European Commission

EMA
EUROPEAN MEDICINES AGENCY

HMA
Heads of Medicines Agencies

ePI pilot report

Experience gained from creation of ePI during regulatory procedures for EU human medicines

An agency of the European Union

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Executive summary

Electronic product information (ePI) for European Union (EU) medicines will benefit patients and healthcare professionals (HCPs) by providing up-to-date information on safe and effective use at the point of need. It contributes to the objectives of the European Medicines Agencies Network Strategy, the European Medicines Agency (EMA) Regulatory Science Strategy and the European Commission (EC) Pharmaceutical Strategy for Europe. Achievements to date include adoption of a harmonised standard for ePI, the EU ePI Common Standard, by the European medicines regulatory network (EMRN), development of tooling for ePI creation and management, and the conclusion of a one-year pilot, the subject of this report. The ePI initiative is supported by the EU funding programme EU4Health.

Key performance indicators

The ePI pilot resulted in successful creation and publication of ePI in real regulatory procedures at EMA, and the National Competent Authorities (NCAs) of Spain (Spanish Agency of Medicines and Medical Devices [AEMPS]), Denmark (Danish Medicines Agency [DKMA]), the Netherlands (Medicines Evaluation Board [MEB]) and Sweden (Swedish Medical Products Agency [MPA]). Key performance indicators (KPIs) defined prior to the start of the pilot included targets for time taken to create ePI, percentage of ePIs from co-opted procedures successfully created and published, usability of the ePI tooling at the Product Lifecycle Management (PLM) portal, usefulness of guidance materials, feasibility of proposed business processes and rating of editor functionality. KPIs largely met or exceeded the predefined targets, with the exception of editor functionality, for which the target was partly met. Use of the editor for adding sections, formatting content pasted from Word and inserting images and tables did not meet the KPI target. These aspects will be included in the planning of future ePI work.

Main recommendations

Recommendations of the pilot were categorised depending on whether they pertained to guidance, business processes or the PLM portal.

The pilot found that existing guidance should be supplemented and highlighted for several topics, especially where new concepts or processes are introduced. In addition, specific guidance is necessary to advise applicants on creation of ePI for product information that diverges from the Quality Review of Documents (QRD) template.

Business processes tested in the pilot introduced ePI as an add-on to the processes currently in place, with the applicant submitting ePI at the PLM portal in addition to the usual process of submitting product information files in the eCTD (electronic Common Technical Document). While further digitalisation of processes is expected in future, it is envisaged that initial introduction of ePI should have as low an impact as possible on core regulatory procedures for evaluation and supervision of medicines. The processes defined in the ePI Procedural Guides were satisfactory for the low number of short, straightforward regulatory procedures in the pilot. However, the guides must be extended to incorporate all regulatory procedures, and linguistic review processes.

In order to promote ePI adoption by companies, it is recommended to consider putting a process in place for a limited time period to allow first-time ePI submission and publication outside of a regulatory procedure.

Importantly, regulators participating in the pilot found that it will be necessary to link ePI submission to the electronic application form (eAF) and, for centrally authorised products (CAPs), to the IRIS procedure management system, which will require a significant development effort.

ePI development at the PLM portal

Applicants can create, manage and submit ePI at the PLM portal, and subsequently regulators can publish ePI. Publication of ePI makes it available at the public webpages of the PLM portal and via a read-only application programming interface (API). Experience gathered in the pilot supports the development of several ePI functionalities before ePI can be implemented into routine business. High-priority features include:

- **Import of FHIR (Fast Healthcare Interoperability Resources) format**, enabling companies to create ePI themselves and import it to the PLM portal for regulator publication, bypassing use of the editor.
- **ePI versioning** to enable access to current and previously authorised ePIs.
- **QRD template versioning** to support ongoing evolution of QRD templates.
- **Linking of ePI to the respective product in the network's Product Management Service (PMS)** so that data from both systems can be leveraged.

Further work is recommended on the ePI data itself and on the flow of information in the business process, notably:

- **Separation of styling and content of ePI**, which has been requested by stakeholders during the pilot and in previous consultations. This enables styling to be added to ePI data by consumers of the data depending on their dissemination platforms and in line with accessibility criteria.
- **Integration of ePI into Product Lifecycle Management**, to facilitate business processes, including further integration with the electronic application form and procedure management system.

In addition to the above-mentioned, resource-intensive developments, multiple smaller-sized enhancements have been recommended, with further details provided in the report.

Pilot conclusion

Although many areas for further development and improvement emerged from the pilot, there were no blocking aspects identified that would prevent inclusion of ePI in regulatory procedures as an add-on to current processes. Therefore, the overall conclusion of the pilot was that the network should progress towards ePI implementation, building on the tooling and guidance already developed and incorporating the recommendations of this report. This should encourage partners and stakeholders, including the regulatory network, pharmaceutical industry, medicine information providers, and patient and HCP representatives, to incorporate ePI into their planning and preparation activities.

Development and enhancement of ePI functionality at the PLM portal is ongoing and focused on features essential for initial go-live. It is anticipated that once these features are in place, ePI will be introduced on a voluntary basis, initially for CAPs. This will be followed by implementation at early adopter NCAs. ePI will then be rolled out across NCAs in a phased approach, taking into account the readiness and resources of the Member States.

Background

ePI refers to the authorised, statutory product information for medicines (including the summary of product characteristics [SmPC], package leaflet [PL] and labelling) made available in electronic format compliant with the EU ePI Common Standard.

EMA and its EMRN partners are working to enable the use of ePI for human medicines in the EU so that benefits of ePI for public health can be realised. ePI facilitates dissemination of information on prescribing, dispensing and using medicines via the web, e-platforms and in print, offering advantages such as improved accessibility, searchability and multilingual capabilities. ePI can also integrate with electronic healthcare systems, enabling HCPs and patients to access accurate and up-to-date product information more conveniently, when and where it is needed. The anticipated benefits and principles guiding ePI development have been established following extensive stakeholder consultation, resulting in the publication of the ePI key principles.

To realise the benefits of ePI for stakeholders across the EU, the harmonised EU ePI Common Standard was developed and adopted by the EMRN. Subsequently, development of tooling for ePI creation and management at the PLM portal began, as a product of the Network Portfolio.

From July 2023 to August 2024, EMA together with the NCAs of Spain (AEMPS), Denmark (DKMA), the Netherlands (MEB) and Sweden (MPA) have run a pilot in which ePI has been created and published in live regulatory procedures.

The objectives of the ePI pilot are:

- To enable EMA and NCAs to assess tooling and processes
- To collect feedback from companies creating and managing ePI
- To support the ePI team in determining outstanding functional requirements and inform progress to implementation

This report outlines the performance and outcomes of the pilot and derives learnings and recommendations that will inform the next steps towards introduction of ePI for EU medicines.

Methodology

NCA-led pilots

A network product owner (NPO) from AEMPS (Spain), and NCA subject matter experts (SMEs) from DKMA (Denmark), MEB (the Netherlands) and MPA (Sweden) were appointed to the ePI team in June 2022 following a call for expression of interest across the network. With their appointments, the NCAs of the NPO and SMEs undertook to run the ePI pilot alongside EMA.

Industry participant selection

Industry participants were selected with the support of trade associations.

Participants for the EMA-run pilot were proposed by ePI team Industry SMEs, in collaboration with the Inter Association Task Force (IATF, representing the Association of the European Self-Care Industry [AESGP], the European Federation of Pharmaceutical Industries and Associations [EFPIA] and Medicines for Europe) and other European trade associations. For the nationally run pilots, participants were selected following calls distributed to national trade associations. Participants were selected mainly based on the availability of upcoming, suitable, regulatory procedures.

In addition to the ePI team, staff of EMA and participating NCAs took part in the pilot, based on their involvement in the relevant regulatory procedures.

Communication

Kick-off calls were held with each participating company and with regulator staff, outlining the business process and functionalities of the PLM portal, and providing the User Guides.

Industry participants could request support by opening EMA Service Desk tickets, by writing to the ePI mailbox or by contacting the NCA NPO/SME.

On completion of the pilot, industry participants provided feedback via surveys and by email.

Regulatory procedures

ePI was included in a total of 23 regulatory procedures. Short-duration procedures were preferred, and parallel variations were not included.

Regulatory procedures included in the ePI pilot

Authority	No. procedures	Procedure types
EMA	5	Type IA Type II Type II Renewal Article 61.3
AEMPS	5	Type IA Type IA Type IB Type IB Type IB
DKMA	3	Type IA Type IB Type II
MEB	5	Type IB Type IB Type IB Article 61.3 Article 61.3
MPA	5	Type IA Type IA Type IB Type II Type II

ePI creation and management

ePIs were created, edited and submitted at the PLM portal by representatives from participating companies who had been granted 'ePI Applicant Manager' roles in the PLM portal.

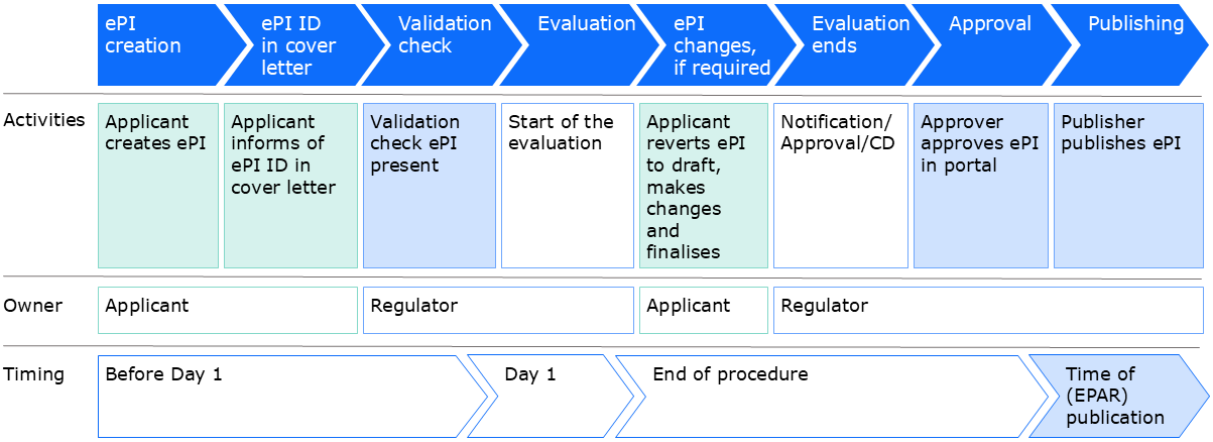
ePIs were approved and published at the PLM portal by regulator staff who had been granted 'ePI NCA/EMA Approver' and/or 'ePI NCA/EMA Publisher' roles in the PLM portal.

Further information on ePI roles is provided in the ePI Registration Guide. Descriptions of creation, management, approval and publication of ePIs are provided in the ePI User Guide for Applicants and the ePI User Guide for Regulators.

Business processes

The business processes followed during the pilot were outlined in the ePI Procedural Guides. In brief, ePI containing the same proposed changes as the Word/pdf product information was created by the company before the start of the procedure. For CAPs, ePI was only in English, and translations were not included. The company informed the regulator in the cover letter included in the eCTD that an ePI was submitted at the PLM portal and provided the EPI ID (identifier for the ePI assigned at the PLM portal). The regulator validated that the ePI with the provided ID had been submitted in the portal. Following validation of the application, the company could move the ePI back to draft and edit as needed. At the end of the procedure, the company ensured that the ePI, incorporating any changes that occurred during the procedure, was submitted in the portal. The ePI was then published by the regulator. Once published, the ePI could be viewed at the PLM portal's Published ePIs page and accessed via the ePI API.

ePI business process with ePI creation and submission at the start of procedure and publication at the end of procedure



Data collection

Data informing pilot outcomes was collected from the following sources:

- Industry participant surveys (23 surveys)
- Service Desk tickets (34 tickets)
- Emails to ePI@ema.europa.eu mailbox (27 emails)
- Direct calls with industry participants
- Additional feedback submitted by industry participants
- Feedback from participating regulator staff
- Observations by ePI team

Key performance indicators

Prior to the launch of the pilot, KPIs were defined by the ePI team, including the NCA and industry SMEs. The purpose of the KPIs was to measure the performance of the tooling, guidance and processes during the course of the pilot against expectations. The KPIs were measured using industry participant surveys and data from the PLM portal.

Time to create ePI

Description

Time (hours) taken by industry participants to create an ePI, including time taken for initial creation and quality control, and excluding time spent updating the ePI following the procedure outcome, perusing the guidance materials, or handling any technical issues.

Objective

To estimate the effort of initial ePI creation, and ensure the effort is proportional to effort currently required for ePI creation using other tooling, systems or for other organisations.

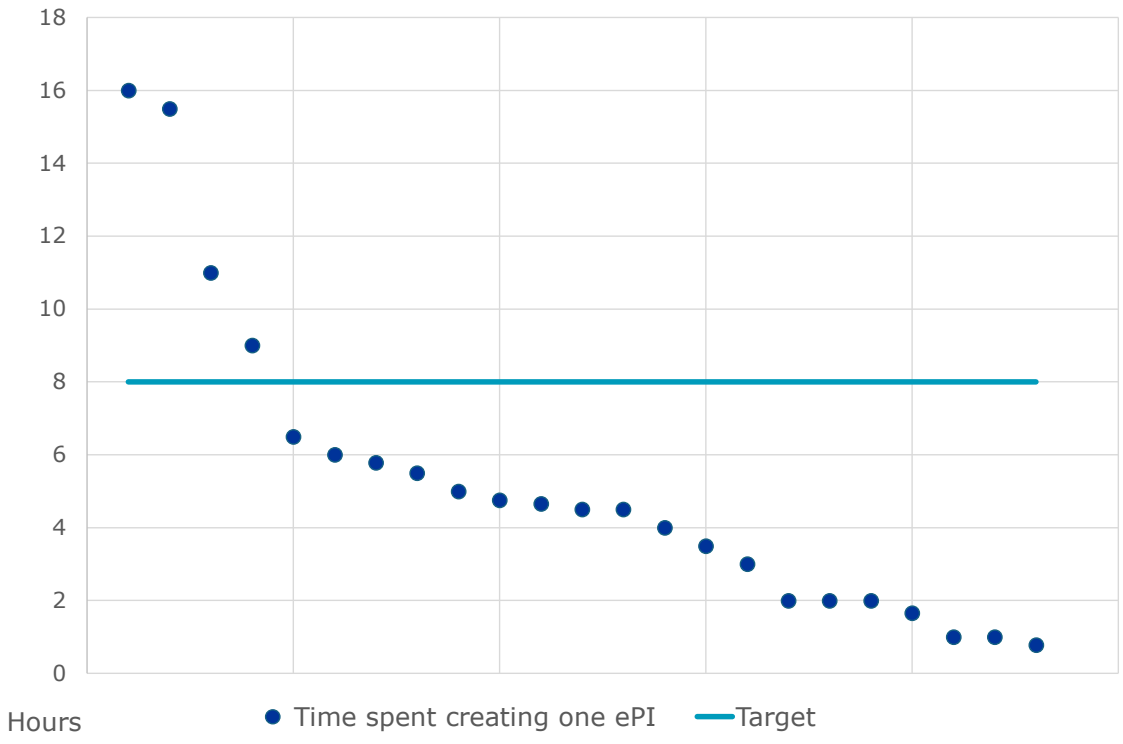
Target

The KPI target was that an average-complexity ePI is created at the PLM portal within 8 hours.

Outcome

ePIs created in the pilot were not notably long or complex. The average time taken to create ePI by industry participants was 5.2 hours. The shortest time taken was around 1 hour and the longest time taken was 16 hours.

Time spent to create one ePI



KPI met

Average time taken for ePI creation was well within 8 hours or one working day. This implies that the effort of ePI creation at the PLM portal is in line with expectations.

Since it can be assumed that the majority of the effort of ePI creation is for the first-time creation of the ePI, and updating ePI in subsequent variations is expected to be less laborious, the effort required in the pilot is considered acceptable.

ePIs created and submitted

Description

Percentage of procedures for which ePIs were successfully created/submitted/updated out of the total number of co-opted procedures.

Objective

To measure whether the business process change is feasible and the tooling fit-for-purpose by ascertaining for what percentage of co-opted procedures ePIs were successfully created, submitted and updated (as needed due to changes during assessment).

Target

The KPI target was that 80% of the co-opted procedures have an ePI successfully created/submitted/updated in the portal.

Outcome

ePIs were created/submitted/updated for 92% (23 out of 25) co-opted procedures.

KPI met

Of 25 regulatory procedures planned for the pilot, 23 resulted in successful creation, submission and update of an ePI. Due to prioritisation of resources at one NCA, the industry participants for 2 proposed procedures were not onboarded to the pilot and therefore no ePIs were created for these procedures.

Guidance, processes and PLM portal functionality were adequate to enable successful ePI creation and submission from participating companies and no blocking factors were identified.

ePIs published

Description

Percentage of procedures for which ePIs were successfully published out of the total number of procedures with a positive outcome for which an ePI was submitted.

Objective

To measure whether the business process change is feasible and the tooling fit-for-purpose by ascertaining what percentage of ePIs were successfully published out of the total number of submitted ePIs for procedures with a positive outcome.

Target

The KPI target was that 90% of the successfully submitted ePIs of procedures with a positive outcome are successfully published to the published ePIs webpage and available via the API after conclusion of the procedure.

Outcome

ePIs were published for 100% of submitted ePIs with a positive outcome. One procedure was withdrawn for reasons not related to ePI.

KPI met

Of regulatory procedures involving 23 ePIs submitted in the pilot, favourable outcomes were reached for 22, and all 22 ePIs were successfully published. One application was withdrawn, however an ePI for the medicine was published outside of a procedure.

Guidance, processes and PLM portal functionality were adequate to enable successful ePI publication by participating regulators and no blocking factors were identified.

PLM portal usability

Description

Rating from industry participants of the PLM portal for user-friendliness, ease-of-navigation, performance, design, text understandability and logic of page organisation.

Objective

To measure portal user experience and gain feedback for future development of user interface and user experience.

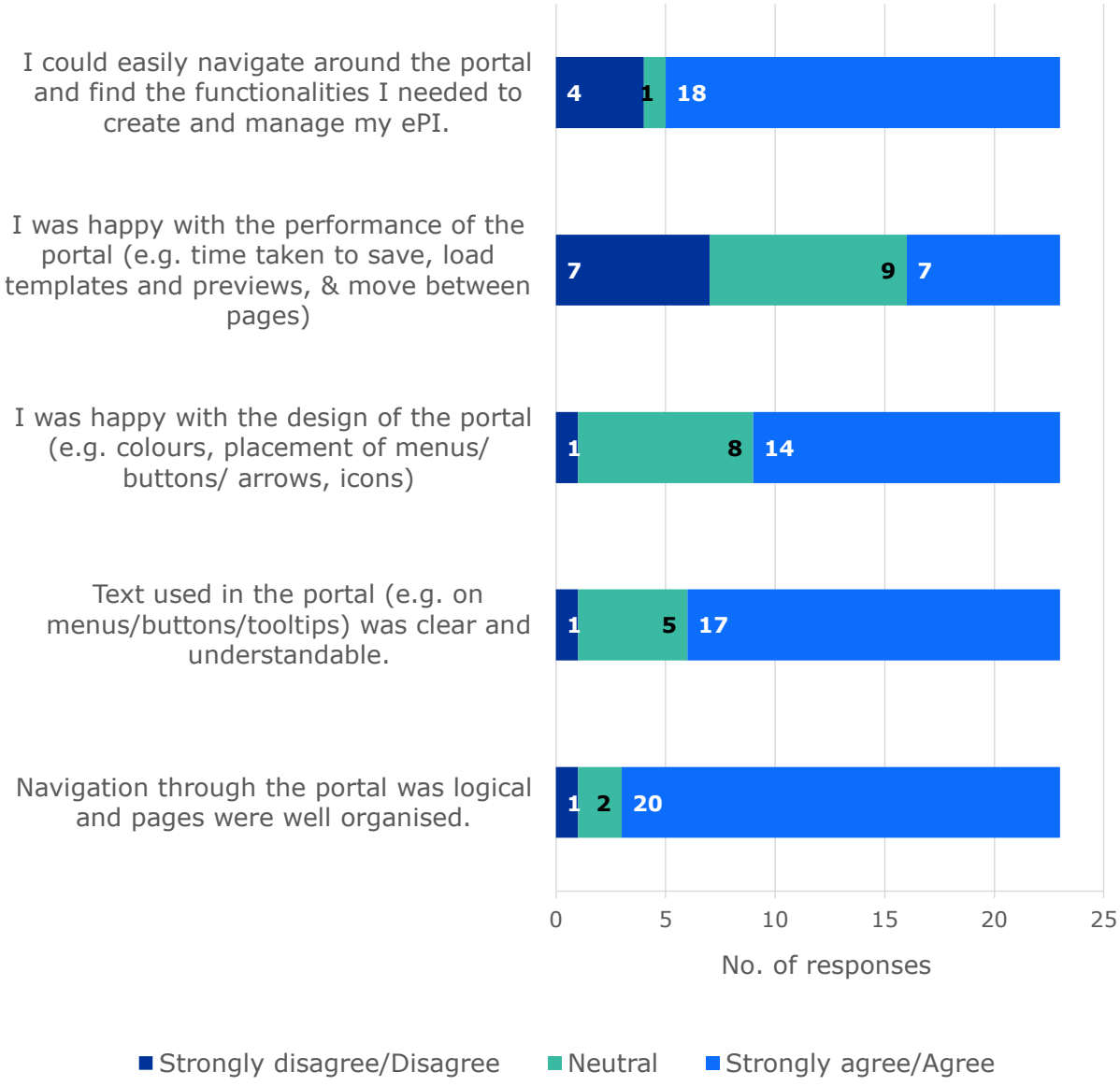
Target

The KPI target was to achieve an average neutral-positive rating (represented by survey scores of 3–5, equivalent to neutral/agree/strongly agree).

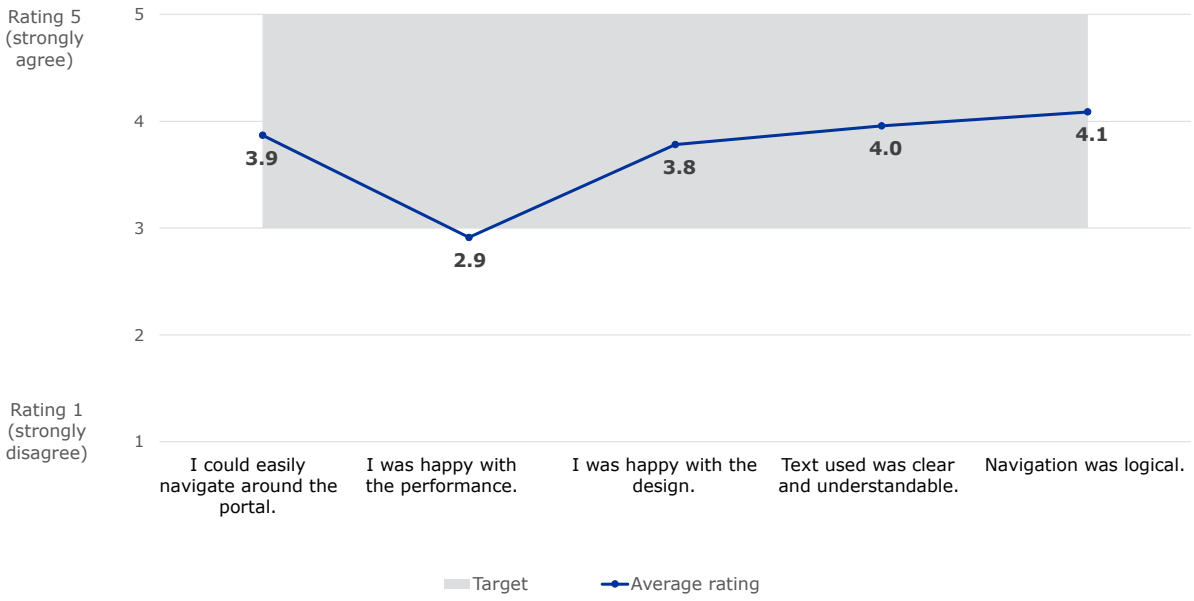
Outcome

Usability parameters were given neutral or positive ratings on average. The performance of the portal (time taken to save, load and move between pages) received the lowest rating. Logical navigation across the portal and organisation of the pages received the highest rating. Participants were also asked about overall user-friendliness of the portal and 14 out of 19 responses rated the portal as user-friendly.

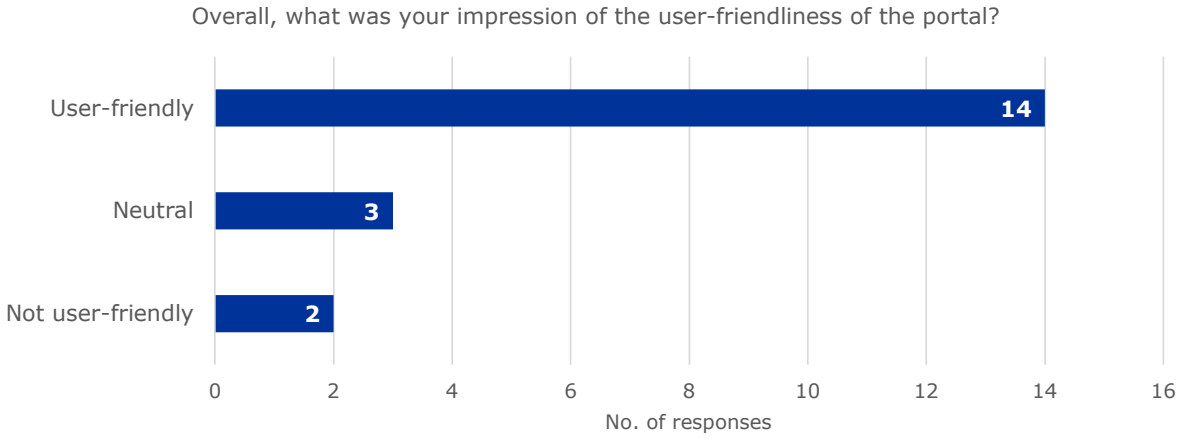
Ratings for usability



Average ratings for usability reached KPI target



Ratings for user-friendliness



KPI met

Industry participants had a positive or neutral response when asked about usability, with navigation through the portal rated highest and performance lowest of all usability parameters. Overall, the portal was considered user-friendly.

Participants provided qualitative feedback on issues encountered and suggested areas for improvement, which will inform future development.

Guidance materials usefulness

Description

Rating from industry participants of the usefulness of the guidance materials, including the Registration Guide, User Guide for Applicants and Procedural Guide for Centrally Authorised Medicines.

Objective

To measure quality of guidance materials to ensure future guides enable users to independently create and manage ePI.

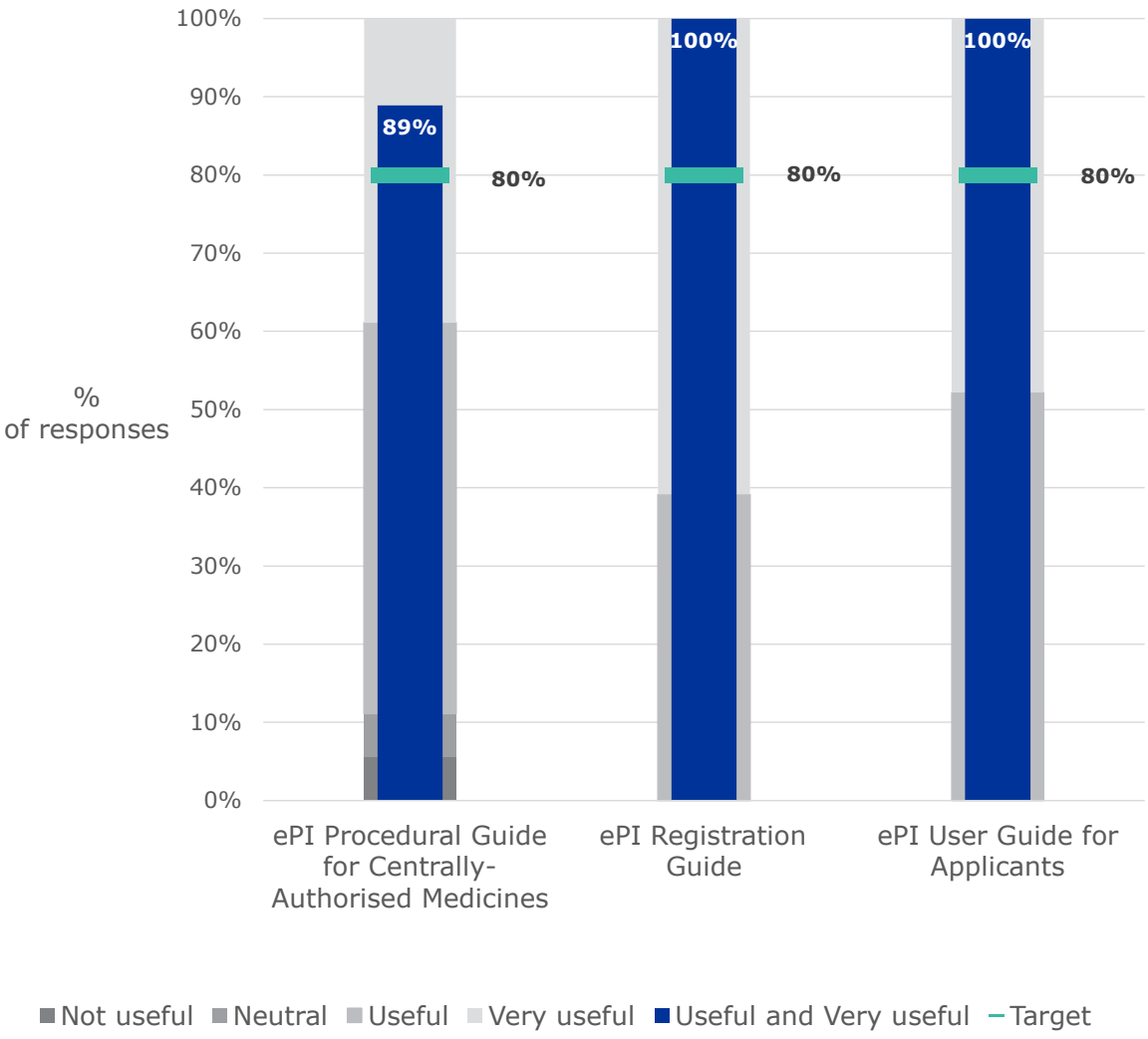
Target

The KPI target was to achieve 80% of industry participants rating the guidance materials as useful or very useful (represented by survey scores of 4–5, equivalent to useful/very useful).

Outcome

Guides covering registration, the portal and procedures were all highly rated with over 80% of participants rating the guidance as useful or very useful.

Ratings for guidance materials usefulness exceeded KPI target



KPI met

Industry participants rated all guides provided positively.

Supported by the guides provided, industry participants were able to request and approve ePI roles, as well as create and submit ePIs.

In addition to the guides, pilot participants were also supported with kick-off calls and exchanges with the ePI team. Wider roll-out of ePI will require significant change management activities to ensure users are adequately supported.

Business process feasibility

Description

Rating from industry participants of the ease or difficulty of implementation of the business process for ePI used in the pilot.

Objective

To measure feasibility of the proposed changes to business processes to incorporate ePI.

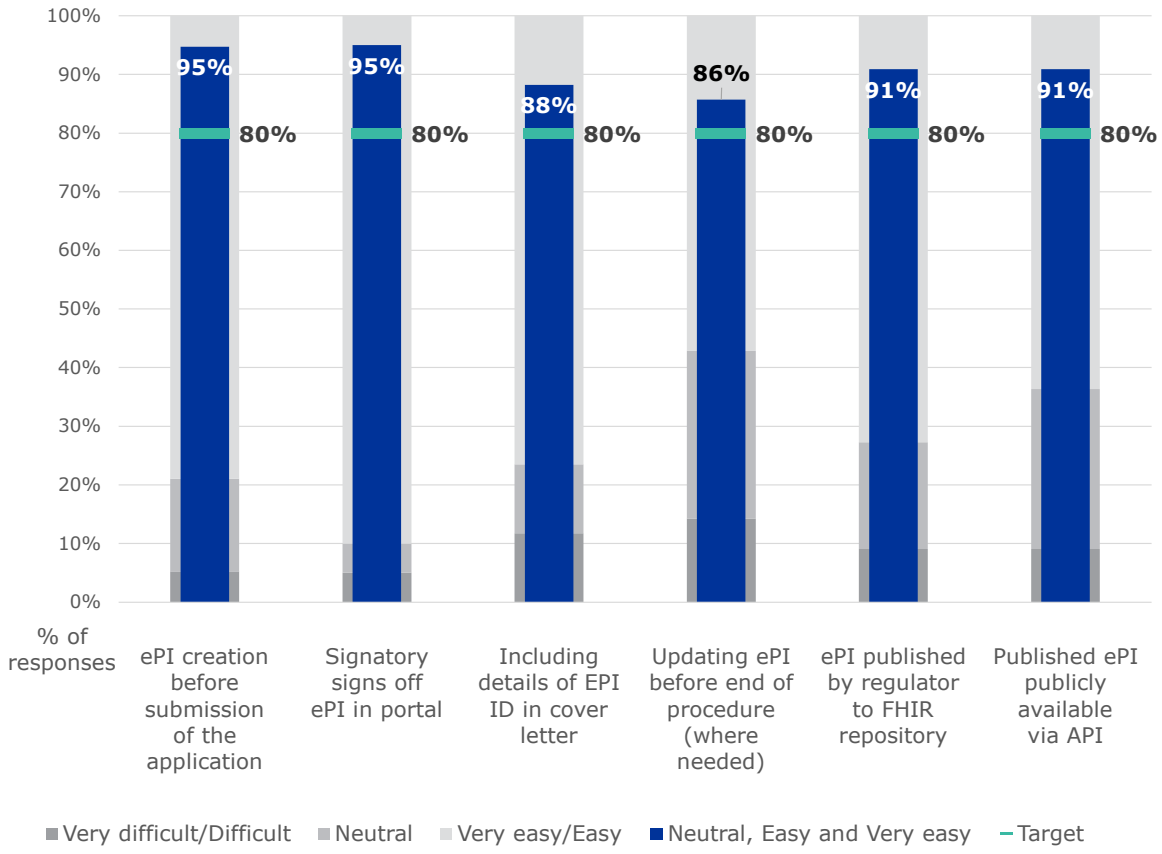
Target

The KPI target was that 80% of industry participants are confident that the newly-proposed business process is viable (represented by survey scores of 3–5, equivalent to neutral/easy to implement/very easy to implement).

Outcome

Aspects of the proposed business process, from ePI creation, sign off, informing the regulator, updating, and publication by the regulator were rated from very difficult to implement to very easy to implement. Over 80% of participants gave ratings from neutral to very easy to implement for business process aspects.

Ratings for ability to implement business process exceeded KPI target



KPI met

Only a minority of industry participants considered the business processes would be difficult or very difficult to implement.

Although areas for improvement in business process were identified during the pilot, the KPI was met and the proposed business processes with appropriate adjustments to accommodate all regulatory procedure scenarios is considered feasible for implementation.

These ratings reflect the views of industry participants. The regulator perspective on processes was collected by feedback to the ePI team, and is incorporated into the business process recommendations.

Editor

Description

Rating from industry participants of the editor used for ePI creation, including navigation, adding documents and sections, pasting content from Word, adding images and creating tables. All industry participants created their ePI using the editor in the PLM portal. In the editor, users can add documents and sections, type and format text, create tables, insert images and paste content from Word.

Objective

To determine whether the editor is fit for purpose for those applicants who will use this method to create ePI.

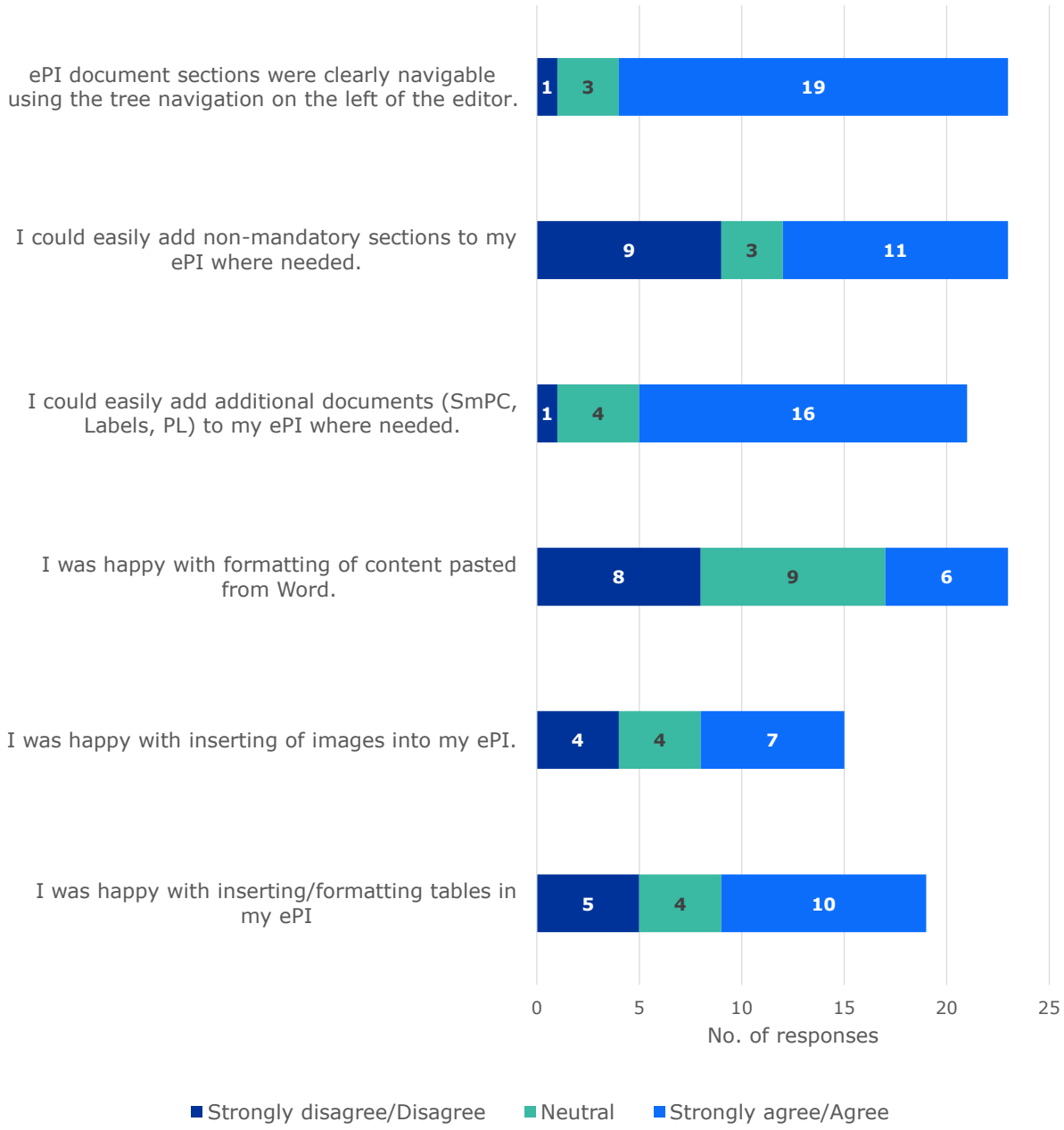
Target

The KPI target was that 80% of industry participants consider the editor at least adequate for ePI creation (represented by survey scores of 3–5, equivalent to neutral/agree/strongly agree).

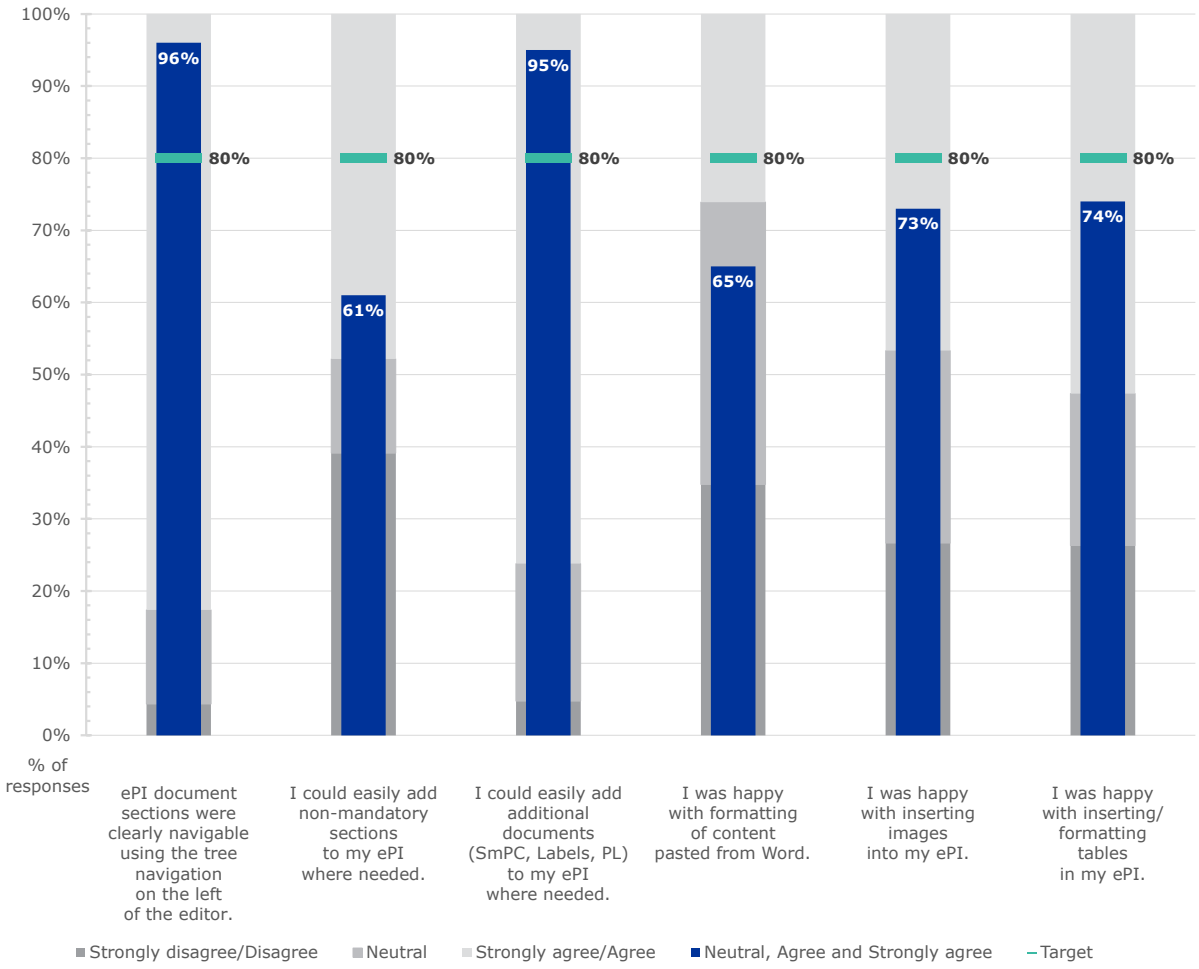
Outcome

The KPI target was reached for 2 editor features: clear navigation through the ePI sections and easy addition of documents to the ePI. Remaining editor features did not reach the KPI target, including addition of non mandatory sections, insertion of images and tables and pasting content from Word.

Ratings for ePI editor



Ratings for editor partly reached KPI target



KPI partly met

Industry participants responded positively regarding navigation in the editor and adding documents in the editor, meeting the KPI target. However, other editor features did not achieve the KPI target, with lowest rating for adding non-mandatory sections and formatting of content pasted from Word.

Detailed feedback was provided on several aspects for improvement, including but not limited to uncertainty on how to manage sections for product information not following the QRD template, difficulty of creation of labelling documents, inability to reorder sections, and the need to format content (e.g., bulleted lists) after pasting from Word.

Learnings and recommendations

Pilot outcomes are based on all data collected during the pilot and are grouped into learnings and resultant recommendations in the following categories:

- **Guidance**: outcomes related to currently available guides or where additional guidance is needed
- **Business process**: outcomes related to the ePI business process used in the pilot or where new processes are needed
- **PLM portal–ePI**: outcomes related to the PLM portal ePI functionality and user experience, as well as potential future portal features

Guidance

Available user guidance

Guidance provided to pilot participants included the ePI Registration Guide, the Procedural Guide for Centralised Procedures/MRP (mutual recognition procedures) and National Procedures, and the User Guide for Applicants/Regulators. These guides were provided as webpages at the PLM portal, except for the Procedural Guides, which were in pdf format. Guidance was only available in English. The pilot participants also attended kick-off calls where instructions and guidance were provided.

The guidance provided was sufficient for participants to create, manage and submit their ePIs and the provided guidance formats (web, pdf) were acceptable. For some topics, additional, focused support would be beneficial.

Recommendation

Guidance webpages should be continually improved, where possible improving navigation and searchability. Although it was not suggested as a requirement by pilot participants, NCAs implementing ePI can consider translating guidance into their local language. Existing guidance materials should be supplemented with short videos on specific topics that require

focused description and explanation. Supplementary activities, such as webinars, should be planned to support implementation.

Naming of ePI documents

Each document of the ePI (i.e. each SmPC, each PL, etc) has a name. The name can be viewed in the PLM portal in the editor, preview and in the published ePI. Default document names in the editor (e.g., Package Leaflet, Package Leaflet (2), Copy1 Package Leaflet) can be changed by the applicant.

The name helps the user to distinguish between documents when working with them in the portal, and is also used for display purposes on the published ePI web pages. The concept of a name for each product information document is new, and it may therefore be unclear how to optimally name the documents. Guidance on naming is provided in the User Guide to Applicants. During the pilot, applicants named documents differently, and possibly underused the potential of this feature.

Document names displayed on the published ePI webpage facilitate navigation

Recommendation

Consideration of how guidance on the naming of documents, currently provided in the User Guide for Applicants, could be more prominent. Information on this feature could also be provided in another format, such as a dedicated, short video.

Product information diverging from QRD template

ePI templates provided in the PLM portal contain mandatory sections, as defined by the QRD templates. It is an advantage of ePI that all ePIs contain the same mandatory sections, as it will support searches for specific sections and comparison across products. Pilot participants requested guidance on how to create ePIs in cases where the product information diverges

from the QRD template. Examples where product information diverges from the QRD template include, but are not limited to:

- Product information with missing mandatory sections
- Product information with sections that do not have a heading
- Product information for medicines with more than one active substance, where extra headings are needed

Recommendation

Guidance should be provided to advise how to create ePI for product information that diverges from the QRD template. This guidance should be consistent across all EU regulators, to ensure that consumers can search, compare and otherwise analyse the product information for all EU medicines.

Correct use of mandatory, non-mandatory and custom sections

ePI follows the QRD templates, having standard mandatory and non-mandatory sections with defined headings. In addition, custom sections and headings can be added at defined lower levels of documents. These are described in the QRD templates, in the User Guide for Applicants and in the Referentials Management Service (RMS) list: Quality Review of Documents Product Information Template. When creating ePI, applicants could erroneously enter text intended for multiple sections into one section or enter text into an incorrect section (e.g. using a custom section instead of a non-mandatory section). These are not the intended or recommended way to create ePI and result in sub-optimal ePI data.

Recommendation

Guidance on use of sections should be improved to ensure it is clear and prominent. Supporting guidance materials such as a short, dedicated video on the topic should be created.

Guidance should emphasise the benefits of correct use of sections, namely that ePI data can be more easily retrieved in searches and used for comparison across products or other analysis. Incorrectly structured sections may result in data for that medicine not appearing in search results, for example.

Translations

For CAPs, ePI created in the pilot was in English only, and ePIs for the additional 25 translations for CAPs were not created. Given the time required for ePI creation using the editor, ePI creation for all languages of a CAP would be unnecessarily labour-intensive.

Recommendation

A more efficient option than creation of all CAP ePI translations using the editor would be translation of the FHIR .xml, followed by import of the translation at the PLM portal. Applicants can provide xml files exported from the PLM portal to translators. Translation services can typically perform translation of xml files. However, guidance will be needed to inform translators of the parts of the file that should be translated and parts that should not

be changed. Testing of this process with translation services will be necessary to confirm the validity of this approach.

Images

Applicants creating ePI need to have images in their product information available in a supported format. In addition, images in product information in Word format are often created using text boxes on top of the image. However, it is not possible to have a combination of images and text boxes in ePI. All parts of the image, including any text, must be in a single image file. It can be the case, that companies do not have the images available in a suitable file format and it may be necessary for image files to be created.

Recommendation

Guidance on images in ePI, currently provided in the User Guide for Applicants could be elaborated and made more prominent to advise applicants that adaptations to existing images or generation of new image files may be necessary. Information on images could also be provided in another format, such as a dedicated, short video.

Finalisation of ePI

Submission of ePI to the regulator requires completion of a declaration by the applicant, including the details of at least one signatory. During the pilot, there was a lack of clarity on the purposes of the declaration and on who should be the signatory. During the pilot, signatories included the authorised contact person for the product, the person responsible for labelling or a regulatory affairs manager.

Recommendation

The text on the declaration page should be updated to cover all regulatory procedures. The text should also be valid for ePI submitted at the start and/or at the end of a procedure. The applicant should decide on what position in their company would be the most appropriate signatory.

ePI roles for applicants

Two roles are available for applicants who wish to work with ePI in the PLM portal: ePI Applicant Manager and ePI Applicant Contributor. (Please note: roles have been made available to pilot participants only). Applicants should apply for only one of these roles. If applicants have both roles, the grants of the role with the highest permissions applies. Some pilot participants requested both roles during the pilot. This could cause confusion for users and for Service Desk staff.

Recommendation

The Registration Guide should include the advice to users to request only one role, ePI Applicant Manager or ePI Applicant Contributor for each marketing authorisation holder they are associated with. The descriptions of the roles in the list of roles in EMA access management should also be updated accordingly.

Summary of recommendations for ePI guidance

1. As creation and management of ePI is a new process, introducing many new concepts, guidance in addition to user guides will be required, including various formats such as webinars, videos and other communication materials and platforms.

2. Translations were not included in the ePI pilot. A dedicated guide should be created for translators to instruct on translation of FHIR-based ePIs.

3. Applicants will require clear guidance, consistent for all EU medicines regulatory authorities, on how to create ePI for existing product information that diverges from the QRD template.

Business processes

'Update' status in PLM portal

ePIs can have several statuses in the ePI portal, as detailed in the User Guide for Applicants. The status 'Update' was intended to be used when a previously submitted ePI was updated with changes following assessment. However, the status was not used or needed during the pilot. Instead 'Submission' status was sufficient throughout the business process.

Recommendation

'Update' status should be removed from the portal and User Guide.

Approval and publication steps

The publication of an ePI by the regulator involves 2 steps, as outlined in the User Guide for Regulators. Firstly, the ePI is approved and next, the approved ePI is published. At NCAs participating in the pilot, the same staff member performed both approval and publication actions at the same time. At EMA, approval and publication were performed by different staff members. However, it was considered that having approval and publication steps may not be necessary. Nevertheless, the 2 steps could help to prevent publication in error.

Recommendation

No immediate action should be taken. Removing the approval step and associated role can be considered depending on requirements of implementing agencies.

Change management for regulators

During the pilot, participating EMA and NCA staff were provided with training and ongoing support for supervision of the regulatory procedures in the pilot. Introduction of changes to the business processes to include ePI will impact all regulatory processes involving product information and therefore a significant number of EMA/NCA staff will be impacted.

Recommendation

Implementation of ePI will require ongoing, consistent and supportive change management within regulatory agencies, including recruitment of change enablers to support, advise and advocate for the change. Change enablers will be staff working within the impacted departments with expertise on the affected processes, who will advocate for change and support the transition to ePI implementation.

Service Desk for questions within NCA scope

Companies participating in the pilot were advised to contact EMA Service Desk with any questions or issues encountered. Some tickets received by Service Desk related to questions about the national ePI that were out of scope of the Service Desk activities and were passed to and answered by the NCA SMEs supervising the NCA-level pilot.

Recommendation

Service Desk processes should be established to manage questions or issues relating to areas of national competence, and to direct where necessary to an NCA contact point.

Communication of ePI details from applicant

Companies submitting ePI in the pilot informed the regulator in the cover letter submitted in eCTD that an ePI was included in the application, and provided the EPI ID. From the regulator perspective, this is not optimal for communication of ePI details and does not ensure that the information reaches the relevant procedure management staff.

Recommendation

The 'Annexed documents' section of the application form accompanying the application could be extended so that it can be used to indicate whether an ePI is included with the application.

For centralised procedures, ePI submission and publication should be integrated with procedure management cases in EMA's procedure management system, IRIS, to ensure visibility by validators, procedure management and publishers at EMA.

First-time ePI creation

All pilot participants were creating ePI for the first time, and therefore required time to become familiar with the portal and processes. Straightforward, single procedures were suited to first-time ePI creation.

Recommendation

First-time creation of ePI for a medicine should be limited to initial marketing authorisation applications or single post-authorisation applications (no parallel procedures). This will ensure that the applicant can create all the documents for the ePI without handling the complexity of potentially needing to merge changes from parallel procedures. In addition, implementation of a dedicated process, for a limited period of time, to submit an ePI for publication outside of a regulatory procedure could be considered.

Process for all procedure types

Regulatory procedures included in the pilot were limited to a small subsection of procedure types. The Procedural Guidance used in the pilot does not cover the full range of regulatory procedures. In addition, guidance on withdrawn procedures or procedures with a negative outcome needs greater clarity.

Recommendation

Procedural guidance will be extended to cover all regulatory procedures involving changes to the product information. Guidance is needed to ensure deactivation of ePI on withdrawal or negative outcome to prevent ePIs remaining in 'Submitted' status.

Process for linguistic review

ePI for centralised procedures in the pilot were created for English language only. The Procedural Guidance used in the pilot does not cover processes for ePI languages that undergo linguistic review.

Recommendation

Procedural guidance should be extended to cover ePIs where the product information content undergoes linguistic review.

Date of last revision

The SmPC and PL include the date of revision of the text in section '10. Date of revision of the text' and section '6. Contents of the pack and other information', respectively. For centralised procedures, in the product information authorised and published, the date is not included and is added later by the company. For some national procedures, the NCA adds the date. In ePI, the regulator roles do not have permissions to edit ePI text, which can only be edited by applicant roles.

Recommendation

Solutions should be explored in order to include the date of revision in ePI documents at the time of publication by the regulator, including the possibility to automatically add the date. It is not desirable for the regulator to directly edit ePI content.

Procedure numbers for ePI

Each ePI is associated with the procedure number of the regulatory procedure in which the ePI was authorised. The associated procedure number will also serve to distinguish between different versions of an ePI for a product: the current, published version and previous, archived versions. The procedure number can be associated with an ePI by manually entering the procedure number at the PLM portal.

Some pilot participants did not complete the procedure number.

Although parallel procedures were not included in the pilot, these should be accommodated in the future. However, it is not currently possible to enter multiple procedure numbers for an ePI.

For purely national procedures, some NCAs participating in the pilot (DKMA, MEB) do not have procedure numbers and advise applicants to complete this field with 'N/A'.

Recommendation

The applicant should be reminded in the PLM portal at an appropriate time to ensure that the procedure number has been entered.

The PLM portal should enable multiple procedure numbers to be entered for one ePI.

NCAs implementing ePI should provide guidance to applicants on how to complete the procedure number for ePIs for purely national procedures.

Summary of recommendations for business processes

1. Business processes need to be elaborated and described in guidance for the full range of regulatory procedures and for linguistic review.
2. To ensure the ePI workflow extends from submission and validation to final approval and publication, involving staff in multiple teams and departments, ePI submission needs to be communicated via the electronic application form, and where possible reflected in the procedure management system.
3. Several changes to the PLM portal are needed due to findings from both company and regulator perspectives.
4. Transition to implementation needs significant change management investment.

PLM portal – ePI

Styling

The text editor used for ePI creation facilitated applicants creating ePI by cutting and pasting content from Word, by preserving formatting and minimising the need to re-format content. Nevertheless, the majority of feedback from users related to formatting/styling issues where formatting was not maintained on pasting or where the user did not achieve the desired formatting or spent significant time on formatting due to insufficient guidance on requirements.

ePI generated in the pilot includes all styling information in-line in the FHIR XML. However, stakeholders interested in consuming ePI data via the ePI API expressed a preference for receiving the data with minimal in-line styling. In this scenario, stylesheets would be used to add desired styles and formats to ePI, for example to add styling required by the QRD template. The separation of styling and content of ePI has been requested by stakeholders during the pilot and in previous consultations. This enables styling to be added to ePI data by

consumers of the data depending on their dissemination platforms and in line with accessibility criteria.

Recommendation

ePI styling aspects should be investigated to provide the optimal solution for users creating and consuming ePI data. Ability of end users of ePI data to implement accessibility features is an important consideration.

Performance

Performance of the portal, in terms of time taken to perform various actions in the portal, was satisfactory for pilot participants, with areas that could be improved. Performance should remain acceptable when there are more users at the PLM portal.

Recommendation

Performance testing will be carried out, and follow-up activities planned where necessary to optimise the performance in areas of the portal where issues may be identified.

API for FHIR upload

For stakeholders with the possibility to generate large amounts of ePI data, it will be too labour intensive to manually upload FHIR ePIs at the PLM portal.

Recommendation

Building on FHIR upload at the PLM portal, FHIR upload via an API POST call should be developed to enable companies or regulators who have large amounts of ePI data to upload efficiently to the PLM portal. While this may not be essential for initial implementation, it will support wider ePI adoption.

Quality control of ePI

ePIs at the PLM portal can be exported in Word format. This functionality could be used by applicants in an 'electronic-first' approach, to derive Word from ePI that could be submitted alongside the eCTD. Export to Word was not used for this purpose by participants in the pilot. However, participants found export to Word useful for quality control purposes, as it enabled ePI to be converted to Word and then compared to other Word documents. Quality control of ePI was an important consideration for both applicants and regulators.

Recommendation

Export to Word functionality should be maintained and improved where possible. Although Word comparison tools are widely available, inclusion of such functionality within the PLM portal could be considered as well as any other functionality supportive of quality control.

Country-specific information

ePI templates provided in the PLM portal follow QRD templates for centralised procedures or mutual-recognition, decentralised and referral procedures. This provides ePI that are harmonised without country-specific sections to accommodate so-called 'blue box' requirements, or additional country-specific information on labelling/PL.

Pilot participants questioned how country-specific information can be included in ePI when the template does not include country-specific headings (e.g., Medicines authorised by AEMPS have a section in the Labelling: '19. Otra información', however this is not included in the ePI template).

Recommendation

It is not desirable to maintain multiple diverse ePI templates that differ from QRD templates agreed at EU level due to the complexity and administrative burden, as well as issues related to introduction of unharmonised elements to ePI. However, it may be a requirement needed to fulfil important use cases, that sections are provided to hold country-specific information. A harmonised solution could be investigated with collaboration of NCA SMEs of NCAs implementing ePI.

Labelling

Creation of labelling in the PLM portal is not user friendly. Labelling is created in the same way as other ePI documents. However, creation of multiple outer and inner labels is not intuitive.

Recommendation

Despite guidance provided in the User Guide for Applicants, Labelling may be created incorrectly resulting in inconsistent Labelling data. Creation of Labelling should be optimised to increase user friendliness and reduce the potential for error.

Adverse Event reporting

For the CAP QRD template, the 'Reporting of suspected adverse reactions' section of the SmPC and 'Reporting of side effects' section of the PL contain standard sentences to inform the healthcare professional or consumer how to report suspected side effects to their national reporting system. Information on the national reporting system is inserted by companies. As a result, ePIs published by EMA in the pilot do not have the details of the national reporting systems and these would need to be added subsequently by consumers of ePI data.

Recommendation

Options to include local details for adverse event reporting in the QRD template for CAPs should be investigated.

Draft status

Prior to submitting ePI to the regulator, applicants create ePI at the PLM portal in 'Draft' status. During the pilot, regulators were able to view, but not to edit, ePIs in 'Draft' status. This was enabled during the pilot to facilitate supporting applicants, responding to questions and troubleshooting issues. Once ePI is implemented into routine business, regulators will not be able to view 'Draft' ePIs. Regulators will only see ePIs in 'Submitted' status.

Recommendation

Currently, ability of regulators to view 'Draft' ePIs is maintained. This will be removed at a timepoint to be determined, in line with the future implementation strategy.

Co-author from another organisation

Several co-authors can work on an ePI. Co-authors with an ePI Applicant Manager role can add other co-authors to the ePI. Only co-authors from the same organisation can currently be added to the ePI.

Recommendation

Adding co-authors from the same organisation was sufficient for the pilot. It will be necessary to extend this functionality to allow adding of co-authors from another organisation. This will facilitate adding of co-authors in procedures involving more than one organisation and involvement of translators and contract organisations.

User interface

Pilot participants found some aspects of the user interface (UI) to be suboptimal when creating and managing ePI.

Recommendation

The UI of the PLM portal – ePI should be aligned with the UI across the PLM portal. UI improvements proposed by pilot participants should be prioritised and implemented according to standard Agile methodology.

QRD template updates

QRD template v10.4 was in use during the ePI pilot. A template update is currently in preparation. A transition plan will be put in place for conversion of existing product information to the new template. In addition to this planned update, QRD templates will continue to be updated intermittently in the future.

Recommendation

The PLM portal – ePI must support update of QRD templates. The co-existence of ePIs in outdated and up-to-date QRD templates should be supported during transition periods.

MRP/DCP procedures

For medicines that are part of an MRP or DCP (decentralised procedure), a separate ePI must be created at the PLM portal for separate submission to each NCA involved in the procedure. When a new ePI is created and the applicant indicates that the NCA is the Reference Member State, both English and local language templates are loaded and must be submitted. Applicants and regulators involved in the pilot expressed the requirement to publish the common text (English) of an MRP/DCP procedure once it is approved and prior to the publication of the national language versions.

Recommendation

Publication of common text ePI on approval can provide multiple advantages for:

- Translators by providing easy access to original text to be translated
- Regulators enabling easy access to common text
- Patients and HCPs by providing English product information as an alternative where their preferred language is not available

Separate publication of common text should be enabled by providing this functionality along with associated business processes and guidance.

API functionality

Participants in the pilot focused on ePI creation, submission and publication. Published ePIs were displayed on the PLM portal. In contrast, the API for retrieval of published ePI data was not tested during the pilot.

Recommendation

Consumers of ePI data using the API should be consulted to inform development of the API and ensure that stakeholders consuming the data can effectively query the API to retrieve the required data for their use cases.

Essential functionality

During the pilot, missing functionality at the PLM portal hampered the business process or the use of ePI data.

When an ePI based on a previously existing ePI was published, the previous ePI had to be identified and unpublished by the regulator in a separate action.

Published ePI were not associated with any medicinal product in PMS, therefore consumers could not match ePI data to the respective PMS data, preventing the leveraging of both data sets.

Limited FHIR import functionality prevented participants who wanted to create ePI by importing data generated by their own systems from doing so. In addition, CAP ePI translations were not included in the pilot due to the absence of this functionality.

Recommendation

Functionality prioritised for development should include:

- **Import of FHIR format**, enabling companies to create ePI themselves or translation services to provide ePI translations and import to the PLM portal for regulator publication, by-passing use of the editor.
- **ePI versioning**, enabling superseded ePIs to be automatically moved to 'Archived' status when updated ePIs are published and consumers to have access to current and previously authorised ePIs.
- **QRD template versioning,** although not needed during the pilot, functionality should be in place to support ongoing evolution of QRD templates.
- **Linking of ePI to the respective product in PMS**, the PLM portal should allow linking of ePI documents (SmPC, PL etc) to the corresponding product(s) in PMS so that data from both systems can be leveraged.

Advanced functionality

Pilot participants and NCAs proposed advanced functionalities that could provide increased efficiencies and streamline workflows, including:

- Highlighting of changes of ePI at the PLM portal so that applicants can see changes made by all co-authors
- Use of ePI as the basis for assessment instead of Word, enabling access by assessors and companies to exchange edits and comments
- Upload of Word documents and subsequent conversion of Word to ePI
- Closer integration of ePI, eAF and PMS data and leveraging of other data coded systems
- Published ePI display showing changes since previous version

Recommendation

Continual improvement and evolution of the ePI product, according to the Agile methodology in place, will lead to development of additional, advanced functionalities according to business needs. Many developments may be in scope of other products or developed by other stakeholders.

Summary of recommendations for PLM portal – ePI

1. Provision of ePI data with styling information in the most suitable format for reuse is an important requirement of consumers of ePI data. At the same time, applicants creating ePI should not have an unnecessarily burdensome creation process. Resolving these requirements is a high priority prior to ePI implementation.

2. Import of FHIR ePI files created by external systems, ePI and QRD template versioning and linking ePI to PMS are essential for successful use of ePI in regulatory processes.

3. Ongoing consultation of NCA SMEs, with a focus on NCAs intending to be early adopters of ePI, will be necessary to ensure correct prioritisation of PLM portal features, specifically those affecting nationally authorised products (NAPs) and country-specific processes, but also wider portal functionality.

4. Many recommendations for portal development, while important, may not be critical for initial go-live of ePI and can be prioritised and worked on as part of ongoing maintenance and development of the ePI product.

5. Proposals for advanced functionalities provide an attractive forecast of benefits and efficiencies that ePI can potentially provide in future. These can be developed in the context of ePI or of other related products, such as the European Medicines Web portal, regulators procedure management systems, third-party health apps, industry initiatives and other stakeholder initiatives.

Pathway to implementation

EMA and NCA implementation

All stakeholders, including pharmaceutical companies and regulators, are expected to commit to implementation of harmonised ePI according to the EU ePI Common Standard. The ePI pilot has successfully included ePIs in both EMA and NCA procedures and has confirmed the validity of a phased approach to implementation by EU authorities.

Timelines and processes for implementation will be flexible and amenable to the available resources and priorities at national level. Such flexibility will allow divergent timelines for implementation, as these will still ultimately lead to a harmonised approach for ePI across the EU.

Regulators involved in the ePI pilot, who have gained first-hand experience of managing ePI in regulatory procedures, support an **initial go-live of ePI at EMA**, followed within a reasonable timeframe by **implementation at early-adopter NCAs**. This will enable controlled, phased introduction of ePI and comprehensive change management targeting regulator staff and applicants. On this solid foundation, roll-out across all NCAs will proceed.

Consultation with Heads of Medicines Agencies and NCA SMEs will be carried out for impact assessment and determination of readiness of NCAs in order to compile a plan for **phased roll out** supported by the ePI product team.

ePI submission for CAPs is expected to be voluntary initially. Transition to mandatory ePI submission will depend on several factors, including Member State decisions and the future revision of the pharmaceutical legislation relating to medicinal products for human use.

Patient access to package leaflet

A pre-requisite for successful adoption of harmonised ePI across the EU will be robust systems in place ensuring that the patient can easily access the package leaflet for their medicine in their chosen format: paper or electronic.

This will involve the following:

- **Easy access to the electronic package leaflet:**
  a user-friendly solution, not requiring high levels of digital literacy, to link the patient from the medicine box in their hand to the electronic package leaflet
- **Availability of a printed copy of the package leaflet:**
  provision of a printed package leaflet should the patient prefer to read the information on a paper copy

As the EMA-HMA-EC ePI initiative progresses towards enabling ePI to be generated, updated and output from regulatory procedures, it is imperative that dissemination mechanisms will be put in place so that ePI can be put to use to deliver benefit to patients.

Post implementation

Following implementation of ePI, the product will continually improve in several directions, including but not limited to:

- **Extending the digital workflow**
  Implementation of ePI is one step in a continual development process towards a smoother and more coherent process of data management, including data capture, analysis, storage and dissemination.
- **Developing advanced functionalities**
  PLM portal functionalities for ePI will be continually improved, and new features prioritised for development according to their business value.
- **Widening scope of ePI for medicines**
  ePI as an outcome of human centralised, national, MRP and DCP procedures can provide the basis to potentially widen the scope to incorporate future product types, such as:
    - parallel traded medicines
    - medicines with Article 126(a) exemption, placed on the market in response to exceptional public health requirements
    - veterinary medicines

Conclusion and next steps

Pilot objectives

Overall, the pilot was successful and fulfilled its objectives of enabling EMA and NCAs to evaluate ePI tooling and processes developed to date. Feedback was collected directly from companies who created ePI in the pilot regulatory procedures. By running the pilot, the ePI team could also ascertain how well tooling and processes worked in practice. Outstanding requirements have been identified and predict the remaining work prior to and beyond implementation.

KPIs defined prior to the start of the pilot met their targets, with the exception of editor functionality, for which the target was partly met. Participant feedback will be addressed as part of relevant recommendations, follow-up actions and continual improvement activities.

Pilot outcomes

Recommendations will be translated to specific action items to be further prioritised and progressed. Other feedback items raised by pilot participants are, where relevant, converted to work items in the ePI backlog, for future prioritisation and development. Prioritisation depends on several factors, but importantly actions considered critical for implementation are to be prioritised over those which could be developed later. Results will be communicated in future system demos and through usual communication channels.

Stakeholder engagement

Stakeholders will continue to participate and provide input and feedback on ePI via Agile ceremonies, roles within product teams and other engagement channels. User Acceptance Testing will be carried out in which testers can engage directly with the PLM portal – ePI. Future change management and training activities are envisaged prior to implementation to support stakeholders in preparing to submit ePI or consume ePI data.

Preparing for implementation

Throughout 2025, ePI development will focus on essential functionalities for implementation.

Following the successful development of essential functionalities, ePI for CAPs is expected to be implemented on a voluntary basis and will be preceded by training and change management activities to support stakeholders who wish to incorporate ePI into their regulatory procedures.

Following CAP implementation, timelines for early-adopter NCAs will be finalised and planning for phased roll out put in place. To support planning initiation, the ePI team will be surveying NCAs to assess readiness, resources and anticipated timelines.

Implementation will be in advance of the upcoming new Directive and Regulation, which revise and replace the existing general pharmaceutical legislation and in which provision for

ePI is expected. The coming into force of that legislation and potentially following implementing acts will impact evolution of ePI.

Glossary

AEMPS	Agencia Española de Medicamentos y Productos Sanitarios
AESGP	Association of the European Self-Care Industry
API	Application programming interface
CAP	Centrally authorised product
CD	Commission decision
DCP	Decentralised procedure
DKMA	Danish Medicines Agency
eAF	Electronic application form
EC	European Commission
eCTD	Electronic Common Technical Document
EFPIA	European Federation of Pharmaceutical Industries and Associations
EMA	European Medicines Agency
EMRN	European medicines regulatory network
ePI	Electronic product information
EU	European Union
FHIR	Fast Healthcare Interoperability Resources
HCP	Healthcare professional
IATF	Inter Association Task Force
KPI	Key performance indicator
MEB	Dutch Medicines Evaluation Board
MPA	Swedish Medical Products Agency
MRP	Mutual recognition procedure
NAP	Nationally authorised product
NCA	National Competent Authority
NPO	Network product owner
PL	Package leaflet
PLM	Product Lifecycle Management
PMS	Product Management Service
QRD	Quality Review of Documents
RMS	Referentials Management Service
SME	Subject matter expert
SmPC	Summary of product characteristics
UI	User interface

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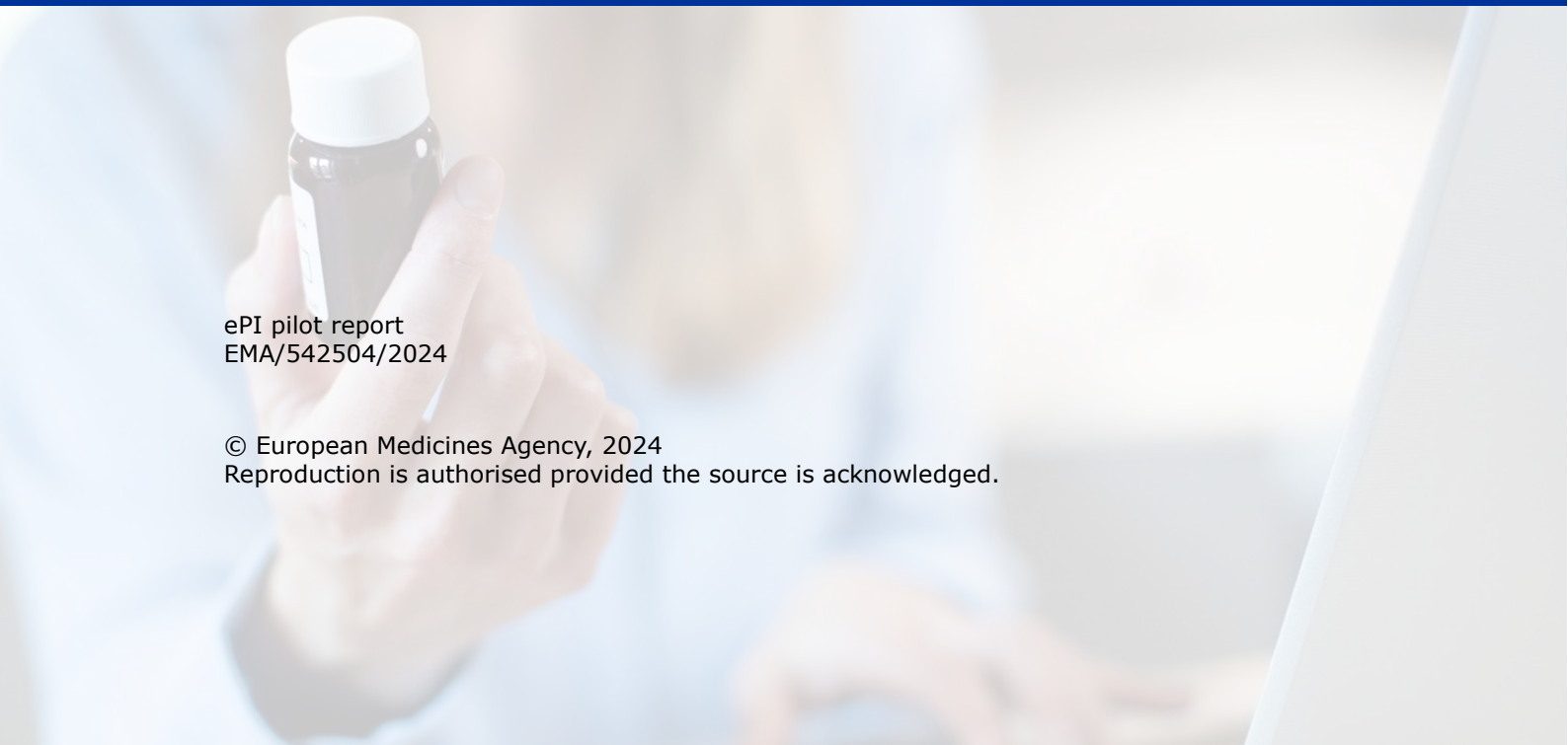

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