Challenges of Trustable AI and Added-Value on Health
B. Séroussi et al. (Eds.)

doi:10.3233/SHTI220558

Using FHIR to Support COVID-19 Vaccine Safety Electronic Case Reports in America

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Abstract. During the COVID-19 pandemic, the Pan American Health Organization (PAHO) promoted several activities to strengthen the countries' emergency response. Vaccines represented a breakthrough in the pandemic evolution, even though they have not been equitably distributed. As most vaccines have received emergency authorizations for their timely delivery, vaccine safety surveillance has been highlighted for detecting early signals of potential adverse events following immunization (AEFI, also known as ESAVI). The objective of this article is to share the different steps, methodologies, and preliminary results of a regional policy to strengthen the ESAVI surveillance system in the Americas, including the adoption of HL7 FHIR for health information exchange between countries and PAHO.

Keywords. vaccine safety, adverse events following immunization, events supposedly attributable to vaccination or immunization, fast healthcare interoperability resources, health information exchange, interoperability.

1. Introduction

Vaccination is one of the most cost-effective methods for the prevention of infectious diseases [1]. Effective vaccines (i.e. vaccines inducing protective immunity) may produce some undesirable side effects which are mostly mild and clear up quickly. An Adverse Event Following Immunization (AEFI), also known as Event Supposedly Attributable to Vaccination or Immunization (ESAVI), is any untoward medical occurrence which follows immunization, and which does not necessarily have a causal relationship with the usage of the vaccine [2]. ESAVI surveillance is one of the most important activities to assure that vaccine products are safe and are being safely administered. Severe reactions following immunization are extremely rare, so several countries have joined forces to pool their ESAVI data in regional and/or global databases.

The COVID-19 pandemic promoted a race for the development of more than 100 vaccine candidates using a wide variety of platforms, some of them being newly available to the public, as the mRNA vaccines. The urgent need for a permanent prevention strategy in response to the pandemic required to fasten not only the development but the regulatory process. Data on efficacy, safety, and quality of manufacturing was limited during emergency authorizations and new strategies to ensure a vaccine-product risk-benefit continuous assessment should be in place. Moreover, considering the new challenges on safety and efficacy that innovation brought, steps were

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needed to develop robust surveillance systems that could effectively and efficiently identify immunization safety signals to facilitate public health decision-making. The process of detecting and reporting vaccine safety data has proven challenging, especially in the Americas.

The Uppsala Monitoring Center (UMC) is a World Health Organization (WHO) Collaborating Center that provides training, guidance, and support to countries in the WHO Programme for International Drug Monitoring [3]. UMC also manages VigiBase, WHO's database of individual case safety reports (ICSR) and the world's largest repository of adverse effects from medicines. Nevertheless, it was noted that only 13 countries from America shared vaccine safety information with UMC in 2021.

The Pan American Health Organization (PAHO) promoted several activities to strengthen the member state's emergency response to the pandemic. Regarding vaccine safety, the need for a regional approach was backed by the PAHO's Technical Advisory Group (TAG), WHO and the United States Center for Disease Control and Prevention (CDC). PAHO proposal included a regional vaccine safety surveillance network, based on the strengthening of national information systems to detect, notify, analyze, and classify the arising ESAVI cases. It would not challenge nor interfere with UMC-WHO data gathering. On the contrary, the enhancement of local capacities would improve data sharing with both PAHO and WHO.

The objective of this article is to share the different steps, methodologies, and preliminary results of a regional policy to strengthen the ESAVI surveillance in the Americas, including the adoption of HL7 FHIR (Health Level Seven - Fast Healthcare Interoperability Resources) for health information exchange between countries and the Pan American Health Organization.

2. Materials and methods

The Pan American Health Organization (PAHO) is the specialized international health agency for the Americas [4]. PAHO engages in technical cooperation with its member states to fight communicable and noncommunicable diseases and their causes, to strengthen health systems, and to respond to emergencies and disasters. To advance these goals, PAHO promotes technical cooperation between its 51 countries and works in partnership with ministries of health and other government agencies, civil society organizations, other international agencies, universities, social security agencies, community groups, and other partners.

The COVID-19 ESAVI project had different phases, starting with a charter, and advocacy activities to support it. After reviewing the proposal, WHO and CDC grants backed its execution. A regional survey was performed to assess each country's infrastructure and capacity building related to vaccine safety surveillance. Then, a phased approach was encouraged to promote progressive improvements in the ESAVI surveillance process and supporting technologies, departing from different baselines. FHIR was promoted for health information exchange between countries and the Pan American Health Organization, including investments in countries' capacity building, implementation guide creation, and the FHIR server deployment at a central level.

3. Results

According to the results of the "Regional Survey on the status of the information systems for the ESAVI surveillance" that was carried out in 2020 by PAHO, 3 different categories could be identified (see Table 1).

Table 1. Regional Survey on the status of the information systems for the ESAVI surveillance.

Category	% of countries	Characteristics
A	62%	based on paper, using spreadsheets to manually aggregate & tabulate data
B	21%	fragmented information system with different unconnected databases
C	17%	robust web based national information system

This heterogeneity motivated a pragmatic approach to quickly get information from countries. As a first step (Phase 1) PAHO asked each country to share a copy of their existing ESAVI database "as is", regardless of their level of development, through a secure File Transfer Protocol (FTP) server. A prior anonymization process was requested to exclude sensitive identification data. Each country's Ministry of Health (MoH) designated a delegate for manually sending the database on a weekly basis. As of January 2022, 16 countries have sent data to PAHO.

The national databases had enormous differences regarding their structure (what data they send, and how it was organized) and heterogeneity in quality (completeness, consistency, coding, among others). Feedback documents were shared with each country including these observations, to generate a continuous improvement process. Using the available information, a manual analysis was carried out to build indicators for the Pan American Advisory Committee on Vaccine Safety (PACVAS) and for country feedback. One of the most important challenges was (and still is) the standardization of the databases, including standard codes, and the mechanisms for sharing and aggregating all the information at the PAHO ESAVI Regional Database, minimizing the workload impact at the country level.

Phase 2 included completing the situation diagnosis and supporting the countries in achieving a robust national ESAVI system, including the 33 recommended core variables, and favoring interoperability between national institutions and automated reporting to PAHO's ESAVI regional database. Therefore, 3 fundamental lines of action were carried out:

1. The deepening of the country baseline assessment, and technical assistance for their national ESAVI information systems improvement.
2. The adequation of the open-source DHIS2 Tracker system, intended for Category A countries as a national ESAVI surveillance system.
3. The adoption of FHIR for the automated reporting of ESAVI cases from each country's information system to PAHO.

Within each country, an advocacy process was carried out, promoting good practices, international standards, inclusion of core variables for the ESAVI surveillance, processes reengineering, among others, which enacted joint efforts with national technical teams.

Category A countries needed a public health information system for ESAVI surveillance. PAHO analyzed different options and decided to promote an open-source system called DHIS2 (District Health Information System 2). DHIS2 is a public global good supported by the University of Oslo (UiO), being a software platform for

strengthening integrated health information management [5]. UiO developed a specific Metadata Package for AEFI surveillance within its Tracker app, as requested by WHO. PAHO requested further changes to DHIS2, including the adoption of semantic standards, the inclusion of extra core variables following its regional manual, among others. There have been countries that have advanced in the use of DHIS2 as a national ESAVI system, such as Ecuador, which will also adopt it for its nominal immunization registry. Other countries in the region such as Paraguay and Bolivia are taking steps in the same direction.

On the other hand, Category B and C countries needed an integration effort to connect their existing systems. This could be achieved internally through a custom extract, transform and load (ETL) process, and using an interoperability approach to send information to the regional database. In this context, we proposed to adopt FHIR, the newest open standard for health information exchange created by HL7 International. Several American countries such as the United States [6], Canada, Argentina [7], Brazil [8], Chile, and Colombia are already using FHIR for public health data exchange. The WHO itself promotes FHIR as a standard for structuring SMART guidelines, as digital certificates for COVID-19 vaccination, among other use cases [9].

The FHIR adoption project for ESAVI Surveillance was based on 4 pillars: Team building; Training; Creation of the ESAVI FHIR implementation guide; and Centralized installation of the FHIR server and client/country support.

The multidisciplinary team was built including people from different PAHO areas: Vaccine Safety, Immunization, Pharmacovigilance, Evidence and Intelligence for Action in Health and Information Technology Services. It was complemented by a team of HL7 FHIR experts from Argentina and Chile, and DHIS2 experts from the UiO. Internal courses were taken to level up the FHIR knowledge.

In the training axis, HL7 FHIR courses were contracted in Spanish, Portuguese, and English for technical representatives from member states' MoH. More than 100 people participated online in the FHIR Fundamentals courses taught by HL7 to date.

Creating a FHIR implementation guide (IG) for ESAVI notification involved an effort to standardize the variables included in the ESAVI Regional Manual, to generate computable specifications. In this way, the FHIR messages sent by the countries to PAHO would have a defined structure, facilitating their automated reporting. In turn, it was proposed to perform a mapping with the E2B XML standard (recommended for the exchange of security reports) to allow bidirectional conversion, and therefore communication with national and global systems that use that standard (Vigiflow, Vigibase, etc). The IG code system proposal was also challenging as many countries have heterogeneous ways of representing core variables (as medications, vaccines, medical background, or adverse events), from plain text to different coding standards as SNOMED, ICD-10, ICD-11, MedDRA, WHODrug, WHO ART, among others. Our approach was to promote coding standards and help countries to adopt them but allowing plain text descriptions in the meantime. There is a need of mapping those standards for coding transformation. Additionally, licensing of selected standards is an issue.

Finally, the installation of a centralized HL7 FHIR server is being carried out to receive and manage the information reported by the countries. At this stage, a group of pilot countries will adopt the FHIR API in their own ESAVI systems with PAHO's support. In this way, the Information System of each country (client) will securely authenticate and send a standardized FHIR message to the PAHO FHIR server, where the data will be received, stored, and processed.

4. Discussion and Conclusion

According to the information systems survey carried out by PAHO in 2020, 83% of the countries in the region DO NOT have information systems mature enough for ESAVI surveillance (categories A and B). Systems with fragmented data were found in multiple national institutions, and there was a lack of semantic standards for vaccines and associated adverse events.

Even though there is a previous standard for Individual Safety Case Reports (ICSR) called E2B XML, it has not been widely adopted for Vaccine Safety reports in the region. Some restrictions could be related to poor national information systems for pharmacovigilance, without semantic standards in place. Additionally, E2B only works for ICSR, requires licensed WHODrug and MedDRA codes, it is quite complex, and has a small community of practice. On the contrary, FHIR is a flexible, simple, easy to adopt standard that works for many health information exchange projects, not only pharmacovigilance. It has a big community of practice, and it is backed by several countries and public health organizations as the CDC and the WHO. Nevertheless, the question is not to replace but to add both standards for suitable circumstances.

Among the collateral benefits of the FHIR project, the capacities acquired by PAHO and by the countries in its management will facilitate its application to any other public health information exchange project. Many of the deliverables of this project can be reused, optimizing successive efforts. Each implementation guide will have its own scope, whether for individual reporting or aggregated data. This vision is aligned with the PAHO Roadmap for the Digital Transformation of the Health Sector in the Region of the Americas [10], and the WHO SMART guidelines proposal [11].

The project using FHIR for ESAVI electronic reporting is a proof of concept (PoC) to demonstrate the impact of this standard on regional public health data management. Future research and evaluation should add evidence on this subject.

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