



Automation in pharmacovigilance: artificial intelligence and machine learning for patient safety

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Abstract

Automation promises to be a game- change for pharmacovigilance decreasing the cost of case reporting and improving data quality to truly add value, including signal detection in drug safety. Pharmacovigilance analytic and benefit – risk assessment. Technology advances are playing a major role in pharmaceutical PV strategy updates. For example more companies are looking towards cloud- based solutions, mobile applications, robotic automation, artificial intelligence and big data analytics as a vital part of clinical safety and regulatory operations in the pharmaceutical industry. Applying innovative technology automation tools and processes to PV strategies is now a critical requirement for managing the safety of pharmaceutical products. The role of artificial intelligence and machine learning in pharmacovigilance can enhance the productivity in identification, detection, management and reporting of ADRs. The main objective of Artificial intelligence is meant to challenges to implementing intelligent automatic solutions include finding / having appropriate training data for machine learning models and the need for harmonised regulatory guidance. AI can analyse and interpret data at lightning speed, never gets tired or sick and can simply work by 24/7. Thousands of adverse effects are processed every month by ICSR in PV that includes native automation and standalone technologies like AI and ML that reduce the manual effort.

Keywords: Automation, health care system, automation in pharmacovigilance, machine learning, artificial intelligence, NLP.

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Introduction

Pharmacovigilance: The etymological roots for the word “pharmacovigilance” are: Pharmakon (Greek) = medicinal substance, and Vigilance (Latin) = to keep watch [1].

As per WHO, Pharmacovigilance (PV) is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug- related problem [2].

Adverse drug events are reported across the world in multiple languages and formats and in structured, unstructured and handwritten documents from affiliates, partners and distributors, mostly many companies receive more than 3 lakh ADRs per annum. Human errors can occur in manual process and cost of the complete project also goes high eventually. It is feasible to use AI-based technology to support extraction from AE source documents and evaluation of case validity [3, 4, 5]. Automation is the process of performing work or reducing work with the help of technology and thereby reducing human dependence [6]. In pharmacovigilance activity various government health authorities daily or periodically. Intelligent automation, as defined by Lewis and McCallum, including machine learning (ML) and artificial intelligence (AI), has started changing the way safety and pharmacovigilance (PV)

Automation in pharmacovigilance

professionals work to process and analyze data in support of decision making [7, 8].

The future of pharmacovigilance and impact of automation in optimizing efficiency:

As one of the fastest growing life sciences disciplines, PV strategies must be optimized for peak efficiency. A well-established principal information technology (IT) framework provides organizations with high performance and scalability, together with systems validation and information security, for effective design and distribution of automation initiatives.

There are four stages of automation they are : Many current IT systems and applications are capable of automating case processing and reporting activities, but overall process still requires significant manual effort, particularly regarding case intake and data entry. There are multiple levels of automation that can serve to make end-to-end safety processes more streamlined and strip down redundant, non-value added steps in existing processes, while increasing human labour efficiency. The first stage is basic process automation, which involves tracking and monitoring tasks and enables the collection of continuous metrics. Basic automation provides reporting and dashboard, and automates a workflow that involves multiple roles, but still requires manual entry, processing and analyzing of safety data into a database or system. Robotic process automation (RPA) is the next level, helps to reduce or eliminate these manual tasks. RPA is often combined with the subsequent level, cognitive automation, which leverages Natural language processing (NLP) to assist human decision making. The system engages in human interaction, whereas the final level, AI, requires little or no human interaction and self-learns through experience, to make predictions based on patterns observed in large volumes of data with the help of machine learning (ML).

For the better part of the past 20 years, not a great deal has changed in how pharmacovigilance professionals handle the processing of adverse drug reaction reports and extraction of health data from individual case safety reports (ISCRs). The system and processes differ slightly between companies and regulatory bodies but remain essentially the same and can be compared. The regulatory requirements differ from country to country, with local differences, but any health safety issue or report must be relayed to a health regulator in the country in which a product is being investigated, provided or sold.

Through a series of information points, a report is passed from the patient to the national competent health authority via health care professionals and drug safety (DS) professionals, who transmit, process and assess this safety information, to ensure the safety of patients and compliance

with regulations. Aggregate reports of these single case reports are generated from the data entered into the database, and analytics are conducted on these reports to discover any additional signals or warnings that a drug manufacturer or regulator should be aware of to ensure public health and safety. More than 1 million reports of drug side effects were received by the US FDA in 2015, a fivefold increase since 2004.

Two imperatives identified to elevate the pharmacovigilance organization's role are (1) capacity management, in which a pharmacovigilance executive needs to improve on timelines and productivity and address the expectations of regulatory agencies; and (2) information and analytics, in which technology needs to deliver significant value across the organization.

Assistive technologies: Automation of jobs and artificial intelligence (AI) has triggered much discussion across all the industries that are either affected or by considering developing this technology to aid in their operations. As with any topic, opinions regarding AI differ. One of the most widely discussed questions is whether AI will replace humans in their roles. A 2013 study conducted at Oxford university posited that as many as 47% of all jobs in the USA are at risk of automation or computerization.

Importance of artificial intelligence and automation in pharmacovigilance –

Implementation of AI and automation in pharmacovigilance practices can help across in signal detection, monitoring, risk management, AE intake and preparation of reports.

Automated case processing and signal detection-Automation can help in case processing at a number of steps along the process. An automated system, once again using NLP (natural language process) to understand both structured and unstructured data from a number of varied sources. Checking for duplications; analysis of data to find keywords or patterns that indicate significant risks to patients or as-yet undiscovered AEs; and submitting data post-review.

Post-marketing surveillance-Post market surveillance (PMS), or monitoring drug safety once a product has reached the market, is another area that AI and automation can improve radically .largely due to the large real-world datasets that can be merged at this stage, from case reports to scientific literature and active surveillance.

Use of Information Technology in Pharmacovigilance

Tools used in automation of pharmacovigilance:

Software used in pharmacovigilance: let's take a look at some software used in pharmacovigilance for management and reporting of adverse events.

1. Oracle Argus safety :

Companies are increasingly shifting their focus to a more holistic view of product safety beginning in

clinical development and continuing through post-marketing surveillance. Oracle Argus safety is a comprehensive platform designed specifically to address the life science industry's complex pharmacovigilance requirements. Argus safety advanced database helps ensure global regulatory compliance, enables sound safety decisions and integrates safety and management functions.

2. Adverse Reaction Information System Global (ARISg):

ARISg is also one of the most used software in pharmacovigilance used by pharmaceutical companies.

It is used by more than 300 companies that maintain their critical drug safety data in ARISg worldwide. ARISg provides all the functionally required to manage adverse event reporting and adverse reaction requirements of different regulatory authorities around the world.

3. Oracle AERS:

Bio pharmaceuticals, vaccines, medical device companies and contract research organizations (CROs) are constantly challenged with meeting time-critical regulatory requirements using limited resources. They must identify and manage safety events before they become issues, and they need to maintain strict compliance with evolving regulations. To manage critical business processes, they require clear visibility into their data.

4. PVNET:

PVNET is a comprehensive pharmacovigilance solution and one of the leading software used in pharmacovigilance with adverse event reporting, adverse drug reaction (ADR) data management and regulatory reporting of ICSR (individual case safety report) that goes beyond more compliance. From early development through post marketing, PVNET helps integrating the safety information, and thus helps user to make critical decisions. PVNET is across the board drug safety successfully audited against GMP standards, 21 CFR compliance and ICH E2B.

5. RepClinical:

RepClinical is a secure web based service that helps you manage critical pharmacovigilance activities in a timely and cost effective manner. With RepClinical you can capture adverse event data, generate regulatory reports and exchange ICRSs with multiple regulatory bodies and business partners. All this in a simple intuitive and efficient way.

Rep Clinical provides clutter free screens and useful features to help generate precise E2B reports easily.

Automation in signal detection in Pharmacovigilance

The recent trends in increasing unknown and unidentified adverse events (signals) have raised the concerns to develop an automated systems to identify and monitor potential signals. The quality of the data collected leads to the decision making based upon the scientific evaluation (12).

Artificial Intelligence for ICSR processing:

Following are the broad two categories of usage AI technologies in ICSR Processing:

- a) Efficiency in decision making – in some scenarios, the quality of information available in INDIVIDUAL CASE SAFETY REPORT is poor in such cases artificial intelligence plays crucial role in devising hypothesis. Artificial intelligence potentially pathway accuracy and rapidness of the content.
- b) Ingestion of structured and unstructured content- Comprises of components for reading incoming case intake information via XML, Documentation, images including PDF and PDF text including forms-tables. Here OCR/ICR along with NLP/machine learning is used to extract ICSR information from information sources in a regulatory compliant manner.

Automation could solve much of the difficulty faced by PV professionals.

Modern work platforms are emerging on the market to enable PV teams to do away with problems in regulatory compliance and reporting – and reduce risks to patients using approved medical products.

Levels of Automation

To achieve full PV transformation, multiple stages or levels of automation are required to ensure processes are completed correctly.

Level-1

Basic Automation

Automatic tracking and monitoring of tasks and enables continuous metrics collection.

Level-2

Robotic Automation

Helps either decrease or eliminate a manual task and results in automatic entry, processing and analyzing of safety data into a safety database or system.

Level-3

Cognitive Automation and Computing

Automation leverages Natural Language Processing (NLP) to help humans make decisions (assist mode) and is often combined with RPA.

Computing involves human interaction to provide the required outcome, with humans driving final decisions.

Level-4

Artificial Intelligence (Ai)

Artificial intelligence involves very minimal or no human interaction.

Effectiveness of Automation in Pharmcovigilance

- a) Faster signal adjudication and reporting.
- b) Increased pharmcovigilance activity stability.
- c) Automated pharmcovigilance task management.
- d) Standardized pharmcovigilance process with local variations.

Some Existing Barriers in Automation Pharmcovigilance – Trust Factor

Life sciences companies like the idea of Artificial intelligence and machine learning, but they are more concerned that automation won't produce the same

Required outcomes as manual case processing.

Uncertainty: Many life sciences companies don't fully understand the capability that automated PV reporting platforms can bring to their processes, making it difficult for them to devise comprehensive specifications for their own developers, or to adequately vet vendors and platforms in the market.

Limited knowledge

The lack of knowledge of full platform capabilities may cause them to restrict their forecast and choose/design solutions that conform to pre-existing processes rather than seek scope to re-think. While this may deliver slow beneficial outputs, that will dramatically reduce the time and cost of their pharmcovigilance operations and improve the quality outcomes

Lack of industry expertise

pharmaceutical organisations may seek out technology experts rather than industry experts, only to realise that these partners have nearly adapted an existing platform for pharmacovigilance applications, but they don't have the expertise in complex rules and regulations of global PV practices.

Extent of usage in under-developed/ developing countries

Usage of contemporary technologies is the major challenge in some countries due to unavailability, unreliable, lack of proper handling knowledge of technology, not inculcating advancement usage.

Advantages of Automation in Pharmacovigilance

When pharmaceutical companies implement advanced PV platforms, they can transform their entire pharmacovigilance workflow.

- * helps in faster case intake and processing.
- * can handle effectively greater extent of incoming case volume and diverse incoming data formats.

* As reporting of ADRs remains poor, ML has been used to identify ADRs from discharge summaries [8].

* Compliance in accuracy and consistency in reporting.

* minimize time, effort, labour costs.

* Speedup the delivery of information.

*It lays a roadmap for use cases within and beyond Pharmacovigilance e.g. landscape analysis, Real World Evidence, Enterprise Knowledge Management and Quantitative Sciences.

*Artificial intelligence allows for the processing and analysis of large amounts of data and can be applied to various disease states [6].

Disadvantages of Automation in Pharmacovigilance

- Costs for investment. Implementing a process automation solution involves a considerable initial investment.
- Loss of flexibility. Modify workflows; tasks and processes may involve certain rigidity.

Conclusion and Discussion

Artificial intelligence in pharmacovigilance: use of technology on scale may enable the pharmacovigilance industry to increase operational efficiency and the consistency of data quality when processing ICSRs.

With the appropriate steps, the future of harnessing and utilizing pharmacovigilance talent is promising in an environment where doctor of science (DS) professionals are assisted by artificial intelligence (AI) in their daily work. While there is a vision for touch less case processing [9], the current state of ML will augment PV professionals by increasing their efficiency and effectiveness [10].

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