AESGP
VOICE OF EUROPEAN SELF-CARE INDUSTRY

efpia
European Federation of Pharmaceutical Industries and Associations

medicines for europe
better access. better health.

ELECTRONIC PRODUCT INFORMATION: FROM PRINCIPLES TO ACTIONS

AESGP, EFPIA and Medicines for Europe reflections on EMA-HMA – EC Key principles for electronic product information

ANNEXES

Annexes

Annex 1: Definitions

Key principles[29]:

Definitions of 'ePI' and 'common electronic standard' are intended to explain the meaning of these terms as they are used in this initiative.

ePI is authorised, statutory product information for medicines (i.e. SmPC, PL and labelling[30]) in a semi-structured format created using the common EU electronic standard. ePI is adapted for electronic handling and allows dissemination via the world wide web, e-platforms[31] and print. ePI fulfils the key principles.

ePI in the EU for all human medicines, including both centrally and nationally authorised medicines, will be created using a **common electronic standard**. The following definition of a common EU electronic standard for ePI is proposed: A common standard for ePI in the EU refers to the technical features of ePI (including mark-up language, controlled vocabularies and interoperability specifications) agreed by EMA, HMA, NCAs, EC, and representatives of the pharmaceutical industry, patients and HCPs. The standard will be used to generate ePI that fulfils the agreed key principles.

Definitions

The definition of ePI encompasses more than information for the prescriber and patients, it also includes labelling, blue box requirements and Annex II information. This seemed to be based on the current PI as PDF provided by the EMA, which contains all annexes to the Commission Decision. The priority for delivering ePI should be the freely accessible provision of trusted (regulator-approved) information to patients, consumers and HCPs. For this reason, we propose a phased approach, which starts with the creation, regulatory processing and dissemination of electronic PLs and SmPCs with the addition in later phase of other value-adding aspects of Product Information plus corrective modifications (from post implementation learning) according to a mutually agreed roadmap. This phased approach should include an analysis with relevant stakeholders, regarding additional information, including from Annex II, which might be considered an added value for patients and HCPs. In this respect, it is proposed to focus on regulatory communications which have an impact on patient care, e.g. risk minimisation materials.

The concept of ePI, including the aspects of structured and unstructured and re-usable elements, should be further explained in a (future) EU implementation guideline for ePI. In our opinion, in future, when ePI will be implemented, QRD template could be updated to align content, technical and design specifications for both PI and ePI. However, to make use of the full potential that ePI can offer to all stakeholders, the specific features of ePI and its re-usable data elements need to be explained in the adapted QRD guidance and the respective xml schema.

Common EU Electronic Standard

The aims of the common standard are 1) to create the technical foundation for the dissemination of trustworthy, regulator-authorised product information and 2) to offer possibilities to streamline, simplify and speed up the regulatory processes involved in the creation and updating (variation) of PI, using existing data, such as SPOR (substance, product, organisation and referential) data.

29 https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/electronic-product-information-human-medicines-european-union-key-principles_en.pdf
30 In certain procedures, Annex II of the marketing authorisation (manufacturer(s) responsible for batch release, conditions and requirements of the marketing authorisation, other conditions or restrictions as applicable) is provided electronically together with ePI. ePI does not include additional information specific to a Member State such as 'blue box' information (see: https://ec.europa.eu/ health/sites/health/files/files/eudralex/vol-2/2018_packaging_guidelines_en.pdf) or artwork of the marketed medicine package. However, it will be possible for NCAs to add such additional information specific to the Member State in electronic format.
31 e-Platforms refer to methods that may be used to access ePI electronically, for example apps, software or websites and tools such as computers, mobile devices and wearables. Access may be online (via devices connected to the internet) or offline (via devices not connected to the internet).

The industry vision is that *"ePI in the EEA for all human medicines, including both centrally and nationally authorised medicines, will be created, submitted, technically validated, reviewed, authorised and disseminated using a common electronic standard"*[32].

The objective set in the key principle *"Efficiency gains for regulatory systems"*[33] can be optimised via the future common electronic standard. It is important that all stakeholders leverage the common standard throughout the life cycle of ePI, including the regulatory process of creation, submission, review, authorisation and dissemination. There is also a need for a common transmission standard for the harmonised exchange of ePI between all stakeholders.

Features such as vocabularies and interoperability specifications are considered important for ePI and should be added at inception because they are key for the specification of ePI. The impact of the statement *"later releases"* on progressing ePI and the Common electronic Standard creates uncertainty for the implementation and may lead to an unnecessary revamp of existing ePI and underlying technology. Further guidance is needed on these aspects. Lessons learned from previous telematics projects such as eCTD, xEVMPD, CESP, should be considered and extensive reworking and hybrid solutions should be avoided wherever possible while transitioning to the stakeholder agreed ePI model.

The programme for developing **ePI must be aligned with all complementary EU telematics** projects including eCTD, SPOR, TOM, CESP Dataset Module, and Regulatory Optimisation of Variations, and be **strongly positioned in the EU Network Strategy**. ePI programme needs to be based on a solid governance model and attribution of roles and responsibilities in the ePI implementation.

In this context a **robust milestone driven roadmap** that is aligned with the different stakeholders and which is based on agreed use cases and takes into account user acceptance testing and post milestone learning would provide the assurance to plan for rapid and agile implementation of ePI and its future enhancement. The roadmap should be drafted with high priority for the benefits of the patients; for that reason, both **new and existing products should be taken into account as part of the first milestone**.

Therefore, from the design of ePI and its Roadmap implementation, it is crucial to start an open dialogue between regulators and industry, with the involvement of the Telematics Management Board, to understand how ePI will fit into the future telematics ecosystem to ensure benefits for end-users. This includes preparatory work-plan for alignment on 'definition' and identifying what business processes and telematics tools must be interconnected, to ensure we gain the efficiencies in the processes while being conscious of the priority to improve health information and HCPs.

To achieve these key objectives and meet these expectations, **urgent and adequate appropriate funding** is required to underpin the project work.

CALL FOR ACTION:

- Start an open dialogue between regulators and industry, with the involvement of the Telematics Management Board (EMA – HMA – EC), to understand how ePI will fit into the future telematics ecosystem to ensure benefits for end-users. This includes preparatory work-plan for alignment on 'definition' and identifying what business processes and telematics tools must be interconnected.
- Agreement on common standard that allows the generation and dissemination of authorised information in the EU/EEA between relevant stakeholders.
- A proposal for an EU Implementation guideline elaborating on the concept of ePI, structured and unstructured and re-usable elements should be developed collaboratively with relevant stakeholders and ultimately provided by EMA.
- Additionally, in future, when ePI will be implemented, QRD template could be updated to align content, technical and design specifications for both PI and ePI.

32 IATF common response is available on https://www.ema.europa.eu/en/documents/other/electronic-product-information-human-medicines-european-union-contributions-received-following_en.pdf
33 https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/electronic-product-information-human-medicines-european-union-key-principles_en.pdf

Annex 2: Benefits for Public Health

Key principles[34]: Benefits for public health. Expanding access to information on medicines as a public health imperative

ePI is a public health priority because it will expand the dissemination of unbiased, up-to-date, regulator approved PI for all medicines in the EU. ePI will support, among other functions:

- Provision of the latest information on a medicine's safety, benefits and conditions of use
- Better delivery of information so that the right information is available to the right HCP and patient / consumer at the point of need.
- Informed decision-making by patients/ consumers and HCPs

Background

Industry believes ePI is a public health priority and respects EMA's willingness to proceed stepwise. However, we think that public health could benefit even more from new advanced technologies and that we could and must go beyond the current scope proposed by the EMA key principles. We fear that buy-in from patients/consumers might be relatively small and hence the positive impact more limited, should ePI simply be provided for a small number of products. To further complement ePI, **having additional information material** available to EU citizens, **video and audio facilities** accessible to support and improve health literacy, and an attractive, presentable and **user-friendly interface** with other potential supportive features would motivate patients to take a more active interest in their health status. Such features, as mentioned above, have also been requested by some national competent authorities in the comments of the 'EMA public consultation on the draft key principles.

We want patients to benefit from the full potential of new technologies, therefore the roadmap should cover all pharmaceutical products. To facilitate the implementation of the project a step wise approach could be envisaged but timelines should remain short in order not to lose momentum and maximise the benefits to HCPs and patients.

The ePI will be very beneficial for products which have been used by patients for many years. For example, in case of chronic diseases, patients are so used to taking their medicines, that they may read the leaflet anymore. With ePI, an alert could be sent if a major update to the leaflet is made and thus helping patients to stay involved in the management of their medicines.

If we are going to equip and empower citizens to be responsive in their health journey, the digital tools must be available. The vision can only be achieved when actionable, understandable, relevant, reliable regulator-approved information is made available using these facilities and tools.

In addition, several specific points still need to be addressed. We have provided them in accordance with the three categories mentioned in the Key Principles document namely, **provision of information, delivery of information and decision-making**.

Provision of the latest information on a medicine's safety, benefits and conditions of use

The availability of ePI facilitates the immediate access to the most recently regulator-approved product information, rather than relying on potentially out of date paper leaflets included in the package product. Once HA approval is granted, time is needed for printing and packaging at the manufacturing/packing facility. Then there is the distribution of the packed product and all the planning necessary and logistics.

On the **Batch specific implementation**, we agree that some parts of the ePI may be applicable to all batches and some only to specific batches (e.g. when excipients change). The need for batch-specific product information is not new and industry has established processes with sufficient control to ensure the right paper version associated with the appropriate batch of the medicine e.g. to reflect changes in the composition of a product. This ensures that any information for which the patient needs to be aware in relation to a particular batch of the medicine, is available when they receive their medicine. However, already today we see situations with divergent sets of product information such as in online compendia. Online compendia always show the latest electronic version of PI which is released by the responsible MAH in sync with the market implementation of a change. Thus, always the newest information is available via the trusted electronic source, but unexpired older goods bearing out-dated product information will remain in the market. Discussion on the batch specific changes and ePI needs to take place as part of the implementation roadmap (including for new classes of medicinal product such as ATMP –in cases of device or batch specific information) but shouldn't hinder the implementation of ePI.

As long as the paper PL is required to be available, it should be taken into consideration that during a certain period of time, there might be an *"inconsistency"* between the paper PL and the ePI, with potentially increased amounts of patient/ consumer queries due to discrepancies between the two versions.

34 https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/electronic-product-information-human-medicines-european-union-key-principles_en.pdf

Therefore, to reduce these queries, as soon as ePI is introduced, the corresponding paper PL should carry **a standardised sentence advising patients/consumers** that the most current version of the product information is provided by ePI with a link to the source as is already described in the guidance on mobile scanning and other technologies in the labelling and package leaflet[35]. Industry and authorities must work together to make sure that this sentence can be added in a pragmatic way to the paper leaflet and avoid any regulatory or administrative burden for all stakeholders.

Delivery of information

Industry supports the EMA's conclusion that there is a need to explore alternative innovative pathways of disseminating information in electronic format. The needs of the patient and HCPs (the ultimate end-users) must be at the forefront of the EC/EMA/HMA implementation strategy and approach. This approach would enable patients to search trusted information sources in a tailored fashion to meet their own needs.

The EMA foresees ePI to be available on a range of platforms throughout the EU and dissemination to patients and HCPs will be implemented regionally and at a National level.

Industry understands this open access approach but considers that **a coherent and consistent solution must be implemented across EU/EEA** to ensure the product information in the correct language is easily located and accessible to both HCPs and patients immediately when a medicine is prescribed or dispensed. **A direct link to the correct text from the pack** is critical, most likely via bar code (for example using the existing 2D code currently on the pack for serialization purposes) or other evolving technologies; but must be as intuitive and simple as possible in order to ensure and encourage that the ePI becomes the definitive and preferred source for users. For clarity to patients, HCPs and pharmacists, and to avoid the risk of mistakes or misunderstanding, only one code should appear on the (secondary) packaging.

Electronic product information should be introduced in a stepwise approach, over a period that allows for a smooth transition from paper and will most probably vary from member state to member state and/or depending on product type. For example, it may be possible to transition to an electronic approach in a hospital or other settings where the patient does not routinely have access to the pack.

For those patients who cannot access their product information electronically, it has to be ensured that they can have the same opportunity as the more digitally advanced patients and get the corresponding, most recent, regulator-approved product information printed in the pharmacy, at the point of sale or via other technologies.

The content of the PI for purely national authorised medicines may differ from one EU member state to another. Also, within one country, the PI may be different for various MAHs, as their products may have different excipients that may for example require different warning statements. Therefore, it is important that the architecture of the web portal (and any other access point) is structured in a way that patients seeking information on their medicine are smoothly and unequivocally guided and directed to the right ePI, without any risk of accessing an ePI that is authorised in another regulatory procedure.

Informed decision-making by patients / consumers and HCPs

It is a priority for the involved stakeholders to provide a European environment with better and easier access to trusted regulator-approved information. It is recognised that an **educational campaign to raise awareness** on this new way of accessing information is key to its widespread adoption as part of the informed decision-making process.

Considerations should also be given on the search results of an internet query regarding product information. **The trusted source should appear first in the search results**, which is not necessarily the case today. This is particularly relevant for the patients and consumers as it is often a key source of information for them.

Patients and consumers should be able to access the product information easily even in situations where they don't have the actual container/ (secondary) packaging such as:

- during their treatment in an hospital, they may not be provided with the Medicines packaging.
- patients may also want to explore information on 'Over the Counter' medicines to better inform their choice of treatment prior to purchase.
- patients may even discard or lose the (secondary) packaging over time.

In all these various scenarios, the ease of accessibility is critical and needs to be addressed to ensure the information is available to aid informed decision making.

Key principles[36]: Benefits for public health. Accessibility to users with diverse abilities

ePI will facilitate creation of PI that is accessible to everyone, including users with print impairments, including physical impairments or learning difficulties, or for whom printed PI is difficult to access for other reasons. ePI allows the use of large fonts or high screen contrast for partially sighted users and audible formats for blind users and those with low literacy levels. ePI on the web will be accessible to screen readers, web and mobile applications, convertible to large font and amenable to other accessible formats. Accessible formats will provide the full and balanced product information to users in formats suitable for their needs.

35 https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/mobile-scanning-other-technologies-labelling-package-leaflet-centrally-authorised-medicinal-products_en.pdf
36 https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/electronic-product-information-human-medicines-european-union-key-principles_en.pdf

Accessibility to product Information for the disabled is about equal opportunity

Regulators and industry recognize people with disabilities, their families and their communities must be given equal opportunities and rights to good health information and education and ePI is a major step toward achieving this objective as it will bring new opportunities to increase accessibility of information. We consider that unnecessary delays in the implementation of ePI in line with the key principles could be perceived as uncaring for those vulnerable EU Citizens, which is far from the case. Therefore, we consider a high level of urgency is now needed, in order to better support the most vulnerable of our community. The importance placed on the patient must not be overlooked and there ought to be an equal focus on the upstream regulatory processes and efficiencies and downstream dissemination activities, to ensure we meet our obligations.

Health literacy: content, readability and lay-out

The NIVEL study[37] identified several shortcomings of the SmPC and PL, e.g. current layout (font size, line spacing, and template), structure and length which may lead to inappropriate consequences, such as the patients not adhering to treatment. Additionally, patients may become confused or worried, for example because of the extensive list of side effects or a lack of balanced benefit-risk information due to lack of clear information about the benefits. In response to the NIVEL study the European Commission in 2017 issued recommendations, to address the shortcomings identified and subsequently, the EMA released an action plan[38] to implement the recommendations made.

Due to resource constraints, the authorities have to prioritize its work on the digital aspects of the product information. However, EMA keeps a keen interest in considering any further stakeholders' input aiming at improving the content of the leaflet.

Independently of the format and the medium, the content of the leaflet is key and should be improved and be part of a broader programme in building citizens' health literacy in partnership with patients, HCPs and authorities. This will be in-line with several wide-ranging actions recommended by the European Commission.

The content should follow general health literacy principles in order to allow individuals to access, understand, appraise and apply health information pertinent to themselves so that they can make appropriate and informed decisions.

ePI will make it easier for patients/consumers to have access to up-to-date product information, and to search and retrieve information in a more suitable and intuitive ways. However, it will not solve issues encountered due to poor compliance or low literacy per se. To address these latter aspects, work on the content and other related information such as instruction videos and risk minimisation materials will need to take place in parallel. In addition, considerations need to be given on how user testing may need to be adapted to take account of new formats.

CALL FOR ACTION

- Health literacy is a key aspect in public health. That's why we think that more information material should be made available to EU citizens. Allowing the creation of easy-to-understand videos and audio content would help and support patients in their treatment journey. It would also help them in their decision-making process.
- Educational campaign to raise awareness on ePI as a new and improved way of accessing information. This is key to its widespread adoption as part of the informed decision-making process.
- Industry aims that all patients will benefit from the full potential of new technologies; therefore, the roadmap should cover all pharmaceutical products.
- Industry and authorities to work on pragmatic implementation of a standardised sentence in the paper leaflet, highlighting the existence of an ePI as the most current version of the product information with a note indicating how to access this information, and avoid any regulatory or administrative burden to the system.
- Discussion between industry and regulators must be undertaken.
  - on how to link ePI with only one code on the box.
  - to ensure that the architecture of the web portal (and any other access point) is structured in a way that patients are smoothly and unequivocally guided and directed to the right ePI, without any risk of accessing an ePI that is not authorised for that specific product.
  - Obtain views, understanding of priorities, identify issues/areas of potential joint working or collaboration of all stakeholders (patients, HCPs, Industry, regulators) to define how the content of the PI can be improved.
- Reflections should be made on how to help countries with fewer resources, and lower digital skill capabilities for ePI implementation. In addition, provisions should be given to support countries where access to digital information is less developed.

37 https://ec.europa.eu/health/sites/health/files/files/committee/75meeting/pil_s.pdf
38 https://www.ema.europa.eu/en/documents/other/european-medicines-agency-action-plan-related-european-commissions-recommendations-product_en.pdf

Annex 3: Efficiency gains for regulatory systems

Key principles[39]: Enabling efficiencies in administration of regulatory procedures

ePI will enable increased efficiency in management of PI during regulatory procedures. By enabling PI changes to be made across all relevant PI annexes and products, ePI could eliminate many manually performed tasks and redundancies that are potential sources of error.

Position

Regulatory efficiencies and operational excellence will be achieved for the benefit of Regulators and Industry via a coherent and consistent implementation of ePI across Europe with significant consequential value for patients and healthcare providers. To achieve this, a standard should be adopted in the creation, submission and review process. The regulatory processes should leverage existing data of the **TOM facilitated SPOR system**.

There are excellent opportunities for efficiencies with ePI in the regulatory system, through improved **interoperability**, which will ensure better accessibility and a high level of regulatory compliance, by using structured and semi-structured data. The main examples of these efficiencies relating to regulatory processes are highlighted below:

- **Automated Data filling from systems (SPOR, supported by TOM) for structured data:** the information only needs to be entered into one system (SPOR) and from there, it will be loaded automatically into the PI. This will reduce workload, but at the same time will increase the compliance of information.
- **Controlled vocabulary:** standardised information that can be included in the PI, e.g. patient friendly translations of indications, warnings/side effects, excipients warnings, storage conditions, etc. Change to the controlled vocabulary should not lead to notification or variation, but be included in process of the transition to ePI.
- **Introduction of referral or health authority requested safety change outcomes:** the new texts provided by the authorities could be included or updated automatically through the system on behalf of the MAH, who then only needs to validate it and confirm that this is correct.
- With the ability to include regulator approved safety information resulting from variations or referrals quickly to the ePI, there should be a possibility for the MAH, to have a **longer implementation time for providing the updated paper leaflet in the box**.
- **Maintenance of text should be easier:** as ePI is structured, only the update to the relevant section of the PI needs to be changed. If information needs to be changed in several places of the PI (e.g. product name), this could be done automatically.
- **Changes made directly into systems:** will speed up the process for update and approval of any change to the PI (e.g. change of pack-size in SPOR, will automatically update ePI as well).
- **Update of the QRD requirements should be reflected in the system**, leading to possibility for an automatic update of the ePI in accordance with the new version of the QRD, being ready for submission (always manual adjustment should be possible).

While being supportive of the implementation of ePI, one significant challenge for industry could be the *"conversion"* of the existing PIs (Word, PDF) into the ePI format. The creation of ePI format for current regulator authorised PIs will be a major logistical burden for companies with a large portfolio. Essential incentives for regulators and industry would be:

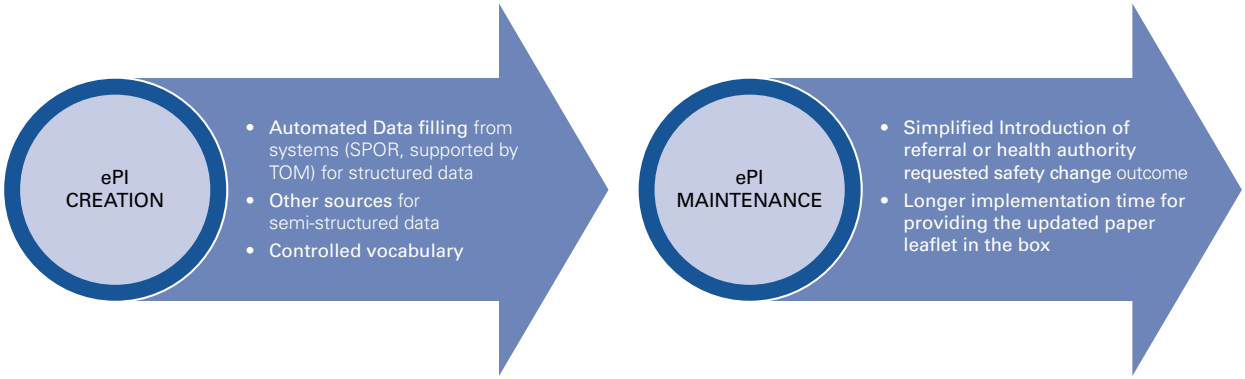
- Efficient process/guidance for having the current PI changed to the new ePI format.
- Process optimisation for changes to the PI. The ePI should not lead to increase of workload on maintenance of PI (after the initial creation phase), it should in fact give opportunity to decrease the workload over time.
- Implementation should be without any regulatory submission/approval process if the change is strictly a conversion from the current format to the new ePI format.
- There should be a reasonable transition time agreed with Industry for companies to change the current PI into ePI.

CALL FOR ACTION

- Stronger collaboration between regulators and industry to establish the needs of both parties in the regulatory processes and submission management.
- Active involvement of the telematics network, to assure processes can be more efficient and linked to other relevant telematics projects.
- Urgent and adequate funding is required, to accelerate the ePI development as highlighted by the recent COVID pandemic and the regulatory and supply chain inefficiencies.

39 https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/electronic-product-information-human-medicines-european-union-key-principles_en.pdf

Efficiency for the Regulatory Network



HOW **Maintenance of text should be easier:** as ePI is structured, only the update of the relevant section of the PI needs to be changed. In case information needs to be changed in several places of the PI (e.g. product name), this could be done automatically.

Changes made directly into systems: will speed up the process for update and approval of any change to the PI

Update of the QRD requirements should be reflected in the system, leading to automatic update of the ePI in accordance with the new version of the QRD

Key principles: Enhancing knowledge of trends in medicines and their evolution

ePI will provide information on medicines that is amenable to analysis and could be used to increase knowledge by facilitating study of characteristics of current EU medicines.

Rationale:

Openly accessible, semi-structured ePI is a valuable resource for research. Academics, the pharmaceutical industry and other researchers will be able to access this resource more easily for studies of active substances, indications, target populations, adverse events and many other pieces of information contained in the PI. Regulators could more easily analyse the PI to assess the relevant evidence to contribute to Committee recommendations or future strategies and policies. Data on nationally authorised medicines could provide a source of information on medicines in countries across the EU. In the future, it could be possible to use ePI to analyse changes in the PI over time and to identify how medicines have evolved and predict future trends.

Position

We recognise that semi-structured data can open the possibilities for future research.

CALL FOR ACTION

- Industry ask for clarity and further discussion on the future use cases given in the rationale of the key principles document. How would the regulators analyse the PI for strategies and policies, and for prediction of future trends?

Annex 4: Existing legislative framework

Key principles[40]: Complementing paper package leaflet

ePI will not supersede or negate the requirement of the pharmaceutical legislation (Article 58 of Directive 2001/83/EC) to include a PL in the packaging of all medicines or directly convey all information required (by Articles 59 and 62 of the Directive) on the outer or immediate packaging. Since the current legislation does not require the use of an electronic version of PI, the use of ePI will not constitute a new legal obligation.

Background

The **current regulatory/legislative framework is being interpreted retrospectively against the backdrop of new digital developments and increasing understanding of health literacy and communication**. However, at the same time industry acknowledges the importance of considering the needs of patients/consumers with low digital literacy, low ability to use digital devices effectively, or limited internet access.

Therefore, it is necessary for the EU network and relevant stakeholders to set out an **ambitious plan considering the needs of patient/consumer groups and the fast pace of technology**. Industry considers that the current legislative framework itself is not limiting in allowing these digital innovations. However, it is realistic to think that in the long term the ePI will be used more widely compared to the paper leaflet due to the advantages it brings. This development will be picked up faster in already highly digitalized markets. This itself should not be a rate-limiting factor when considering the different levels of digitalisation uptake within Europe.

Today there are situations where it would be **reasonable to consider that the paper PL could be removed** from their individual packs and substituted by ePI while still ensuring patients' needs and interests are respected.

Industry believes that **ePI shall have the same value as paper PL and that** this evolution requires **a change in** the legislation. As pointed out in the EC pharmaceutical Strategy, Regulators, Members State and industry need to collaborate to develop and implement ePI for all medicines in Europe with involvement of Member States and industry, **evaluate and revise relevant provisions in the legislation**[41].

However, a stepwise approach needs to be developed, with relevant stakeholders, to ensure suitable and appropriate implementation occurs to safe-guard patient needs. The development of a roadmap for ePI would need to focus on two main elements.

Firstly, it is important to consider current practices of hospital- / healthcare professional-administered products where patients rarely receive the package leaflet.

Secondly, for all other products there is a need for an agreed legal interpretation of how information can be conveyed on the outer or immediate packaging and whether this can be sufficiently met with 2D-codes, which will provide access to the relevant information. Allowing for cases where patient information has been incorporated into the information present on outer packaging it is assumed that the requirement for an ePI will not become mandatory.

Replacing paper with ePI for hospital / HCP administered products

It is important to consider current practices with hospital / healthcare professional-administered products where patients rarely receive the package leaflet. These settings show no reason not to remove the paper leaflet which is not used or seen and direct patients toward the ePI, thereby potentially improving accessibility to appropriate information.

Industry proposes an EEA-wide pilot study to investigate the current practices for provision of information to patients and possible future alternatives such as the replacement of paper package leaflets with ePI (or other alternatives, such as printing at pharmacy level).

Such a pilot could be expanded to products directly dispensed to (and used by) patients in highly digitalised markets. Experiences from various ongoing national initiatives such as, i) the Italian practice[42] of printing at pharmacies of the most up-to-date package leaflet, ii) Belgium / Luxembourg pilot project[43] at hospitals and iii) the German pilot for distributing flu-vaccination[44] with French labelling in Germany should be taken into account when planning further expansion.

Industry welcomes further discussion on additional 'use cases' that further explore the benefits of ePI considering:

- faster dissemination of relevant regulator approved changes to product information, (operational excellence).
- decreased risk of drug shortages (opportunity of redistribution of packages in different languages).

40 https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/electronic-product-information-human-medicines-european-union-key-principles_en.pdf
41 https://ec.europa.eu/health/sites/health/files/human-use/docs/pharmastrategy_com2020-761_en.pdf
42 AIFA official decree dated 14.04.2014 (in force since 2 June 2014), updated with AIFA official decree no. 821 of 24.05.2018, effective from 11.07.2018
43 More information available at the following links: The Belgian Federal Agency of Medicines website (https://www.afmps.be/fr/news/projet_pilote_e_pil_la_notice_papier_fait_place_a_la_notice_electronique; https://pharma.be/fr/projects/e-pil-fr.html); https://www.famhp.be/en/news/is_the_electronic_patient_information_leaflet_just_as_effective_as_the_paper_version_e_pil; The Ministère de la Santé in Luxembourg website https://sante.public.lu/fr/actualites/2020/08/e-pil-call-for-candidates/index.html
44 https://www.pei.de/DE/newsroom/hp-meldungen/2020/201028-vaxigrip-tetra-influenza-impfstoff-frankreich-eingefuehrt.html;jsessionid=A430493D5264328B80407ABB09444254.2_cid354?nn=12248480

- the Green deal and the EU Commission agenda to minimise environmental impact; we see a possible upside of the ePI by removal of the paper leaflet, starting in the hospital setting providing a positive outcome is seen from the Belgian pilot[45], to reduce the volume of paper and ink (and all industrial activities) that is currently used to have a paper leaflet available in all boxes of medicinal products. Other industry sectors have already showed positive results of replacement of paper instructions by digital information. This will contribute to the decrease of the carbon footprint.
- reduced packaging/distribution and wastage costs arising from implementation of safety changes and recall costs of batches.
- immediate access to the latest product information via ePI could enable a more flexible transitional period for the provision of up-to-date paper leaflets following safety relevant updates.
- efficiencies in the size of packaging materials thereby reducing transport and storage space, (especially important for products requiring controlled temperature storage).

Key principles[46]: Open access to regulator-approved information only

ePI is intended for the delivery of the full and complete regulator-approved medicine PI only. ePI will not be used for delivery of promotional information.

ePI should always be published as freely accessible open data.

Industry fully acknowledges this key principle and supports that ePI will not be used for delivery of promotional information and will be freely accessible open data. However, industry recommends having a transparent and open discussion regarding the *"data stewardship"* of the content of the Product Information. The responsibilities for the paper leaflet are very clear: after approval of the final version, that text should be included in the boxes of medicinal products. For Type IA changes, the MAH is allowed to make this change in the printed leaflet but has to notify the regulatory authority of this change. The MAH is in this way always responsible and can be held liable for the leaflet that reaches the patient. This is considered *"data stewardship"*.

With introduction of digital information, this information can be used by parties other than the MAH or regulatory authorities. The MAH can only control the information that originally published in the trusted database, so only have *"data ownership"* for this information.

Industry recommends having a transparent and open discussion, with the goal of confirming *"data stewardship(s) and data ownership(s)"* of the content of ePI.

With regard to *"data stewardship"* of the content of the Product Information, clear assignment of responsibility is required to clarify the accountability and liability for each step; in particular for the release of the final content that is publicly available. We believe this openness will facilitate an efficient collaboration between Industry and Authority(s) in order to improve the governance aspect for ePI.

Industry is convinced that besides the data stewardship, also the **data ownership** should be discussed. Dissemination of trusted information via ePI to patients and HCPs is the primary objective and due to its digital nature and accessibility ePI might be reproduced in various ways. While patients and HCPs are expected to benefit from well-controlled ePI services, less controlled reuse of data and dissemination by third parties always comes with the risk that the reproduced data set is not kept accurate e.g. when the data in the original source changes. Therefore, it needs to be clarified that such a scenario is beyond the control of MAHs.

Key principles[47]: Data protection

ePI itself will not include any personal data. In any event where processing (e.g. collecting or handling) of personal data may occur in relation to the implementation and use of ePI, for example in the context of a mobile application developed for the use of patients to access ePI, personal data processing must be in accordance with applicable European data protection legislation. This includes, in particular Regulation (EU) 2016/679 (GDPR) and Regulation (EU) 2018/1725 applicable to EU institutions.

Given the fact that ePI itself contains no personal data and should be published as open data, data protection is not an issue for the key principles.

Mobile applications developed for the use of patients to access ePI should ensure that personal data, e.g. on what information a given patient has accessed, or information the patient has submitted (e.g. reporting a possible side effect),

45 See footnote 42
46 https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/electronic-product-information-human-medicines-european-union-key-principles_en.pdf
47 https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/electronic-product-information-human-medicines-european-union-key-principles_en.pdf

will not be collected inappropriately or passed to third parties without consent. Any informed consent provisions must be explicit, clear, and understandable. Application by third parties of the EU data protection legislation must be ensured.

CALL FOR ACTION

- Expansion of Pilot projects investigating the benefit of replacing paper with ePI for hospital/HCP administered products.
- Supporting stakeholder discussions on additional 'use cases' and the positive benefits associated with them.
- Conduct legal framework analysis, to allow for the development of an ambitious ePI roadmap.
- Industry recommends having a transparent and open discussion, with the goal of confirming "data stewardship(s) and data ownership(s)" of the content of ePI.

Annex 5 Processes: High-level Governance & Flexibility in Implementation

Key principles[48]

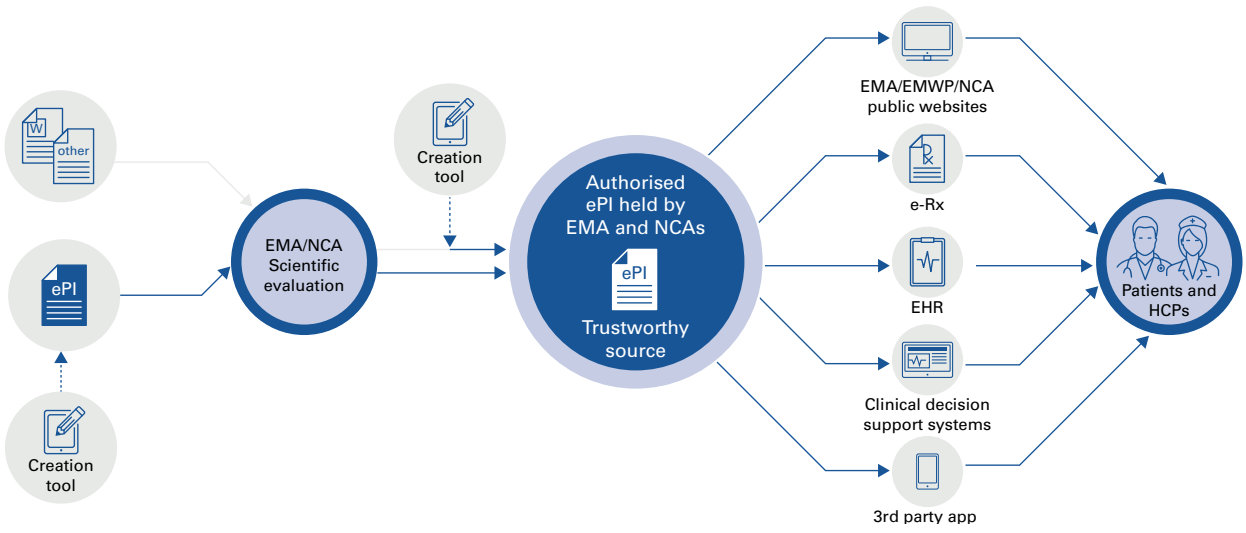
High-level governance

It is envisaged that, eventually, ePI format will be used for the PI of all human medicines authorised in the EU through EMA and NCAs from the point of submission and throughout the evaluation process. However, in the short and medium term, some regulatory authorities may decide to continue to perform assessment as is done currently, and that ePI should be created once the regulatory procedure is complete. The ePI implementation process will depend on the findings of feasibility analyses and will be described in a future roadmap to guide implementation. ePI will be made available to users (e.g. patients / consumers and HCPs) through websites at EMA level and if available, Member State level. ePI data will be made available for use in other e-health systems, such as electronic health records and e-prescribing systems. ePI will also be available for use by third-parties, who can reproduce ePI and make it available to patients and HCPs (as is already the case for PI today).

Flexibility in implementation

All stakeholders, including pharmaceutical companies and regulators, are expected to commit to implementation of the common electronic standard for creation of ePI for all EU medicines. However, timelines and processes for implementation will be flexible and amenable to the available resources and priorities at national level. A roadmap will be proposed by HMA and EMA to define the steps for development, which allows implementation in the EU on the basis of the key principles.

Proposed model for ePI proess in the key principles



(Subject to change following feasibility analysis once ePI project is started)

High-level Governance & Flexibility in Implementation

Processes relates to the implementation of ePI, including processes, roles & responsibilities. For a successful implementation of ePI across Europe for the interest of the patients, **technology and process have a crucial role to achieve the goals**. The value of ePI is well recognised in the **EU Commission Pharmaceutical Strategy**[49] as well as in the **EMRN Strategy**[50], and to achieve the objectives set out in the Strategy a Plan for a coherent and consistent EU implementation is needed. Currently there are more and more national health authorities' initiatives starting to be planned or implemented; this is a cause for concern for the industry because there is high risk that the major benefits that patients can obtain, especially in

48 https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/electronic-product-information-human-medicines-european-union-key-principles_en.pdf
49 https://ec.europa.eu/health/sites/health/files/human-use/docs/pharmastrategy_com2020-761_en.pdf
50 https://www.ema.europa.eu/en/about-us/how-we-work/european-medicines-regulatory-network/european-medicines-agencies-network-strategy

a cross-border setting, will be missed because of lack of harmonised ePI development and implementation. **As pointed out in the EC pharmaceutical Strategy, Regulators, Members State and industry need to collaborate to develop and implement ePI for all medicines in Europe**. Therefore, there is a need to **establish soon an open dialogue between regulators and industry on how ePI will fit into the future telematics ecosystem** to ensure benefits for all end-users (such as patients, HCPs and carers).

A very pertinent example of the need for a harmonised approach, is how the COVID19 pandemic has clearly demonstrated the need for transparency of patient information dissemination. As new medicines or updates of PIs for already existing medicines are approved and made available over short development timeframes, the offering of ePI will be immense as it will enable the most up to date HA approved benefit/risk information becoming available to prescribers and patients in real time and via an effective method which will support risk minimisation and patient safety.

The objective set in the key principle *"Efficiency gains for regulatory systems"*[51]is of significant importance for Regulators and industry. This objective can only be achieved if the ePI implementation plan will take it into account in the first planning phase. To improve the ePI processes both in the creation and updating processes (via variations), these regulatory processes should leverage existing data of the TOM facilitated SPOR system, both for the benefit of the regulators and the pharmaceutical industry. Industry's aim is to avoid complexity, offer possibilities to streamline, simplify, reduce administrative burden, to manage paper versioning vs ePI.

The Key Principles paper suggests that a broad margin of flexibility is given for national implementation of ePI across Europe. However, if **flexibility** is not being accompanied by a **clear and binding phased roadmap and value-added milestones**, the consequence will be a fragmented and costly implementation process that will miss the opportunity for development of optimal and common practices across the EU regulatory network. Variable timelines, together with multiple standards and sources of information will undermine the main objective of providing updated and trustworthy product information to patients and HCPs based on one authoritative source and to one EEA-wide standard.

With the vast experience from industry and agencies of telematics programmes, industry endorses the key learnings of eCTD, CESP and xEVMPD programmes (phased approach and the mandated milestones) to build a successful ePI implementation roadmap, with reliable timelines for all stakeholders. A phased-approach roadmap should include a **proof-of-concept phase** in which the level of acceptable flexibility for an ePI approach can be tested and improved accordingly.

Industry welcomes collaboration with the regulator network to define the success criteria for a phased and meaningful EU/EEA-wide ePI implementation and would welcome an open dialogue to build an **effective governance model**.

Roles & responsibilities: Data-stewardship/accountability/liability

Industry recommends having a **transparent and open discussion regarding the** *"data stewardship"* **of the content of the Product Information**. The responsibilities for the paper leaflet are very clear: after approval of the final version, that text should be included in the boxes of medicinal products. For Type IA changes, the MAH is allowed to make this change in the printed leaflet but has to notify the regulatory authority of this change. The MAH is in this way always responsible and can be held liable for the leaflet that reaches the patient. This is considered *"data stewardship"*.

With introduction of digital information, this information can be used by parties other than the MAH or regulatory authorities. The MAH can only control the information that originally published in the trusted database, so only have *"data ownership"* for this information.

Industry recommends having a transparent and open discussion, with the goal of confirming *"data stewardship(s) and data ownership(s)"* of the content of ePI.With regard to *"data stewardship"* of the content of the Product Information, clear assignment of responsibility is required to clarify the accountability and liability for each step; in particular for the release of the final content that is publicly available. We believe this openness will facilitate an efficient collaboration between Industry and Authority(s) in order to improve the governance aspect for ePI.

Industry is convinced that besides the data stewardship, also the **data ownership** should also be discussed. Dissemination of trusted information via ePI to patients and HCPs is the primary objective and due to its digital nature and accessibility ePI might be reproduced in various ways. While patients and HCPs are expected to benefit from well-controlled ePI services, less controlled reuse of data and dissemination by third parties always comes with the risk that the reproduced data set is not kept accurate e.g. when the data in the original source changes. Therefore, it needs to be clarified that such a scenario is beyond the control of MAHs.

Access to ePI

The Key principles suggest that *"A pan-European web portal could provide a central point for access of ePI for all centrally and nationally authorized medicines"*.

In the ePI key principles document, it is envisaged that *"ePI will be made available to users (e.g. patients / consumers and HCPs) through websites at EMA level and if available, Member State level. ePI data will be made available for use in other e-health systems, such as electronic health records and e-prescribing systems. ePI will also be available for use by third-parties, who can reproduce ePI and make it available to patients and HCPs (as is already the case for PI today)."* This is the reason why *"ePI should always be published as freely accessible open data and will be accessible by third-parties for example, for use in websites and patient / consumer apps"*.

51 https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/electronic-product-information-human-medicines-european-union-key-principles_en.pdf

Industry understands the value of ePI being available on a range of platforms throughout the EU but most importantly Member States must follow **a coherent and consistent approach to develop and use ePI** (from the point of submission). In addition, it is critical to have a safe and secure access to the correct ePI from the medicinal pack. This process should be intuitive and as simple as possible.

We support the concept to have **a single access-point to extract and re-use ePI as described in the Key principles – process chart**. This will ensure that patients are guaranteed to have access a trusted source of regulator approved ePI. It is important that the architecture of the web portal (and any other access point) is structured in a way that patients are smoothly and unequivocally guided and directed to the right ePI, approved for that specific product.

Since platform will be accessed by millions and millions of people, particular attention should be given to cybersecurity aspects to ensure there will be in place a strong protection from unauthorised changes of data/information or any cyber-attack.

Technical considerations need to take into account other patient benefits such as access to alternative language versions. For nationally authorised medicines interchangeability of language versions across member states is not guaranteed by the frameworks applicable to this procedure. National authorisations are the result of individual member state assessment of marketing authorisation applications and the resulting label agreed between the NCA and the MAH. National Authorisations which are the outcome of a DCP or MRP procedure may include national requirements to support better understanding in an individual country and therefore a one-to-one translation between these national authorisations cannot be confirmed in all cases. Approved national language versions will only become available at the time of final MA approval in each Member state included in the MRP or DCP procedure and would not become available simultaneously. For those products authorised via the DCP or MRP it should be permissible to provide links to other the language versions approved in other member states where interchangeability can be assured by the MAH.

Once a common standard and governance process are established, stakeholders must plan for their implementation in their jurisdictions according to a roadmap, which includes timelines, determined at HMA and EMA level **in collaboration with industry**. **Those prerequisites will allow development of systems for ePI dissemination from the trusted source database (downstream). These developments can occur in parallel without jeopardising the building of this one integrated, common network that is fully integrated with all the related telematics projects**.

CALL FOR ACTION

For the all above considerations, industry have identified as crucial to:

- Establish a central coordination of all "ePI like" initiatives, to ensure key benefits to all stakeholders is delivered.
- Start an open dialogue with regulators and industry in early 2021, to understand how ePI will fit into the future telematics ecosystem to ensure benefits for end-users (such as patients, HCPs and carers), as COVID19 demonstrated the need for transparency of patient information dissemination. This includes preparatory work-plan for alignment on 'definition' and identifying what business processes and telematics tools must be interconnected.
- Agree on Common Standard: Common standard should be developed in collaboration between the Industry, Regulators and impacted stakeholders. Optimising the PI review process is important for timely updates to be shared with the patients. Ensure the technical foundation of the ePI is designed with ease of implementation and ease of maintenance in mind. The easier ePI is to implement, then the more likely MAH's are to adopt the new format. This will lead to a faster transition from the current unstructured PI's to the structured ePI format.
- Identify a clear Governance structure and ownership of the ePI project, that will take care of assuring the appropriate funding for a harmonised and coordinated implementation in all EU member States. The implementation phase of ePI should have a clearly defined transition period and production to fulfil use cases ePI will serve and an agreed binding Roadmap for the implementation in all EU member States.
  - Pilots that are conducted by the associations are beneficial to identify the benefits of ePI to patients.
- Industry recommends having a transparent and open discussion, with the goal of confirming "data stewardship(s) and data ownership(s)" of the content of ePI.
- Building up the technical foundation of ePI to make access of all EU and national authorised product information in a faster and easily accessible way within the EU in order to leverage ePI to mitigate shortages, regulatory efficiency and support the adoption of multilingual package.

Annex 6: Multilingual ePI

Key principles[52]: Multilingual ePI

ePI shall support all official EU languages and Icelandic and Norwegian so that EU citizens will be able to read ePI in their preferred language when authorised ePI in that language is available.

Position

The availability of different official languages is accomplished by translations as part of the applicable EU procedure. This ensures that the PI for a centrally authorised medicine is available in all official EU languages (plus Norwegian and Icelandic) and the PI for a nationally authorised medicine is available in one or more official language(s) of the Member State where the medicine is placed on the market.

For nationally authorised medicines interchangeability of language versions across member states is not guaranteed by the frameworks applicable to this procedure. National authorisations are the result of individual member state assessment of marketing authorisation applications and the resulting label agreed between the NCA and the MAH. National Authorisations which are the outcome of a DCP or MRP procedure may include national requirements to support better understanding in an individual Country and therefore a one-to-one translation between these national authorisations cannot be confirmed in all cases. Approved national language versions will only become available at the time of final MA approval in each Member state included in the MRP or DCP procedure and would not become available simultaneously. For those products authorised via the DCP or MRP it should be permissible to provide links to other the language versions approved in other member states where interchangeability can be assured by the MAH. It could be considered that NCA validated translation tools could be utilised in the future to facilitate provision of other language versions.

The availability of ePI in multiple languages will facilitate the **mitigation of product shortages** enabling easier supply without the need for relabelling. This is especially important in times of increased risk of medicinal shortages as observed with the COVID19 pandemic and as recognised in the EU Pharmaceutical strategy ePI can *"support wider availability of medicines across Member States".*

Broader use of multilingual packages could increase availability of medicines and improve management of the supply chain. Increasing the possibility of using multilingual labelling would offer significant benefit for countries where the size of the market is not big enough to respond to patients' needs. Promoting the possibility of having common labels between large and small markets would have several benefits in improving access to medicines for patients across Europe. However, due to the challenges in providing printed paper leaflets in various languages in the final packaged product, this is complex.

In particular, the limited space available to accommodate the multilingual text and lack of harmonisation of national requirement for PI contents are the major challenges to implement Multilingual packages. For injectable medicines it is even more complex to add languages in the paper leaflet, due to the size of the boxes that have to be as small as possible to facilitate storage in refrigerated conditions.

ePI represents a game-changer tool to address those challenges, if individual EU / EEA member states will agree to **accept packaging potentially with one language only and have the other official approved language versions available electronically**. This would also facilitate the supply to small markets.

CALL TO ACTION

Open dialogue between industry and regulators on recognition of ePI as main source in the following scenarios:

- Mitigation of shortages by stock sharing between countries, without the need for repacking because the PL is available as an ePI.
- Flexibility in language versions required in the paper leaflet for multilingual packs when the full text can be provided in ePI.
- Possibility for use of packs from other markets to increase availability in small markets.

Removal of the paper and use of the ePI as single source will facilitate multi-country packs.

52 https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/electronic-product-information-human-medicines-european-union-key-principles_en.pdf

Annex 7: Interoperability with EU and Global initiatives

Key principles[53]:

ePI will interface and interact with many ongoing and foreseen eHealth initiatives. eHealth and related services should work together, within and across organisations or domains. ePI interoperability with cross-border prescription, electronic health records, the future European medicines web portal, pharmacovigilance systems, SPOR data management services, future ePI for veterinary medicines, a future European common data model, current electronic application procedures and national ePI systems must be considered in the design of EU ePI. Use of ePI in both an EU and global context should also be taken into account.

Position

Industry warmly welcomes the ePI principle of interoperability by design with other ongoing initiative in the digital environment such as eHealth initiatives and EU Telematics projects.

It is strongly recommended that interoperability with the future European medicines web portal, pharmacovigilance systems, SPOR data management services, future ePI for veterinary medicines, a future European common data model, current electronic application procedures and national ePI systems will be included as criterion for the design and implementation of ePI from the start.

This will be **essential to achieve significant objective for patients and HCPs**, such as alert of significant changes in the PI content, like safety measures, but also to achieve efficiencies in the regulatory systems. **SPOR Data management service, current electronic application procedures and national ePI systems represent the foundation of ePI for its effective implementation**.

Therefore, there is a need to have an **open dialogue with between regulators and industry to agree on how ePI will fit into the future telematics ecosystem** to ensure benefits for all end-users (such as patients, HCPs and carers).

The objective set in the key principle *"Efficiency gains for regulatory systems"*[54] is of significant importance for Regulators and industry. This objective can only be achieved if the ePI implementation plan will take it into account in the first planning phase. To improve the ePI processes both in the creation and updating processes (via variations), these regulatory processes should leverage existing data of the TOM facilitated SPOR system, both for the benefit of the regulators and the pharmaceutical industry.

In addition, it will be crucial to establish interoperability with cross-border prescription, electronic health records as well for an effective functioning of the overall eHealth initiatives. As for example, in order to promote cross–border prescription, ePrescription and support EU Citizens in managing their health abroad connection between SPOR, ePI and eHealth initiatives is an essential link.

CALL FOR ACTION

- ePI interoperable by design should be a successful criterion for its harmonized implementation, especially to connect and transform regulatory processes and data into useful information provided to patients, consumers, HCPs and caregivers.
- Recognise ePI as a part of the eHealth strategy.

53 https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/electronic-product-information-human-medicines-european-union-key-principles_en.pdf
54 https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/electronic-product-information-human-medicines-european-union-key-principles_en.pdf

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medicines for europe
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