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

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Reader guidance

The document is structured with an opening 'executive summary' which summarises the drivers for ePI and the benefits for all Stakeholders, the way forward to move from principles to action and the key asks.

The following paper includes the content and key points from the individual sections which relate to the EMA Key Principles guidance document.

In addition to the paper, there are a series of seven stand-alone annexes, that provide more in-depth detail that can be used separately in discussion or as an integrated document about the ePI Key Principles. At the end of each section is a 'Call for Action' which is a practical list of recommended actions to be initiated.

Executive summary

Electronic product information: from Principles to actions

The European Medicines Agency (EMA), the Heads of Medicines Agencies (HMA) of EU Member States and the European Commission (EC) have published in 2020 the **key principles paper outlining a common approach to develop and use electronic product information (ePI)** for human medicines across the European Union[1].

The pharmaceutical industry fully supports the provision of comprehensive, accurate and up-to-date regulator-approved information on medicinal products, both for patients and healthcare professionals (HCPs) and EMA/HMA's conclusion that there is a need to explore alternative innovative pathways of disseminating information in electronic format.

The value of ePI has been clearly recognised in the **European Medicines Regulatory Network Strategy**[2] **(EMRN)** where multiple benefits for patients' empowerment, operational excellence and sustainability of the Regulatory Network have been envisaged for the healthcare and pharmaceutical environment.

Also, the European Parliament (EP) has called for the urgent implementation of ePI *"in order to facilitate the moving and sales of medicines within the single market and thus mitigate shortages"* in the **EP Report on shortages**[3].

Moreover, the recent **European Pharmaceutical strategy**[4] has highlighted how the *"better use of product information in electronic format (ePI) could facilitate the delivery of information on the medicine to healthcare professionals and patients in the EU's multilingual environment and support wider availability of medicines across Member States". In the next years, the European Commission (EC) will collaborate with Member States and industry "to develop and implement electronic product information (ePI) for all EU medicines"* and *"evaluate and revise relevant provisions in the legislation by 2022".*

Moreover, the need for flexibility by using ePI was recognized in the context of the preparedness work of COVID-19 vaccine development and the associated logistics of early printing packaging activities.[5]

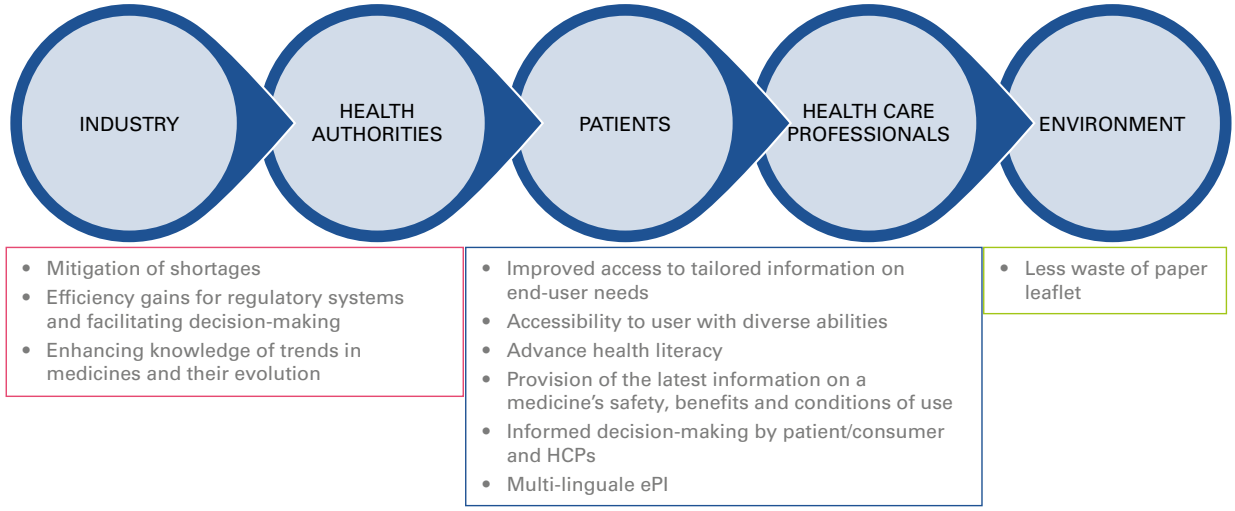
This paper provides the industry views on the 'Key Principles' document but also provides a holistic vision of what is needed to deliver timely and easily accessible and up-to-date medicinal product information to patients and HCPs, contributing to the overall health literacy of EU Citizens.

1 https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/electronic-product-information-human-medicines-european-union-key-principles_en.pdf
2 EP REPORT on the shortage of medicines – how to address an emerging problem (2020/2071(INI)), para 75.
3 https://ec.europa.eu/health/sites/health/files/human-use/docs/pharmastrategy_com2020-761_en.pdf
4 https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/electronic-product-information-human-medicines-european-union-key-principles_en.pdf
5 https://www.ema.europa.eu/en/documents/other/questions-answers-labelling-flexibilities-covid19-vaccines_en.pdf

ePI: Drivers and benefits for all stakeholders

All stakeholders (patients, healthcare professionals, caregivers, regulators and industry) can benefit from ePI implementation.

The needs of the patient and HCPs (the ultimate end-users) must be at the forefront of the EC/EMA/HMA ePI implementation strategy and approach.



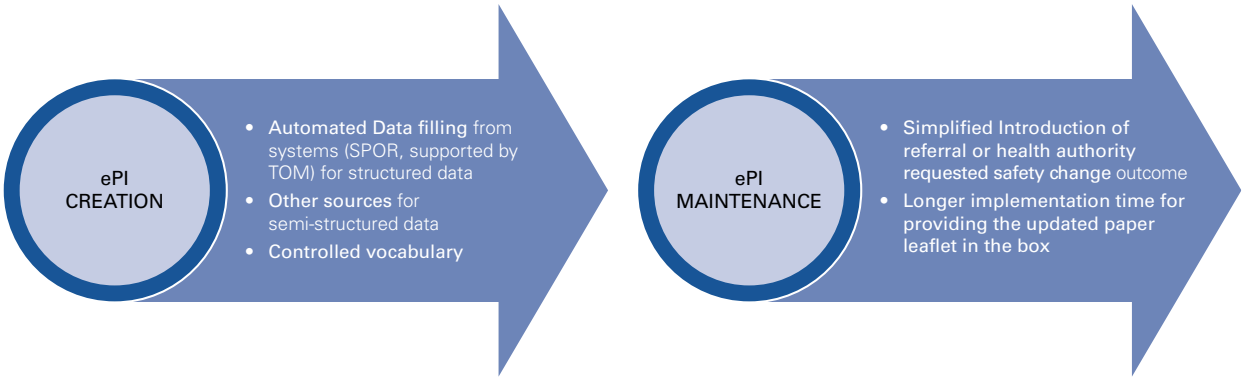
Industry believes that public health could benefit enormously from a coherent and consistent ePI implementation across the EU. Considering new advanced technologies, we could and must go beyond the current scope proposed by the EMA key principles.

Some examples of benefits and functionality that ePI could bring:

- Immediate access to the most recently regulator-approved product information.
- Attractive, presentable and user-friendly interface with other potential supportive features (e.g. user font modification) would motivate patients to take a more active interest in their health status.
- Availability of additional materials to the statutory information: video and audio facilities[6] accessible to support and improve health literacy and safe use of the product.
- Alerts for major updates to the leaflet.

However, ePI will not solve issues encountered due to poor compliance or low literacy per se, so work on the content (readability, user testing, QRD template, etc) and other related information such as instruction videos, audio content, additional materials and risk minimisation materials will need to take place in parallel.

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

Regulatory efficiencies and operational excellence will be achieved for the benefit of regulators and industry via a harmonised implementation of ePI across Europe. There are excellent opportunities for efficiencies with ePI in the regulatory system

6 https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/mobile-scanning-other-technologies-labelling-package-leaflet-centrally-authorised-medicinal-products_en.pdf

through improved interoperability, ensuring better accessibility and a high level of regulatory compliance, by using structured and semi-structured data. These regulatory processes should leverage existing data of the TOM facilitated SPOR system.

The Environment

The **Green deal and the EU Commission agenda to improve the environment:** we see a huge potential upside of the ePI by successively replacing the paper leaflet, starting in the hospital setting and outside of the hospital setting with products that are directly administered by HCPs (e.g. vaccines), to reduce the volume of paper and ink (and all associated industrial activities) that are currently used. This will also contribute to the decrease of the Carbon footprint.

The way forward to move from principles to action

1. Need to collaborate at different levels of the pharmaceutical network to establish Governance model and balance flexibility with patients and stakeholders needs

Industry has reached out for a strong collaboration with regulators and other stakeholders including the Telematics Management Board, to ensure we gain the efficiencies in the processes while being conscious of the priority to improve health information.

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. The ePI programme needs to be based on a **solid governance structure** and attribution of roles and responsibilities in the ePI implementation.

There is a need for a **robust milestone-driven roadmap that is aligned with the different stakeholders and which is based on agreed use cases**. The roadmap should be drafted with high priority given to the benefits of the patients; for that reason, both **new and existing products** should be considered as part of the first milestone.

- To achieve these key objectives and meet these expectations, **urgent and adequate funding** is required to underpin the project work.
- For a successful implementation of ePI across EU/EEA in the interest of the patients, **technology and process have a crucial role to play in achieving the goals**.
- It would also be important to start urgently an open dialogue with industry and regulators 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 ePI Key Principles paper suggests that a broad margin of **flexibility** is given for national implementation of ePI across EU/EEA. However, this flexibility should be accompanied by a **clear and binding phased roadmap and value-added milestones** that include a **proof-of-concept phase** in which the level of acceptable flexibility for an ePI approach can be tested and improved accordingly.

2. ePI definition and common standard

The definition of ePI encompasses more than information for the prescriber and patients, it also includes labelling, blue box requirements and Annex II information[7].

The priority for delivering ePI should be the freely accessible provision of trusted (regulator-approved) information to patients, consumers and HCPs. Therefore, we propose a phased approach, which starts with the creation, regulatory processing and dissemination of **electronic Package Leaflets (PL) and Summary of Product Characteristics (SmPCs); a mutually agreed roadmap** defines the subsequent addition of other value-adding aspects of ePI, plus corrective modifications (from post-implementation learning).

One of the first key enablers for the adoption of ePI is a **common standard** that allows the generation and dissemination of authorised information in the EU/EEA. Features such as **vocabularies and interoperability specifications** are considered important for ePI.

3. Existing legislative framework to coexist with digital innovation

The EC Pharmaceutical Strategy[8] formulates as an action to *"develop and implement ePI for all EU medicines with involvements of member states and industry".* In addition, it recognised the need to *"evaluate and revise provisions in the legislation".* Industry believes that the **ePI shall have the same value as paper PL**, however this evolution requires further practical experience following the implementation of ePI and should be considered as part of the evaluation of the legislation.

There are situations where the paper PL could be removed from the pack and substituted by **ePI while still ensuring patients' needs** and interests are respected (e.g. by providing printed leaflet at point of dispensing).

Current practices with hospital / healthcare professional-administered products where patients rarely receive the package leaflet, show there is no reason not to remove the paper leaflet from the pack. By directing patients toward the ePI, it will fill the gap of information that is a reality in today scenarios.

Therefore, industry proposes to expand current national pilot[9] into an **EEA-wide pilot study to investigate the current practices** and benefits **of replacing paper with ePI for hospital/HCP administered products**. Such a pilot could be expanded to products directly dispensed to (and used by) patients in highly digitalised markets **to investigate the current**

7 https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/electronic-product-information-human-medicines-european-union-key-principles_en.pdf , page 4.
8 https://ec.europa.eu/health/sites/health/files/human-use/docs/pharmastrategy_com2020-761_en.pdf, pages 15 and 16.
9 More information available at the following links: https://www.afmps.be/fr/news/projet_pilote_e_pil_la_notice_papier_fait_place_a_la_notice_electronique; The Ministère de la Santé in Luxembourg website https://sante.public.lu/fr/actualites/2020/08/e-pil-call-for-candidates/index.html

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).

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

- faster dissemination of relevant regulatory approved changes to product information
- mitigation of medicines shortages (by redistribution of packages in different languages)
- reduced packaging/distribution and wastage costs (arising from changes and recall of batches)
- immediate access to the latest information via ePI following approval, enabling a more flexible transitional period for the provision of up-to-date paper leaflets
- possible removal of the paper leaflet to reduce the volume of packaging and use of paper and ink and decreased carbon footprint
- efficiencies in the size of outer packaging materials thereby reducing transport and storage space, (especially important for products requiring controlled temperature storage)

4. ePI as main source of product information

The availability of ePI in multiple languages will facilitate the **mitigation of product shortages** by 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. 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. However, due to the challenges in providing printed paper leaflets in all languages in the final packaged product this is complex. ePI represents a game-changer tool to address this, if individual EU and EEA 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.

5. Access to ePI: intuitive and friendly for an informed decision-making by patients / consumers and HCPs

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.

Industry understands the value of ePI being available on a range of platforms throughout the EU but most importantly each Member State 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**.

- **Outer package:** further discussion is needed in light of current and evolving technologies and standards, to facilitate **one code**[10] **only on the (secondary) packaging** to ensure clarity to patients, HCP and pharmacists and to avoid the risk of mistakes and/or misunderstanding.
- **The architecture of the web portal**[11] must be structured in a way that patients are smoothly and unequivocally directed to the correct regulatory ePI, for that specific product.
- Patients who cannot access their product information electronically should have the **same opportunity as those who have** (e.g. by providing printed leaflet at point of dispensing).
- **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.

6. Interoperability by design

Industry welcomes the ePI principle of **interoperability by design** employed in other ongoing initiatives in the digital environment such as eHealth initiatives and EU Telematics projects and recommends including it as a criterion the design and implementation of ePI from the start. This will be **essential to achieve significant objectives for patients and HCPs**, such as alert of significant changes in the PI content or specific, 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**.

10 A code can be achieved using different technology including but not limited to QR codes, 2D data matrix codes, linear barcodes.
11 A pan-European medicines web portal providing a central point for access of ePI for all centrally and nationally authorised medicines (see EMA/HMA/EC paper 'Electronic product information for human medicines in the EU: key principles').

Key Asks

Launch the ePI project

Governance/Guidance/Regulatory

- Identify a clear Governance structure and ownership of the ePI project, that will take care of ensuring the appropriate funding, which is required to accelerate the ePI development
- An agreed binding Roadmap for a consistent and coherent ePI implementation in all EU member States, covering all pharmaceutical products
- Establish a central coordination of all "ePI like" initiatives
- Start an open dialogue between regulators and industry in early 2021, to fit ePI into the future telematics ecosystem
- Active involvement of the telematics network, to ensure processes are more efficient and linked to other relevant telematics projects
- A future EU Implementation guideline elaborating on the concept of ePI, structured and unstructured and re-usable elements should be provided by EMA
- Develop a Common standard in collaboration between the Industry, Regulators and impacted stakeholders
- ePI interoperable by design should be a successful criterion for its coherent implementation
- Stronger collaboration between regulators and industry to establish the needs of both in the Regulatory processes
- Pragmatic way to include a standardised sentence in the paper leaflet, highlighting the existence of an ePI on reference websites, and avoid any regulatory or administrative burden to the system.
- Architecture of the web portal (and any other access point) should be structured in a way that patients are smoothly and unequivocally guided and directed to the right ePI
- Supporting stakeholder discussions on additional 'use cases' and the positive benefits
- Discussion between Industry and regulators must be undertaken on how to link ePI with only one code on the (secondary) package

Policy and legal aspects

- A transparent and open discussion, confirming "data stewardship(s) and data ownership(s)" of the content of ePI
- Expansion of Pilot projects investigating the benefit of replacing paper with ePI for hospital/HCP administered products
- Dialogue between industry and regulators on recognition of ePI as main source in scenarios where it can mitigate shortages or increase availability of medicines in small markets.
- In future, removal of the paper on voluntary basis and ePI as single source will facilitate multi-country packs
- Conduct legal framework analysis, for the development of an ambitious ePI roadmap

Patients and HCPs

- Educational campaign to raise awareness on ePI
- Discussion on how to secure safe and easy access to ePI for patients
- Collaboration of all stakeholders (patients, HCP, Industry, regulators) to define how the content of the PI can be improved.
- Recognise ePI as a part of the eHealth strategy

Introduction

The EU product information (PI) for medicinal products consists of two main documents: the Summary of Product Characteristics (SmPC) and the Package Leaflet (PL), which are regulated regarding their content, structure, and layout. To be effective, ePI has to be actively referred to, read, understood, trusted and remembered. The SmPC is primarily directed to Healthcare Professionals (HCPs), while the PL addresses patients and caregivers, requiring different language and layout principles to suit the reader.

The **NIVEL study**[12] 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 unintended 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 that would help them understand the benefits and potential consequences the medicine would have on them[13].

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**[14] to implement the recommendations made. The recommendations focus largely on improving content, layout and readability (including patient involvement) and electronic formats of product information.

The pharmaceutical industry fully supports the provision of comprehensive, accurate and up-to-date regulator-approved information on medicinal products, both for patients and HCPs. Such information must be safely and easily accessible, allowing the patients/HCPs to obtain, identify and use the information necessary to meet their individual needs. Patients' role in their own health care is changing from patient compliance to patient engagement. Therefore, the importance of the product information is increasing, and content, readability and layout are considered key pillars for its correct and appropriate use. Consequently, the pharmaceutical industry believes that the enhancement of product information content is considered critical and should be further developed as part of a broader programme in building citizens' health literacy in partnership with patients, HCPs and authorities. 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[15].

The pharmaceutical industry supports the EMA's conclusion that there is a need to explore alternative innovative pathways of disseminating information in electronic format. The use of existing and evolving technologies could allow immediate access to the most recent regulator-approved 'real-time' product information, rather than relying on potentially out of date paper copies or electronic information from non-trusted sources. This approach would enable patients to search trusted information sources in a tailored fashion to meet their own needs. Furthermore, a direct link from the medicines packaging would enhance accessibility without the need to rely on search engines pointing towards trusted sources of ePI.

Prioritisation has been given to the development of an electronic approach to the creation and dissemination of product information in a structured format (ePI). EMA, the Heads of Medicines Agencies (HMA) of EU Member States and the European Commission (EC) have published **key principles outlining a harmonized approach to develop and use electronic product information (ePI)**[16] for human medicines across the European Union. These principles represent a collaborative guidance on ePI and form the basis of follow up implementation plans for ePI.

The value of ePI has been clearly recognised in the **European Medicines Regulatory Network Strategy**[17] **(EMRN)**, where the multiple benefits for patients' empowerment, operational excellence and sustainability of the Regulatory Network have been envisaged for the healthcare and pharmaceutical environment. Recently, also the European Parliament (EP) in the **EP Report on shortages** have called for the urgent implementation of ePI *"in order to facilitate the moving and sales of medicines within the single market and thus mitigate shortages"*[18].

Moreover, the recent **European Pharmaceutical strategy** has reinforced how the *"better use of product information in electronic format (ePI) could facilitate the delivery of information on the medicine to healthcare professionals and patients in the EU's multilingual environment and support wider availability of medicines across Member States"*. The European Commission (EC) will collaborate Member States and industry *"to develop and implement electronic product information (ePI) for all EU medicines"* and *"evaluate and revise relevant provisions in the legislation"*[19].

12 https://ec.europa.eu/health/sites/health/files/files/committee/75meeting/pil_s.pdf
13 https://ec.europa.eu/health/sites/health/files/files/committee/75meeting/pil_s.pdf at page 8 and 9
14 https://www.ema.europa.eu/en/documents/other/european-medicines-agency-action-plan-related-european-commissions-recommendations-product_en.pdf
15 Sørensen K, et al. Health literacy in Europe: comparative results of the European health literacy survey (HLS-EU). Eur J Public Health. 2015 Dec;25(6):1053-8.
16 https://www.ema.europa.eu/en/electronic-product-information-human-medicines-european-union-key-principles
17 https://www.ema.europa.eu/en/about-us/how-we-work/european-medicines-regulatory-network/european-medicines-agencies-network-strategy
18 EP REPORT on the shortage of medicines – how to address an emerging problem (2020/2071(INI)). Para 75
19 https://ec.europa.eu/health/sites/health/files/human-use/docs/pharmastrategy_com2020-761_en.pdf

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 seems to be based on the current combined product information in PDF format provided by 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, therefore, we propose a phased approach, which starts with the creation, regulatory processing and dissemination of electronic PLs and SmPCs, with the addition in later phases 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.

A main key enabler for the adoption of ePI is a **common standard** that allows the generation and dissemination of authorised information in the EU/EEA. In addition, we propose to stress the 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 aims of the common standard are:

- to create the technical foundation for the dissemination of trustworthy, regulator-authorised product information and
- 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, both by regulators and the pharmaceutical industry

The programme for developing **ePI must be aligned with all complimentary 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 ePI implementation.

There is a need for a **robust milestone driven roadmap that is aligned with the different stakeholders and which is based on agreed use cases**. 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.

Industry has reached out for a strong collaboration between regulators and industry, with the involvement of the Telematics Management Board (EMA – HMA – EC), to ensure we gain the efficiencies in the processes while being conscious of the priority of bringing improvements in health information to patients and HCPs.

To achieve these key objectives and meet these expectations, **urgent and adequate 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, when ePI will be implemented, the QRD templates could be updated to align content, technical, design specifications and standard for both PI and ePI.

Benefits for Public Health

The needs of the patients and HCPs (the ultimate end-users) must be at the forefront of the EC/EMA/HMA ePI implementation strategy and approach

Industry believes that public health could benefit enormously from an ePI implementation in EU. Considering new advanced technologies, we could and must go beyond the current scope proposed by the EMA key principles. There is a risk that buy-in from patients/consumers might be relatively small, should ePI simply be provided for a small number of products available on the market. Any implementation that is not coordinated across health authorities risks that some of the benefits of ePI noted in the EMRN Strategy (e.g. in case of shortages) and in the EU Pharmaceutical Strategy[20] cannot be achieved. For that reason, **industry support the EC vision of collaboration between Regulators, Members State and industry to develop and implement ePI for all medicines in Europe**.

Some examples of benefits and functionality that ePI will bring:

- The availability of ePI facilitates the **immediate access to the most recently regulator-approved product information** and the ability to search and retrieve information in a more suitable and intuitive way.
- **Additional information materials (video and audio facilities) to the statutory information[21] available to EU citizens, that will support and improve health literacy and inform on the correct use of the medicine**. An attractive, presentable and user-friendly interface with other potential supportive features motivate patients to take a more active interest in their health.
- **In the case of chronic diseases**, patients are so used to taking their medicines, that they do not read the leaflet anymore. With ePI, **an alert could be given in the event of a major update to the leaflet**. This is of particular importance for medicines that are already available on the market and used by patients.

However, ePI will not solve issues encountered due to poor compliance or low literacy per se. To address these latter aspects, **work on the statutory information (QRD template, readability etc.) and possible connection to other related information such as instruction videos, audio content, additional information materials 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.

Intuitive and straightforward access to ePI to enable an informed decision-making by patients, consumers and HCPs

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*" and will be *"also be available for use by third-parties, who can reproduce ePI and make it available to patients and HCPs".*

We support the concept to have a **single access-point to extract and re-use ePI as described in the Key principles – process chart**. Industry understands the value of ePI being available on a range of platforms throughout the EU but most importantly each Member State 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.

- **Outer package:** further discussion is needed in light of current and evolving technologies and standards, to facilitate one code[22] only on the (secondary) packaging to ensure clarity to patients, HCP and pharmacists and to avoid the risk of mistakes and/or misunderstanding.
- The **architecture of the web portal** (and any other access point) must be structured in a way that patients are smoothly and unequivocally directed to the right ePI, approved for that specific product. 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".* This will ensure that patients are guaranteed to have access to a trusted source of regulator approved ePI.
- 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** to get the corresponding, most recent, regulator approved product information printed in the pharmacy, at the point of sale or via other technologies.
- **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.

20 https://ec.europa.eu/health/sites/health/files/human-use/docs/pharmastrategy_com2020-761_en.pdf
21 Include EMA guidance on Mobile scanning technologies as reference. https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/mobile-scanning-other-technologies-labelling-package-leaflet-centrally-authorised-medicinal-products_en.pdf
22 A code can be achieved using different technology including but not limited to QR codes, 2D data matrix codes, linear barcodes.

ePI Implementation and patients' need

While industry recognises a need for allowing **flexibility** in implementation of ePI across EU countries, 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.

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

As long as the paper PL is required to be available, it should be taken into consideration that over a certain period of time, there might be an *"inconsistency"* between the paper PL and the ePI, caused by the immediate availability of the ePI while printing and packaging takes significantly longer. Therefore, as soon as ePI is introduced, the corresponding paper PL should carry a **standard sentence** advising patients/consumers that the most current version of the product information is provided by ePI with a note indicating how to access this information. Industry and authorities have to 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.

CALL FOR ACTION

- Patients must benefit from the full potential of new technologies; therefore, the ePI implementation roadmap should cover all pharmaceutical products.
- 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 and authorities to work on pragmatic implementation of a standardised sentence in the paper leaflet, highlighting the existence of an ePI on reference websites, and avoid any regulatory or administrative burden to the system.
- Discussion about current and evolving technologies and standards how to link to ePI in a long-term with only one code on the (secondary) packaging.
- Architecture of the web portal (and any other access point) should be structured in a way that patients are smoothly and unequivocally directed to the correct ePI, that is approved for that specific product.
- Obtain views, understanding of priorities, identify issues/areas of potential joint working or collaboration of all stakeholders (patients, HCP, 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.

Efficiency gains for regulatory systems

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 common standard should be adopted in the creation, submission and review process and 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 (e.g. data from SPOR), by using structured and semi-structured data. The main examples of these efficiencies relating to regulatory processes are:

- **Automated Data filling from systems (SPOR, supported by TOM) for structured data.**
- **Controlled vocabulary for standardised information**, e.g. patient friendly translations of scientific terms.
- **Simplified introduction of referrals or health authority requested safety change outcomes.**
- Potentially a **longer implementation time for providing the updated paper leaflet in the box.**
- **Maintenance of text should be easier**, only the relevant section of the PI needs to be updated.
- **Changes made directly into systems, which** will speed up the process for updates and approval of any change to the ePI (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.

While being supportive of the implementation of ePI, **the creation of ePI format for already existing PIs should equally be prioritised by providing incentives** i.e. an efficient process/guidance for the conversion of the current PI to the new ePI format, process optimisation for changes to the PI, possible implementation without any regulatory submission/approval process (if strict conversion) and there should be a reasonable transition time agreed with Industry.

CALL FOR ACTION

- Stronger collaboration between regulators and industry to establish the needs of both parties in regulatory processes and submission management.
- Active involvement of the telematics network, to ensure processes are 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.

Existing legislative framework

The EC Pharmaceutical Strategy[23] formulates as an action to *"develop and implement ePI for all EU medicines with involvements of member states and industry"* in addition it recognized the need to *"evaluate and revise provisions in the legislation."* Industry believes that **ePI shall have the same value as paper PL**, however this evolution requires further practical experience following the implementation of ePI and should be considered as part of the evaluation of the legislation. However, a stepwise approach needs to be developed, with relevant stakeholders, to ensure suitable and appropriate implementation occurs to safe-guard patient needs.

There are situations where the **paper PL could be removed from the pack** and **substituted by ePI while still ensuring patients' needs** and interests are respected (e.g. by providing printed leaflet at point of dispensing).

Current practices with hospital / healthcare professional-administered products where patients rarely receive the package leaflet, show there is no reason not to remove the paper leaflet from the pack. By directing patients toward the ePI it will fill the gap of information that is a reality in today scenarios.

Therefore, industry proposes to expand current national pilot[24] into a **EEA-wide pilot study to investigate the current practices and benefit of replacing paper with ePI for hospital/HCP administered products**. Such a pilot could be expanded to products directly dispensed to (and used by) patients in highly digitalised markets **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).

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

- faster dissemination of relevant regulator approved changes to product information.
- mitigation of medicines shortages (by redistribution of packages in different languages as it was used in Germany for flu-vaccination[25]).
- possible removal of the paper leaflet, starting in hospitals providing a positive outcome is seen from the Belgian pilot, to reduce the volume of paper and ink currently used for the paper leaflet and 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).
- quick access to the latest product information via ePI after the approval process, could enable a more flexible transitional period for the provision of up-to-date paper leaflets.
- efficiencies in the size of packaging materials thereby reducing transport and storage space, (especially important for products requiring controlled temperature storage).

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.

23 https://ec.europa.eu/health/sites/health/files/human-use/docs/pharmastrategy_com2020-761_en.pdf, pages 15 and 16.
24 More information available at the following links: 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; The Ministère de la Santé in Luxembourg website https://sante.public.lu/fr/actualites/2020/08/e-pil-call-for-candidates/index.html
25 https://www.pei.de/DE/newsroom/hp-meldungen/2020/201028-vaxigrip-tetra-influenza-impfstoff-frankreich-eingefuehrt.html;jsessionid=A430493D5264328B80407ABB09444254.2_cid354?nn=12248480

Processes, flexibility and Governance

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 **European Commission Pharmaceutical Strategy**[26] as well as in the **EMRN Strategy**[27], 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 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 States and industry need to collaborate to develop and implement ePI for all medicines in Europe**.

Therefore, there is an urgent need to establish 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).

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 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.

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 regulatory 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

With regard to **data stewardship**[28] of the content of the Product Information, clear assignment of responsibility is required to clarify the accountability and liability for each step of the ePI process; in particular for the release of the ePI final content that will be publicly available. We believe this openness will facilitate an efficient collaboration between Industry and Regulator(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.

CALL FOR ACTION

For all the above considerations, industry has identified as crucial the following actions:

- Establish a central coordination of all "ePI like" initiatives, to ensure that key benefits to all stakeholders are delivered.
- Agree on Common Standard: A 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 ensure 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 use cases that ePI will serve and an agreed binding Roadmap for the implementation in all EU member States.
- 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.

26 https://ec.europa.eu/health/sites/health/files/human-use/docs/pharmastrategy_com2020-761_en.pdf
27 https://www.ema.europa.eu/en/about-us/how-we-work/european-medicines-regulatory-network/european-medicines-agencies-network-strategy
28 "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".

Multilingual ePI

The availability of different official languages is accomplished by translations as part of the applicable EU regulatory procedure. While PI for a centrally authorised medicine is available in all official EU languages (plus Norwegian and Icelandic), 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. This means that for nationally authorised medicines interchangeability of language versions across member states is not guaranteed by the frameworks applicable to this procedure.

For MRP or DCP procedures, ePI will be available in multiple languages but due to different timelines of national approvals, they will not be available simultaneously. For those products, it should be permissible to provide links to other language versions where interchangeability can be assured by the MAH.

The availability of ePI in multiple languages will facilitate the **mitigation of medicines shortages** enabling easier supply without the need for relabelling. This is especially important in times of increased risk of medicines shortages as observed with the COVID19 pandemic. 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. 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 FOR ACTION

We call for an open dialogue between industry and regulators on recognition of ePI as the 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 leaflet and reliance on ePI as the single source will facilitate multi-country packs.

Interoperability with EU and global initiatives

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

In addition, it will be crucial to establish interoperability with cross-border prescription, electronic health records to ensure effective functioning of the overall **eHealth initiatives**. 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 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.