Exploring the Application of Automation and Cognitive Technologies for Vaccine Pharmacovigilance

Dr. Vivek Ahuja
Vice President, Global Pharmacovigilance

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AGENDA

1. INNOVATIONS IN VACCINES
2. CURRENT GAPS IN VACCINE SAFETY
3. TECHNOLOGIES IN VACCINE SAFETY MANAGEMENT
4. AUTOMATION IN VACCINE PHARMACOVIGILANCE
5. EXPECTED BUSINESS OUTCOME OF AUTOMATION
Innovations in Vaccines
Current Gaps in Vaccine Safety
Vaccine Pharmacovigilance

Definition:

The science and activities relating to the detection, assessment, understanding and communication of AEFI and other vaccine- or immunization-related issues, and to the prevention of untoward effects of the vaccine or immunization.
Vaccine Safety?

Canadian Journal of Infectious Diseases and Medical Microbiology

Rotavirus Vaccine Withdrawal in the United States: The Role of Postmarketing Surveillance

Science

Why a pandemic flu shot caused narcolepsy
Vaccine Safety as Important as Efficacy

- Vaccines are required to have a higher-level of safety and lower levels of risk as compared with therapeutic medicinal products.
- Most of the vaccination programs are aimed at children or infants, whose tolerance of risk is very low.
- Adverse effects that follow immunization are promptly noticeable as compared to the target disease.
- Safety issues arising from vaccination require rapid action.
- Therefore, the systems for handling AEFI data should be robust, flexible, reliable, and accurate.
Challenges with Vaccine Safety

1. Vaccine safety signals may include complex syndromes
2. Complex quality concerns, and new technical issues due to rapid scientific advances
3. Current routine PV systems insufficient
4. Safety of multivalent and multi-dose schedules
5. Safety concerns only in sub-groups
6. Cost, time, resources
**Challenges with Vaccine Safety - Action Plan**

1. **Rapid Response**
   - Any safety issues with vaccines should be dealt with rapidly; delays can result in loss of public confidence in vaccine.

2. **Replacing Manual Methods**
   - Manual methods for collection and assessment of individual cases may cause unnecessary delays and can be error prone.

3. **Effective PV Systems**
   - AEFI reporting system should be highly responsive, effective and should allow quality improvements.

4. **Automation Technologies**
   - Advanced automated systems should be incorporated for collection, processing, transmission of safety reports.
Software Solutions for Vaccine Safety Management
Vaccine Pharmacovigilance Paradigm

**STEP 1**
Collection and processing of spontaneous reports of AEFI

**STEP 2**
Detecting any possible relation between an event and vaccine

**STEP 3**
Development of a causality hypothesis

**STEP 4**
Confirming or refuting the hypothesis

- **Spontaneous Reports**
- **Signal Detection**
- **Causality Hypothesis**
- **Testing Causality Hypothesis**
Spontaneous Reports- Case Processing is Complex!

**RECEIPT AND INTAKE OF INFORMATION**

**STRUCTURED**
- LITERATURE
  - PDF
  - XLS
  - EMAIL
- REGULATORY AUTHORITY
  - PDF
  - XLS
  - EMAIL

**UNSTRUCTURED**
- PHYSICIAN / PATIENT
  - PDF
  - XLS
  - EMAIL
  - HANDWRITTEN
- SPONTANEOUS

**TRANSLATE TO ENGLISH**
- STANDARDIZE THE INFORMATION BY ENTERING DATA IN A SAFETY DATABASE

**VALID**
- INITIAL AE (S)
- FOLLOW UP AE (S)
- DATA ENTRY IN SAFETY DATABASE

**INVALID**
- DETERMINE SUSPECT PRODUCTS
- DETERMINE SERIOUSNESS
- DETERMINE CAUSALITY
- DETERMINE LABELEDNESS
- DETERMINE PRODUCT CODING

**SEND ACKNOWLEDGMENT WITH CASE ID TO SOURCE**
- PQC, MI
- PQC & MI MANAGEMENT GROUP

**ACKNOWLEDGMENT OF RECEIPT**
- QC ENHANCEMENT
- TO FLAG MEDICAL CONCEPTS

**DISTRIBUTE APPROPRIATE DOCUMENTS FOR SUBMISSION**
- ALSO IN LOCAL LANGUAGE AS REQUIRED
- MARK AS NOT TO BE SUBMITTED & ARCHIVE

**SUBMISSION REQUIRED**
- QC ENHANCEMENT TO FLAG MEDICAL CONCEPTS
- DISTRIBUTE REPORTS
- DOCUMENT SUBMISSION OR DECISIONS
- END OF STUDY UNBLINDING USING IVRS

**UNBLINDING USING IVRS**
- CONSIDERING MAH STATUS
- ACTIVE PV AGREEMENT
- STUDY CONFIGURATION

**MONITOR SUBMISSIONS**
- SUCCESSFUL
- REJECTED
- FIX & REDISTRIBUTE

**BUILD NARRATIVES**
- QC ENHANCEMENT TO FLAG MEDICAL CONCEPTS
- DISTRIBUTE APPROPRIATE DOCUMENTS FOR SUBMISSION
- CREATE F/U LETTERS
- TRACK & RECREATE FOLLOW UPS AS REQUIRED
Where is Automation Likely to Impact the Most in Pharmacovigilance?

<table>
<thead>
<tr>
<th>Categories of work that have higher automation potential</th>
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<tbody>
<tr>
<td>Time spent in all US occupations</td>
</tr>
<tr>
<td>Manage¹ Expertise² Interface³ Unpredictable physical⁴</td>
</tr>
<tr>
<td>9</td>
</tr>
<tr>
<td>18</td>
</tr>
<tr>
<td>20</td>
</tr>
<tr>
<td>26</td>
</tr>
<tr>
<td>Collect data</td>
</tr>
<tr>
<td>64</td>
</tr>
<tr>
<td>69</td>
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<tr>
<td>81</td>
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</tbody>
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- Most susceptible activities
- 51% of total working hours
- $2.7 trillion in wages

- Manage & Develop People
- Applying expertise to decision making, planning & creative tasks
- Interfacing with Stakeholders
- Performing physical activities & operating machinery in unpredictable environments
- **Performing physical activities & operating machinery in predictable environments** Source: US Bureau of Labor Statistics, Mckinsey Global Institute Analysis 2017
Automation Technologies

01 NLP, NLG
Analysis and synthesis of natural language and speech.

02 Chatbots
A computer program designed to simulate conversation with human users.

03 Knowledge generating tools
Cognitive tools that work in a structured framework: Data>>Information>>Knowledge.

04 Machine learning & data mining
Provides systems the ability to automatically learn and improve from experience without being explicitly programmed.

05 Image processing & visualization
Extracts information from an image and performs analysis.

06 Information retrieval, Classification and filtering
The storage and representation of knowledge and the retrieval of information relevant for a specific user problem.

07 Pattern recognition, Decision support systems
These systems:
- observe the environment,
- learn to distinguish patterns of interest
- make sound and reasonable decisions.
ArisGlobal is the leader in bringing to market IT-based solutions for the Life Science Industry, with a focus on the following industry specific domains:

- Clinical Development
- Regulatory Affairs
- Safety/Pharmacovigilance
- Medical Affairs

Locations in the U.S., Europe, and Asia

- 200+ Current Clients, Including 30 of the Top 50
- 8 Health Authorities using ArisGlobal Solutions
- More than 1,000 Employees Worldwide
- More than 30 Years of Experience
- Visit [www.arisglobal.com](http://www.arisglobal.com) to learn more
- Regulated Cloud 110+ Customers
Why ArisGlobal

Innovative
• First to market with Fully E2B R3 Compliant & xEVDMP/IDMP Ready solution
• First PV solution to have cognitive capabilities on the market
• Achieved 20% reduction in case processing time from day one
• First to introduce cloud to PV market

Proven
• 25+ years of Experience
• 200+ Current Clients
• 100+ customers on ArisGlobal Cloud
  - Largest PV solution on GxP complaint cloud
• 30 Customers on ISP-based, multi-tenant platform

Trusted
• 8 Health Authorities using ArisGlobal Solutions
• 30 out of 50 large pharma
• Ongoing commitment by ArisGlobal to Life Sciences industry
• Proven track record in all areas of regulatory compliance including PV
LifeSphere Safety Multivigilance™

Integrated and streamlined end-to-end process for capturing, processing, reporting and benefit-risk analysis of adverse event cases.

Intake, Triage & Receipt
- E2B
- Email
- Fax
- Documents
- LifeSphere Mobile MA™
- LifeSphere Call Center™
- 3rd-party data source (ex: clinical)
- Remote Data Capture

Case Processing
- LifeSphere Safety Database™ (including Japanese version)
- Data Entry
- Document Quality
- Safety Review
- Quality Review
- Medical Review
- Submissions Decision
- LifeSphere Central Coding™
- Medical Dictionary Coding

Electronic Submissions
- agXchange ESM™ (Electronic Safety Submissions)
- LifeSphere Submissions Tracking™
- LifeSphere Signal and Risk Management™
- Signal Detection and Benefit-Risk Management
- LifeSphere SUSAR Reporting™
- LifeSphere Reporting and Analytics™
- Investigator Reporting
- Safety Data Warehouse

ArisGlobal
ArisGlobal’s Automation Approach

01

Consortium

We have built a consortium with our 5 largest customers, together to achieve touchless non-serious processing of cases this year.

02

Regulators

Regulatory authorities are reviewing our technology/algorithms for seriousness/triage as we work with 8 agencies across the world.
Potential Impact of Automation on Case Processing

- **Current State**
- **Year 1 (15%)**
- **Year 2 (30%)**
- **Year 3 (50%)**

- **Increase in Cognitive Capability**
- **Increase in Efficiency, Quality & Compliance**
- **Decrease in FTEs & Cost**
Automation in Vaccine Pharmacovigilance
Areas in which automation is being applied in vaccine pharmacovigilance:

**Case classification**
To classify cases as AEFI's or not.

**Medical Review**
Review of case attributes.

**Identification of new AEFIs**
To identify previously unknown adverse events related to vaccination.

**Social media surveillance**
To capture AEs not reported to spontaneous reporting systems.

**Medical literature monitoring**
To monitor new cases reported in medical literature.
Automation in AEFI Case Classification

Automation of case classification of reports can increase reliability of the safety signals detected.

Automatic Brighton Classification (ABC) Tool:
- It is an online tool for case definition
- Has a rule-based algorithm
- Allows the confirmation of AEFIs based on user input on signs and symptoms of a case
- Assessment is based on Brighton Collaboration (BC) defined criteria for a specific AEFI

01 User has to confirm if a case is that of Guillain-Barré syndrome (GBS)
02 The user is asked to respond to a set of questions
03 User provides ‘Yes’ ‘No’ or ‘Don’t Know’ based on signs and symptoms
04 ABC tool processes user input
05 Classifies a report as not a case of GBS when the criteria are not met
06 Classifies a report as Level-1, 2 or 3 diagnostic level of GBS when BC criteria met
Application of Information Retrieval (IR) systems result in case classification with higher sensitivity and specificity.
Key functions of an automated text mining system are:

- Can **recognize** essential text in the narrative
- Can **differentiate** a reported symptom and an actual diagnosis in the narrative
- Can **extract** key features of a case
- Can perform **organization** of key medical concepts in a narrative
Automation in Medical Review

The text mining system components and functions:

01 Pre-processor
  Prepares the text for the main processing

02 VAERS dictionary
  Includes 55,000 entries (each entry includes a term and its tag that corresponds to a semantic type)

03 Semantic tagger
  Tags the tokens based on the dictionary entries

04 Grammar rules
  Define the relationships between tags

05 Rule-based parser
  Parses the text by executing the grammar rules

06 Features extractor
  Extracts the predefined features
Automated Definition of New Adverse Events

Automation with literature-based reasoning:

- The technology builds new case definitions based on cross-case patterns in literature.
- The case definitions are built using text mining, information retrieval systems and knowledge discovery systems from biomedical literature.
- The findings from biomedical literature are translated into algorithms.
- The algorithms automatically identify the cases of a specific condition.
- The algorithms can be updated continuously based on new findings.
Automated Definition of New Adverse Events

Workflow for literature-based new AEFI case definitions:

- Search through PubMed for a specific AEFI (e.g., anaphylaxis)
- Abstracts containing the related terms filtered
- Processing and extracting the relevant terms
- Build relationship trees linked to medical dictionaries

Create a corpus of all related terms

Text mining, information retrieval, knowledge discovery systems

Generate case definitions

The algorithms can auto-identify new cases meeting the identified case definitions real-time with minimal human intervention.
Advanced cognitive tools can be applied to auto-detect vaccine names and reaction terms from social media posts.

Machine learning algorithms can be applied for performing complex statistical analyses.

Hidden AE reporting patterns can be detected.

PV data from various sources can be combined.

Results in potentially neutralizing biases from different sources such as spontaneous reports, literature, social media, PASS.
Medical Literature Monitoring & Automation

- Robotic automation
- NLP & data mining
- Machine learning
- Information retrieval systems
- Classification & filtering systems

Automated PV Tools

- Real-time comprehensive literature search
- Auto-detection of relevant articles
- Auto-extraction of info for case creation
- Improve precision of database search
- Audit trail of all searches and articles scanned

Automation of Literature Monitoring
Expected Business Outcome of Automation
Automation - Productivity Gains

- Automation in case processing is expected to have significant productivity gains.
- Up to 30% increase in productivity can be achieved in tasks such as narrative redaction.
- An estimate of the gains in productivity that can be achieved through automation in case processing is presented here.
Automation-Impact on Quality

Quality Parameters
- Accuracy
- Completeness
- Conformity
- Consistency
- Current
- Duplication
- Integrity
- Precision
- Relevance
- Understandability

Automation
Quality
Automation - PV Resource Redistribution

Case processing staff

PV experts for data analysis, signal detection, risk management

40% budget

Medium-high skill resource

Estimated X% budget

Pharmacovigilance staff distribution

Case processing staff

PV experts for data analysis, signal detection, risk management

Medium-high skill resource
Automation leads to disruptive growth in performance
**Total Cost of Ownership**
- SaaS solution eliminates costly internal infrastructure and support costs
- Annual upgrades and quarterly releases/updates included
- Standard ISP configuration reduces setup & implementation fees and facilitates seamless upgrades
- End-to-end product suite eliminates costs associated with multiple vendor offerings

**Productivity**
- Embedded automation and cognitive computing for higher productivity
- Seamless integration eliminates redundancy between systems
- Embedded workflow and superior easy of use drives productivity

**Compliance**
- Common technology stack for efficient, scalable and seamless data integration across ArisGlobal Life Sciences suite of products and other systems
- Facilitates compliance with data privacy and other industry/regulatory obligations
- Multi-tenant cloud architecture continuously delivers rapid innovation and ensures seamless updates

**Quality**
- Established QMS, leveraging over 30 years of experience with building regulatory compliant solutions for life sciences
- SOC 2 compliant
- ISO 27001 certified development
Benefits of LifeSphere Safety™

01 Total cost of ownership
02 Productivity
03 Improved decision making
04 Compliance
Thank You
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