Hospitals use different EHRs as a result of the fact that, current post market safety studies largely depend on the submission of spontaneous case reports where underreporting is a major problem. The need for a more proactive approach is apparent, where safety data from multiple sources are actively monitored, linked and analyzed. Effective integration and utilization of electronic health records (EHR) can help to improve post-market safety activities on a proactive basis. SALUS aims to facilitate this through the following subtasks:

- Provide functional interoperability profiles and supporting open source toolsets enabling EHR systems and clinical research systems to communicate and exchange EHR data
- Implement semantic interoperability solutions enabling meaningful interpretation of the exchanged EHR data
- Implement security and privacy mechanisms and open source toolsets ensuring that clinical information is shared in an ethical and safe way
- Provide a novel exploratory analysis framework for open-ended temporal pattern discovery for safety studies on top of disparate, distributed, heterogeneous EHR systems

The need for a sustainable proactive post market safety study protocol to several healthcare centers (hospitals, primary care centers) and collect concomitant symptoms, diagnoses, allergies, medications of the qualified patients for statistical assessment and by investigating other underlying conditions that may have initiated the oedema. This can be achieved through the SALUS interoperability architecture, although the participating hospitals use different hospital information systems, EHR standards and terminology systems.

**Objectives of the Project**

Pre-approval clinical trials cannot guarantee that drugs will not have serious side effects after they are marketed. Post-approval drug safety data studies aim to address this problem; however, their effectiveness is started to be discussed especially after recent examples of drug withdrawals. This is due to the fact that, current post market safety studies largely depend on the submission of spontaneous case reports where underreporting is a major problem. The need for a more proactive approach is apparent, where safety data from multiple sources are actively monitored, linked and analyzed. Effective integration and utilization of electronic health records (EHR) can help to improve post-market safety activities on a proactive basis. SALUS aims to facilitate this through the following subtasks:

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**Project Description**

In SALUS we aim to create the necessary infrastructure to enable secondary use of EHRs in an efficient and effective way for reinforcing the post market safety studies so that patient safety can be ensured through early detection of rare adverse events.

In particular we aim to:

- Strengthen the spontaneous reporting process by automated adverse drug event (ADE) detection tools screening EHRs in a hospital so that ADE reporting burden can be weakened within a clinical institute. This will increase data accuracy as it eliminates manual screening of clinical care data for identifying ADEs.
- Enable ADE reporting by extracting the available information from the EHRs into the individual case safety reports, to avoid duplicate data entry. This will ensure delivering timely feedback to the regulatory bodies via EHR supported adverse event reporting.
- Strengthen the current signal detection processes in Spontaneous Reporting System (SRS) centers for tracing case reports to their corresponding patient records to allow absolute reporting rates to be computed, and to provide additional information on extended parts of the underlying medical history of the patient. This will combine the strengths of case reports and secondary use of EHRs.
- Enable real time screening of multiple, distributed, heterogeneous EHRs for early detection of adverse event signals. This will facilitate proactive safety monitoring as a complementary approach to reactive signal detection based on spontaneous reports.
- Enable sustainable and scalable EHR re-use architecture facilitating wide scale outcome and effectiveness research, to be able to observe selected cohorts of patients over an extended period of time screening multiple, distributed, heterogeneous EHR systems to identify long term safety issues of a product.
- Enable the execution of post-market analysis for different subpopulations selected from multiple, distributed EHRs as target cohorts. This will offer new opportunities for addressing a fundamental dilemma: the trade-off between safety and access: we will have a chance to determine that an

**Practical Example Scenario**

After a new “calcium channel blocker” is marketed, several hospitals report « leg oedema » cases as an adverse event to the regulatory body. This reporting process is very easily maintained within their EHR platform connected to the SALUS interfaces. As a result, the regulatory body initiates a post market safety study to assess the validity and importance of this adverse event. Through SALUS interfaces, regulatory body can send the study protocol to several healthcare centres (hospitals, primary care centers) and collect concomitant symptoms, diagnoses, allergies, medications of the qualified patients for statistical assessment and by investigating other underlying conditions that may have initiated the oedema. This can be achieved through the SALUS interoperability architecture, although the participating hospitals use different hospital information systems, EHR standards and terminology systems.
adverse event is restricted to a small, identifiable segment of the population, so that the drug could remain on the market and continue to benefit those who are not subject to the event.

Expected Results & Impacts & Preliminary Results

The SALUS project will foster integration of clinical care information from EHRs into clinical research systems to enable proactive post-marketing safety studies for early detection of potential safety issues. Such an environment will:

- increase data availability for the clinical research community;
- increase data accuracy as it eliminates manual process of detecting ADEs to the extent possible;
- reduce time spent on data entry for filling individual case safety reports, or filling forms to be sent to the disease or drug registries established to run observational studies by flawlessly retrieving data from EHRs;
- support wide scale longitudinal observational studies by enabling access to clinical care data stored in multiple distributed EHR systems for enabling comparative effectiveness research;
- decrease the time to detect the adverse drug events, as access to distributed EHR systems will drastically increase the scale of the safety studies;
- facilitate participation by a greater number of clinicians and healthcare institutes in safety research;
- eliminate unnecessary litigation costs due to drug withdrawals; more funds will be available to medication innovation.

Figure 2 SALUS Pilot Applications

SALUS
Scalable, Standard based Interoperability Framework for Sustainable Proactive Post Market Safety Studies

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Partners:
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- European Institute for Health Records (France)
- Stiftelsen WHO Collaborating Centre for International Drug Monitoring (Sweden)
- OFFIS E.V. (Germany)
- AGFA Healthcare N.V. (Belgium)
- Electronic Record Services B.V. (Netherlands)
- Lombardia Informatica SPA (Italy)
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