Development of a SMART-on-FHIR-enabled Semi-Automated Adverse Event Validation and Reporting Application

Shayan Hobbi, IBM
Agenda

1. Current state of adverse event (AE) reporting
2. Development of a semi-automated solution for adverse event validation and reporting
3. Challenges and Lessons Learned
   • Challenges with Provider-facing SMART connections
   • Data element needs for biologics surveillance and gaps between USCDI Profiles
   • Use of FHIR and USCDI Profiles for Validation and Reporting of Biologics-related Adverse Events
4. Next Steps
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CBER Biologics Effectiveness and SafeTy (BEST) Initiative Mission

Conduct active surveillance for post-market safety and effectiveness of biologic-products

Current Need

More robust post-market adverse event reporting

CBER Regulated Products

- Vaccines (preventative and therapeutic)
- Blood (components and derived)
- Human Tissues and Cellular Products
- Gene Therapies
- Xenotransplantation Products
Current biologic product AE reporting systems are manual, passive, and voluntary. As a result, CBER receives fewer and lower quality reports than needed for its post-market surveillance.
Adverse Event (AE) Validation and Reporting:

Current State

- **Manual Reporting**
  - Data re-entry to report
  - Lack of granularity in report evidence

- **Manual Validation**
  - Time-intensive to review
  - Potential AEs not always
  - Case definitions separate

- **Manual Detection**
  - Under-recognition of
  - Individual flagging of potential AEs

- Clinical exposure and outcome

Providers & Industry

- Manual **burdensome** process
- *Voluntary* with few incentives
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4. Next Steps
Solution demonstrates use of innovative methods to **reduce burden**, while increasing quantity and quality of AE reports.

**Semi-automated AE Validation and Reporting:**

**Improved Efficiency and Accuracy**

<table>
<thead>
<tr>
<th>Current</th>
<th>IBM BEST Pipeline</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Manual Detection</strong></td>
<td><strong>Automated Detection</strong></td>
</tr>
<tr>
<td>Under-recognition of outcomes</td>
<td>AI algorithm scores potential cases</td>
</tr>
<tr>
<td>Individual flagging of potential AEs</td>
<td>Batch detection, more focus on patient care</td>
</tr>
<tr>
<td><strong>Manual Validation</strong></td>
<td><strong>Semi-Automated Validation</strong></td>
</tr>
<tr>
<td>Time-intensive to review dispersed data</td>
<td>Evidence integration reduces burden</td>
</tr>
<tr>
<td>Potential AEs not always communicated</td>
<td>Flagged and prioritized cases sent for review</td>
</tr>
<tr>
<td>Case definitions separate</td>
<td>Case definition integrated</td>
</tr>
<tr>
<td><strong>Manual Reporting</strong></td>
<td><strong>Semi-Automated Reporting</strong></td>
</tr>
<tr>
<td>Data re-entry to report externally</td>
<td>Auto-population of granular ICSR evidence</td>
</tr>
<tr>
<td>Lack of granularity in report evidence</td>
<td>Generation of evidence-based ICSR narrative</td>
</tr>
</tbody>
</table>
Current BEST Infrastructure:

Semi-automated AE Validation and Reporting

Provider Network

Component 1: Provider EHR Data Extracts (or SMART connection to FHIR endpoint)

Quality Assurance

Component 2: HAPI FHIR Server

Component 3: FHIR-based AE Detection

Component 4: SMART-on-FHIR AE Validation & Reporting Tool

AE Report (ICSR XML)
Semi-Automated Outcome Validation

SMART-on-FHIR Chart Review Tool: Enables semi-automated clinical assessment with an intuitive UI, that can plug into SMART-on-FHIR enabled EHR endpoints

Abstraction: Allows for simplified visualization of patient EHR information

Classification: Reviewers efficiently document information related to classification, including:

- Certainty of exposure
- Assessment of causality
- Evidence for conclusions
- Certainty of adverse event
- Severity of reaction

*Simulated data
**Features:** Auto-population and generation of ICSR from FHIR to XML format (with functionality for final review and editing)

**Impact:** Increased efficiency through auto-population of ICSR

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**Reviewer confirms evidence and other information prior to submission**

**Reviewer clicks to auto populate ICSR report**

**Reviewer completes final check and then submits**

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*Simulated data*
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4. Next Steps
Challenges with Provider Facing SMART-on-FHIR Connections

1. Often documentation for EHR-hosted SMART sandboxes was far more complex for provider-facing connections, compared to the patient-facing scope.
   1. This was relatively minor, and was resolved by contacting teams hosting SMART sandboxes

2. Time for providers to review and approve SMART app connection to production FHIR endpoint
   1. This is a significant investment and can take up to 7-9 months, depending on the provider.
   2. Often, test data in the test environments are not reflective of production data (especially for transfusion patients)
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Detection Features

- Flu_Vaccine_Administered = True
- Viral_rule-out = True
- Relevant_Diagnosis = True
- GBS_Diagnosis = True
- Post_exposure_diagnosis = True

EHR Data Elements of Interest
(Vaccine AE Example)

**Exposure**

**Labs**
- Hemoglobin – 7.2 grams/L
- Hematocrit – 25%
- WBC count – 7,200/mcL
- Viral Panel Test - Negative

**Diagnoses**
- Guillain-Barre Syndrome, Other neurological symptoms

**Notes**
- Physician Progress Note: *6-weeks following influenza vaccination*, patient exhibited symptoms for Guillain-Barre Syndrome. Other viral tests *rule-out other viral causes of GBS*
  - Blood pressure increase – 111/72 to 123/95 mmHg
  - HR increase from 92 to 119 bpm
  - Viral Serology Test– Negative

*Simulated data*
## EHR Data Elements of Interest (Transfusion AE Example)

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Labs</th>
<th>Diagnoses</th>
<th>Notes</th>
</tr>
</thead>
</table>
| **2017-02-17 11:20** – Packed RBC transfused (ISBT Product: E4306) | • Hemoglobin – 7.2 grams/L  
• Hematocrit – 25%  
• WBC count – 7,200/mcL  
• Brain natriuretic peptide - 110 pg/mL  
• AST – 150 IU/L, ALT – 71 IU/L | • Anemia, Abnormal liver function tests, Dysmenorrhea | Physician Progress Note: 3 hours following the second transfusion, developed **dyspnea**, drop in SPO2, mild edema, increase in blood pressure and tachycardia. CXR showed bilateral **pulmonary edema**. Patient was then treated with **Lasix** and O2 and vital signs returned to baseline within two hours. **Vital Signs:**  
• Blood pressure increase – 111/72 to 123/95 mmHg  
• HR increase from 92 to 119 bpm  
• SpO2 decrease – 97% to 88% |

**Detection Features**

- Transfusion_Administered = True
- BNP>100 = True
- Relevant_Diagnosis = True
- Dyspnea = True
- Pulmonary_Edema = True
- New_Diuretic = True
- SpO2<90 = True

*Simulated data*
## EHR Data Elements of Interest for Biologics AE Reporting

<table>
<thead>
<tr>
<th>Data Element</th>
<th>Direct EHR Extract</th>
<th>HL7 CDA</th>
<th>FHIR R4 (USCDI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unstructured Data</td>
<td>Available in native format</td>
<td>Available in XML Format</td>
<td>Linked via DocumentReference Resource</td>
</tr>
<tr>
<td>Refresh</td>
<td>Live, but queries return static extracts.</td>
<td></td>
<td>Live, but queries return static extracts. Subscription/push model is live.</td>
</tr>
<tr>
<td>Vaccine Exposures</td>
<td>Identified by RxNORM, CPT, HCPCS and NDCs.</td>
<td>Identified with CVX. NDCs not included.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lot number and manufacturer available if recorded with administration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood Component Exposure</td>
<td>ISBT-128 + HCPCS/CPTs available if recorded.</td>
<td>ISBT-128 codes and other transfusion elements NOT included</td>
<td></td>
</tr>
<tr>
<td>Outcome Diagnoses</td>
<td>Diagnoses and Problems recorded with sufficient granularity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other fields needed for ICSR Reports</td>
<td>Generally available</td>
<td>Following general availability</td>
<td>Minor additions needed for patient and organization resource</td>
</tr>
</tbody>
</table>

- **Vaccine Exposures**: Identified by RxNORM, CPT, HCPCS and NDCs. Lot number and manufacturer available if recorded with administration.

- **Blood Component Exposure**: ISBT-128 + HCPCS/CPTs available if recorded.

- **Outcome Diagnoses**: Diagnoses and Problems recorded with sufficient granularity.
ICSR Generation Overview

Map ICSR data elements to FHIR

FAERS (R2) + VAERS (R3) ICSR Specs (ICH)

FHIR Data Elements (R4 and DSTU2)

Flag elements of interest in the Validation and Reporting Application

VR App Generates ICSR

FAERS ICSR Message (XML)

VAERS ICSR Message (XML)

Clinician-originated data during case validation + EHR-originated patient data

Note: Any images, videos, or other representations of an individual’s health record shown on slides is synthetic and does not contain actual patient data.
Identify Data Elements Needed for Outcomes Detection

Transfusion-related Outcomes: All 12 CDC NHSN AE Case Definitions

Vaccine-related Outcomes: Brighton Collaboration Vaccine AE Case Definitions

Extract Case Definition Components (Allergic Reaction example)
- generalized urticaria (hives) or generalized erythema
- angioedema, localized or generalized
- generalized pruritus with skin rash
- measured hypotension

Identify relevant terms in structured and unstructured clinical terminologies

FHIR Profiles and Valuesets

Outcome/Exposure Detection Algorithm

SNOMED Terms
ICD Diagnoses
LOINC Lab Results
UMLS Concepts

Note: Any images, videos, or other representations of an individual’s health record shown on slides is synthetic and does not contain actual patient data.
Identify Data Elements Needed for Exposure Detection

- Transfusion-related Exposure Logic
- Vaccine-related Exposure Logic

FHIR Profiles and Valuesets

Outcome/Exposure Detection Algorithm

- ICD10 Procedures
- CPT/HCSCPS Procedures
- NDC Codes (Vaccines)
- ISBT-128 Codes (Transfusions)

Identify relevant terms in structured and unstructured clinical terminologies

Note: Any images, videos, or other representations of an individual’s health record shown on slides is synthetic and does not contain actual patient data.
Compile Data Needs into Implementation Guide

Transfusion-related Exposures

Vaccine-related Exposures

Transfusion-related Outcomes: All 12 CDC NHSN AE Case Definition Components

Vaccine-related Outcomes: Select Brighton Collaboration Vaccine AE Case Definition Components

FAERS (R2 + FAERS Blood DTD) ICSR Specs (ICH)

VAERS (R3) ICSR Specs (ICH)

Outcomes/Exposure Detection and Validation

ICSR AE Reporting

FHIR Data Elements and Valuesets

FHIR Profiles and Implementation Guide

Note: Any images, videos, or other representations of an individual's health record shown on slides is synthetic and does not contain actual patient data.
1. Patient, Practitioner, Organization, Observation, Procedure, Condition, Immunization

2. New Resources for USCDI: MedicationAdministration, AdverseEvent, BiologicallyDerivedProduct

3. Main data element gaps between current surveillance needs and USCDI:
   - **MustSupport: ISBT-128 codes** for blood and tissues
     - Added BiologicallyDerivedProduct to capture transfusion exposure details, and link to Procedure resource
   - **MustSupport: NDC codes** for Vaccines and other blood products, allergenics, and advanced therapies to sufficiently identify granular details for products
   - **Other fields needed for ICSR reporting**
     - Added AdverseEvent resource so EHRs can store AE reports directly in EHR
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4. Next Steps
Goal is to add in data elements to future versions of the USCDI for safety and effectiveness surveillance of biologic products, in addition to coordination of care for patients.

- FDA CBER and IBM have created a FHIR Implementation Guide for capturing the data elements needed for biologics surveillance (including ISBT codes for blood, and NDC codes for Vaccines)

- IG to be circulated in appropriate HL7 workgroup(s) for review

Source: https://www.healthit.gov/sites/default/files/draft-uscdi.pdf

US Core FHIR Implementation Guides: https://www.hl7.org/fhir/us/core/
Questions?