the Finalisation page in the portal
Day 0 to day 30	Validation	Even though this procedure does not foresee PI changes requested by authorities, it might do so sometimes. If so, update ePI according to comments any time, but at the latest at Day 30 - Approval. Change status from ´*Draft*´ to ´*Update*´ in the Finalisation page in the portal.
Day 30 (may be closed earlier)	Validation and acknowledgement of acceptable/ unacceptable notification.	At the EoP day the Applicant will update the ePI – both the common and translated text – with approval/revision date. The NCA will change status from ´*Submission*´ to ´*Approved*´ and ´*Published*´ in the Finalisation page in the portal. Should the texts (common, translation or both) be delayed for some reason, the ePI should be

		updated at the same time as actual approval of each and respective text.

Type IB

Variation type IB is a variation not significantly affecting quality, safety or efficacy; however, it needs some assessment. After completing submission, the assessment is allowed for 30 days. If no comments within 30 days, the Applicant may consider the variation as approved and could implement the variation. If any comments from CMS, there may be another period of 30 days for response time. Variations type IB may affect all parts of the product information.

There is an auto-validation phase of 7 calendar days from submission to all concerned CMS. If there are no validation comments from any CMS, the procedure will start. RMS may comment, usually no formal report (email conversation). If CMS do not comment, it is interpreted as support. National phase with review of translated product information is performed in parallel.

Timetable

Days	**Procedure Activity**	**ePI Activity**
Day -7 to day 0	Validation	Create/Update **common** ePI. Change status from *´Draft´* to *´Submission´* in the Finalisation page in the portal. Create/Update **translated** ePI. Change status from *´Draft´* to *´Submission´* in the Finalisation page in the portal.
Day 0	Procedure start	
Day 20	RMS comments	
Day 27	CMS comments	
Day 30	Approval or clock stop	Update ePI according to comments any time, but at the latest at Day 30 - Approval. Change status from *´Draft´* to *´Update´* in the Finalisation page in the portal. At the EoP day the Applicant will update the ePI – both the common and translated text – with approval/revision date. The NCA will change status from *´Submission´* to *´Approved´* and *´Published´* in the Finalisation page in the portal. Should the texts (common, translation or both) be delayed for some reason, the ePI should be updated at the same time as actual approval of each and respective text.

30 days	*Await response from applicant*	
New day 0 (after clock stop)	Start of second round	
New day 20	RMS comments	
New day 27	CMS comments	
New day 30	Approval/Rejection	Update ePI according to comments any time, but at the latest at the EoP Day. Change status from ´*Draft*´ to ´*Update*´ in the Finalisation page in the portal. At the EoP day the Applicant will update the ePI – both the common and translated text – with approval/revision date. The NCA will change status from ´*Submission*´ to ´*Approved*´ and ´*Published*´ in the Finalisation page in the portal. Should the texts (common, translation or both) be delayed for some reason, the ePI should be updated at the same time as actual approval of each and respective text.

Variations according to Article 61(3)

Variation according to Article 61(3) is a variation not significantly affecting quality, safety or efficacy; however, it needs some assessment. Variations according to Article 61(3) may not affect the SmPC.

After completing submission, the assessment is allowed for 25 days. Between day 25 and 90 the RMS may comment. If no comments within 90 days, the Applicant may consider the variation as approved and could implement the variation. If there are comments from RMS/CMS, there may be a period of 10 days for response time.

There is an auto-validation phase of 7 calendar days from submission to all concerned CMS. If there are no validation comments from any CMS, the procedure will start. RMS may comment, usually no formal report (email conversation). If CMS do not comment, it is interpreted as support. National phase with review of translated product information is performed in parallel.

Timetable

Days	**Procedure Activity**	**ePI Activity**
Day -7 to day 0	Validation	Create/Update common ePI. Change status from *´Draft´* to *´Submission´* in the Finalisation page in the portal.
Day 0	Procedure start	
Day 15	RMS comments	
Day 20	CMS comments	
Day 25	Approval or allowance for response time	Update ePI according to comments any time, but at the latest at Day 25 - Approval. Change status from *´Draft´* to *´Update´* in the Finalisation page in the portal.
10 days	*Await response from applicant. The RMA may allow further response time.*	
Day 25-90	Any comments and changes agreed upon between the Applicant and the RMS. RMS communicating with the Applicant and the CMS.	
At the latest day 90	Approval/Rejection	Update ePI according to comments any time, but at the latest at the EoP Day. Change status from *´Draft´* to *´Update´* in the Finalisation page in the portal At the EoP day the Applicant will update the ePI – both the common and translated text – with approval/revision date. The NCA will change status from *´Submission´* to *´Approved´* and *´Published´* in the Finalisation page in the portal. Should the texts (common, translation or both) be delayed for some reason, the ePI should be updated at the same time as actual approval of each and respective text.

Type II

Variation type II is a variation that may significantly affect quality, safety or efficacy, and needs assessment. The Applicant is not allowed to implement the variation before any approval. Variations type II may affect all parts of the product information.

There are three timetables for type II variations:

- **Short timetable**: *30 days*. Urgent safety updates.
- **Standard timetable**: *60 days*. Standard.
- **Long timetable**: *90 days*. Change or extension of indication. Or for complex grouping variations or when nationally approved product up for PI harmonisation.

There is an auto-validation phase of 14 calendar days from submission to all concerned CMS. If there are no validation comments from any CMS, the procedure will start. RMS will always circulate a report. CMS may comment. If CMS do not comment, it is interpreted as support. National phase with review of translated product information starts after the EoP.

Short timetable	**Standard timetable**	**Long timetable**	**Activity**	**ePI Activity**
Day -14 to day 0			Validation	Create/Update common ePI. Change status from *´Draft´* to *´Submission´* in the Finalisation page in the portal.
Day 0			Procedure start	
Day 15	Day 40	Day 70	RMS circulates the PVAR	
Day 20	Day 55	Day 85	CMS comments on PVAR	
Day 21	Day 59	Day 89	Clock stop if questions	
Day 22	Day 60	Day 90	Approval if no questions	Update ePI according to comments any time, but at the latest at Day 22/60/90 - Approval. Change status from *´Draft´* to *´Update´* in the Finalisation page in the portal.
10 days	*60 days*	*90 days*	*Await response from applicant*	
10 days	60 days	60 days	RMS formulating FVAR	

Day 22	Day 60	Day 90	RMS circulation of FVAR, start of second round	
-	*(Day 75)*	*(Day 105)*	*Breakout if needed*	
Day 25	Day 80	Day 110	CMS comments on FVAR	
Day 30	Day 90	Day 120	Approval/ rejection/ referral	Update ePI according to comments any time, but at the latest at the EoP Day. Change status from *´Draft´* to *´Update´* in the Finalisation page in the portal. At the EoP Day the Applicant will update the common ePI with approval/revision date. The NCA will change status from *´Update´* to *´Approved´* and *´Published´* in the Finalisation page of the portal.
Within 7 days after EoP Day			Applicant submits the PI translations.	Create/Update translated ePI. Change status from *´Draft´* to *´Submission´* in the Finalisation page in the portal.
Within 30 days after EoP Day			Communication between the NCA and Applicant regarding translation.	When translation is agreed upon, the Applicant will update the translated ePI with national approval/revision date. The NCA will change status from *´Submission´* to *´Approved´ and ´Published´* in the Finalisation page in the portal.

7. Abbreviations

AEMPS	The Spanish Agency of Medicines and Medical Devices
CMS	Concerned Member State
CMDh	Coordination group for mutual recognition and decentralised procedures (human)
DKMA	The Danish Medicines Agency
eCTD	A common technical document in electronic format. The Common Technical Document (CTD) describes the organisation of modules, sections and documents to be used by an Applicant for a Marketing Authorisation for a medicinal product for human use. The eCTD allows for the electronic submission of the CTD from applicant to regulator according to a certain structured format, the submission of PDF documents, stored in the eCTD directory structure, accessed through the XML backbone.
EMA	European Medicines Agency
ePI	Electronic product information for medicines in a semi-structured format created using the common EU electronic standard
EoP	End of Procedure
FHIR	Fast Health Interoperability Resources, a standard specification for Healthcare Interoperability
FVAR	Final Variation Assessment Report
MEB	The Medicines Evaluation Board (the Netherlands)
MPA	The Swedish Medical Products Agency
MRP	Mutual Recognition Procedure
NCA	National Competent Agency – in the ePI pilot AEMPS, DKMA, MEB, MPA respectively
PI	Product Information (authorised, statutory product information for medicines i.e. SmPC, PL and labelling)
PLM	Product Lifecycle Management (Portal)
PVAR	Preliminary Variation Assessment Report
RMS	Reference Member State
RSI	Request for Supplementary Information