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An Agile Approach to Accelerate Development and Adoption of Electronic Product Information Standards

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Abstract. The Medical Product Information found in most medication boxes offer a wealth of information, including terms of active ingredients, excipients, indications, dosage, route of administration, risks, and safety information. Digital health services that help patients, their care givers, and health professionals to manage medication, can be improved with tailored information based on user profile, the patient's Electronic Health Record (EHR) summary, and Medicinal Product Information. The electronic Product information (ePI) comprises the summary of product characteristics, package leaflet, and product label. The European Medicines Agency released in 2021 the first version of the EU proof-of-concept ePI standard based on HL7 FHIR. The Gravitate-Health project uses this common standard as a springboard to implement a federated open-source platform and services that helps advance access, understanding, and adherence by providing trusted medicinal information in an interoperable and scalable way. In this paper, we present the agile technical approach and co-creation process to design, test, and progressively mature interoperability working with the HL7 Vulcan Accelerator and FHIR connectathons.

Keywords. Citizen Empowerment, interoperability, electronic product information, International Patient Summary, HL7 FHIR, regulatory science

1. Introduction

In the European Union, a medicine's product information refers to the summary of product characteristics (SmPC) that is intended for healthcare professionals (HCPs), labelling (outer and inner packaging information) and package leaflet (PL) intended for for patients / consumers that is generally included as a printed copy in the medicines package [1]. The regulated and scientifically validated information included in SmPC assists HCPs in prescribing and dispensing the medicine. PLs included in the medicine

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package inform patients and consumers about safe use. Prior to marketing authorization, a rigorous regulated process ensures that the paper PL can be read and understood by its users, patients and caregivers. However, in a digital world, the content of the paper PL is considered as a trusted yet underexploited information resource.

A report from the European Commission in March 2017, and a subsequent European Medicines Agency (EMA) action plan [2], identified areas where the SmPC and PL could be improved. Developing key principles for an ePI format was identified as the most pressing priority from a public health perspective and these key principles were finalized and published in January 2020 [1]. Further to this, the EMA ePI SetUP project was established to develop a common European format for ePI based HL7 FHIR® [3]. This ePI setup project started early in 2021, to create a proof-of-concept EU common standard specification in line with the key ePI principles. The draft specification was published in June 2021, together with an exploratory FHIR server that hosted sample data. A hands-on workshop was organized in July 2021, followed by a stakeholder consultation. Then, the common standard specification was approved by the EU Network Data Board [4], the next ePI implementation phase started. Despite the shift towards use of electronic formats, the primary form of delivery for Medicinal Product Information is still paper and regulatory processes built around this paradigm. While there are procedures and guidance on testing understanding of paper leaflets [3], such guidance is missing for ePI.

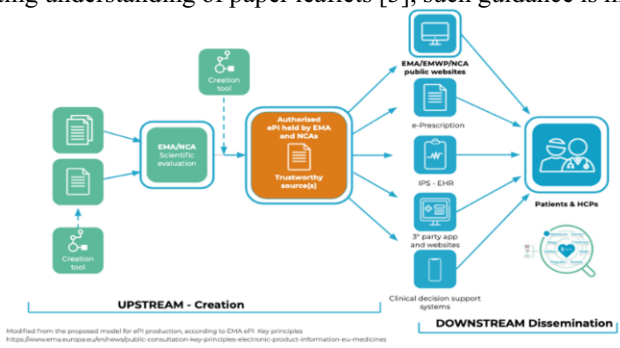

Figure 1. Gravitate-Health engages upstream, when creating and assessing ePIs and downstream, when tailoring ePI to user needs and preferences optimizing its impact on the understanding of the information.

The Gravitate-Health public-private partnership (www.gravitatehealth.eu) aims to offer citizens services that are tailored to their needs and help them access, understand and adhere to their medication therapy, supported by information conveyed by ePIs. To that end, the G-lens® combines users profile information with a summary of curated excerpt to their EHR, to highlight important ePI information. This approach will be tested in concrete user scenarios, starting in Europe and USA, and sharing experiences globally. The figure 1, above, describes the proposed data flow and process from the ePI creation (upstream) to ePI dissemination (downstream). Gravitate-Health aims to test the understanding of ePIs informing upstream. Furthermore, the G-lens® is envisaged to accelerate progress, in the 'Downstream dissemination' space, offering value to patients and their support network. Employing an HL7 FHIR standard-driven methodology, Gravitate-Health collaborates with the HL7 Vulcan accelerator's ePI project to incrementally advance and test solutions in HL7 FHIR connectathons (FCAT) three times a year. This methodology will be incorporated in the development of the Gravitate-Health HL7 FHIR IG (Implementation Guide). This methodology and preliminary findings are presented in the following sections. The discussion section reflects on the impact of the Gravitate-health approach and concludes with key points and next steps.

2. Methodology

Open standards and specifications are key to the vision of Gravitate-Health to improve access, understanding and adherence to medication treatment and exploit ePI along with information from EHRs, ePrescription Systems, and Appointment Booking. Gravitate-Health has defined personas with diverse use profiles and medication needs. Elements of the personas and associated scenarios will be used to gradually increase the complexity of the ePI scripts, while introducing step-by-step the G-lens® functionality. Among open standards, Gravitate-Health focuses on HL7 FHIR®, Web Accessibility Guidelines (WCAG2.1), and patient outcome measures like ICHOM. The G-lens® can be thought of as a set of rules that relates information in the user profile and one's patient summary to what is highlighted in ePI, or how the information from multiple ePIs is presented. HL7 FHIR® involves numerous resources and profiles. HL7 FHIR® profiles are adaptations of FHIR® resources to specific needs described in Implementation Guides (IGs). Typically, HL7 FHIR® IGs are complemented with (a) source code repositories in GitHub and (b) FHIR® servers that are populated with sample data. The Gravitate-Health IG will detail the HL7 FHIR® resources used to realize the G-lens®. The methodology adopted comprises this iterative process:

1. Identify test scenarios that mimic common real-life situations.
2. Select the FHIR® resources in-scope.
3. Identify product(s) and the SMPC/PL structured or semi-structured content
4. Convert to FHIR shorthand instances and deliver to Github workflow, to IG, to renderings of the content to HTML, XML and JSON.
5. Test at the FCAT ePI track and repeat.

The agile methodology adopted by Gravitate-Health is to progressively develop, test, and validate the resources in the IG based on FHIR shorthand (FSH), Github workflows and FHIR Release 5.0.0-snapshot1. The maturity model of HL7 FHIR® associates a level to each FHIR® resource corresponding to how extensively the resource has been tested, adopted, and used in the community. This is in line with the Gravitate Health agile methodology that entails joining the HL7 Vulcan accelerator with a dedicated ePI project, and working in a FCAT ePI dedicated track in regular sprints to incrementally advance and gradually mature the functionality of the Gravitate Health IG.

3. Results

Gravitate-Health initiated collaboration with the Vulcan Accelerator (https://confluence.hl7.org/display/VA), seeking to connect clinical research and healthcare. Gravitate-Health joined Vulcan through its coordinator early in 2021, Vulcan approved the ePI project in Aug 2021. From September 2021, Gravitate-Health committed to organizing a dedicated track in each of the three FCAT organized annually. The dedicated Vulcan ePI track develops and tries out ePI scenarios using synthetic data. In addition to the Gravitate-Health team members participating in each FCAT, all FCAT participants are invited to join and help validate the latest developments in the Gravitate-Health FHIR® IG. Parallel to each FCAT, a LinkedIn® event helps share the progress made more widely. The key ePI principles of EMA [1], advocate for "accessibility by design", so that medicinal product information is accessible to people with print impairments e.g., physical or sensory impairments, or learning difficulties. For this purpose, voice and video formats should be considered by regulators to complement

printed information and facilitate patient accessibility needs, to support use of preferred modality to perceive, understand, navigate and interact with the Internet. Thus, in terms of accessibility standards, we need to examine: (a) accessibility regulations applicable in the EU; (b) readability guidance provided by medicinal agencies applicable to patient leaflets [3]; (c) global accessibility standards; (d) accessibility of structured definitions in HL7 FHIR. The EU in the guidance already provided highlights the use of adequate font size, appropriate capitalization, uniform heading style, and line space. It also recommends short bullet lists, short sentences, and actionable guidance. A sample protocol is provided for assessing the understanding of the content by the users of the patient leaflet. Preliminary results from FCAT28 and FCAT29 are very encouraging, showing a steady increase in the participation in Gravitate-Health ePI track. Attendance in the associated LinkedIn® event also increased. Active participation in the hand-on sessions increased as well, along with the availability of tools, servers, and sample data. In fact, the use of FHIR tools like FSH and clinFHIR helped accelerate the development of sample data. **Figure 2** shows a FHIR ePI use case demonstration with CAPABLE one of the four applications that tested elements of the Gravitate-Health FHIR® IG and demonstrated elementary functionalities of the G-lens®, highlighting or suppressing ePI sections based on patient information. The ePI information is retrieved from Felleskatalogen the official product dictionary in Norway. Manually extracted knowledge linked ePI sections (*FHIR ClinicalUseIssue)* is coded in ICPC-2 with Patient demographics, allergy and conditions in *AllergyIntolerance* and *Condition* resources.

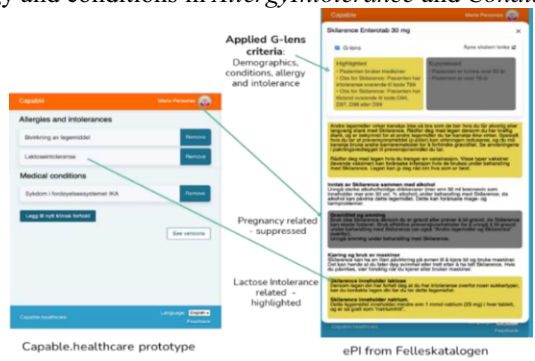

Figure 2. Example prototype from CAPABLE [5] developed in the course of FCAT29 (January 2022).

4. Discussion

The key ePI principles [1] identify ePI as a public health priority that can improve access, support adverse-event report, provide automatic update notifications and lead to more efficient regulatory processes, safety and inclusion of all. Although ePI will coexist with paper, paper and ePI will point to the newest version available in all European languages. Safeguarding these key ePI principles, Gravitate-Health collaborate with EMA, FDA, and selected national regulators to advance interoperability of resources in iterative sprint cycles and open collaboration leading to global alignment. After analyzing the landscape of standards for interoperability and accessibility, organizing two FCAT tracks, and exploring the EMA common ePI standard, there are five elements to be explored in future FCATs. First**,** knowledge representation of the ePI structured information and dictionaries connecting the elements of the user profiles and the patient summary

components is key to sustainable progress. Second, PL style and readability guidance [3] should be assessed for ability to meet the future needs for ePI and G-lens® implementations with comprehensive and real-world user scenarios with all relevant stakeholders, perhaps focusing on specific groups of pharmaceutical products. Appropriate WCAG2.1 compliant style sheets should to cater to the accessibility needs of ePI users. Third, Gravitate-Health should incorporate testing and validation guidance of EU readability and WCAG2.1, to demonstrate real-world testing of the understanding of ePIs with G-lens® use. Fourth, the federated open-source platform of Gravitate-Health could develop tools to curate and validate ePIs resources and their stylesheets, to be tested in future FCATs. Gravitate-Health should document the maturity of HL7 FHIR® ePI resources, as strategy to facilitate global adoption and regulatory alignment.

5. Conclusions and Next Steps

Interoperability driven by the HL7 FHIR® standard is at the core of the Gravitate-Health project. HL7 FHIR® is a living standard comprising of resources. The resources of interest to Gravitate-Health relate to ePI, SPOR, the International Patient Summary (IPS), and patient outcome measures. These FHIR® resources are currently at different levels of maturity and Gravitate-Health agile methodology can help accelerate their process of maturity. In addition, the open process to engage stakeholders and software developers can contribute to capacity business and community knowledge, collaborating with HL7 Vulcan accelerator for clinical research. Gravitate-Health comes into play with an agile methodology across the life cycle of ePIs that assesses understanding in the upstream and personalization in the downstream. Still there are many challenges to overcome to bring G-lens® to reality, including knowledge representation, multiple HL7 FHIR® versions, and terminology management. We expect that the agile approach adopted by Gravitate-Health will steadily move us towards advanced interoperability that drives access and understanding of medication information from trusted sources.

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