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ARTIFICIAL INTELLIGENCE AND AUTOMATION IN PHARMACOVIGILANCE

TRANSFORMATIVE TRENDS AND FUTURE OUTLOOK

Contents

Introduction

The technological transition from manual tasks in Pharmacovigilance (PV) to digital solutions has taken many directions and forms. Parallel to adopting safety databases to host safety data and adopting software to allow the migration of analogic processes to the digital environment, multiple efficiency breakthroughs have been possible using technology. For many years, automation has been in place to allow machines to handle laborious and repetitive tasks, liberating skilled employees for more critical tasks. Using the Cambridge Dictionary[i] definition of automation as the use of machines and computers to operate without human control, we can look at automation as a goal leveraged by digital transformation.

According to CIOMS Working Group XIV[ii], we can define Artificial Intelligence (AI) as systems that can perceive their environment, act autonomously to achieve certain goals, and adapt their behaviour over time. In recent years we have observed a rapid and extraordinary dissemination of generative AI in our daily lives. Its pervasiveness is raising great expectations for PV as well.

To feel the pulse of this race for the applicability of AI in the PV space, we were interested to understand how companies are deploying this technology. Therefore, we conducted an open survey, completed by 17 participants from 15 companies. We observed that AI is deployed principally by medium- and large-sized companies. The most influential criterion for PV leaders to consider using AI in PV is the annual average volume of Individual Case Safety Reports (ICSRs). However, we observe broader AI dissemination among companies with medium ICSR volumes.

Advancement of Automation in Pharmacovigilance

In PV, the escalating volume of adverse event (AE) reports and the diversification of AE sources[iii] underscore the critical need for automation. The increasing regional regulations and unique requirements for product types further compound the complexity[iv].

Automation has transitioned from being an optional enhancement, limited to a few use cases such as rule-based ICSR submission to regulatory authorities, to an essential component of effective PV systems. These developments illustrate the natural evolution of PV, driving the need for a simultaneous evolution of technologies designed to meet this field's growing demands. The recent widespread visibility of generative AI and consequent raise of expectations on this technology, has extensively motivated the industry players to explore solutions using AI.

Blend of automation and complementing technologies

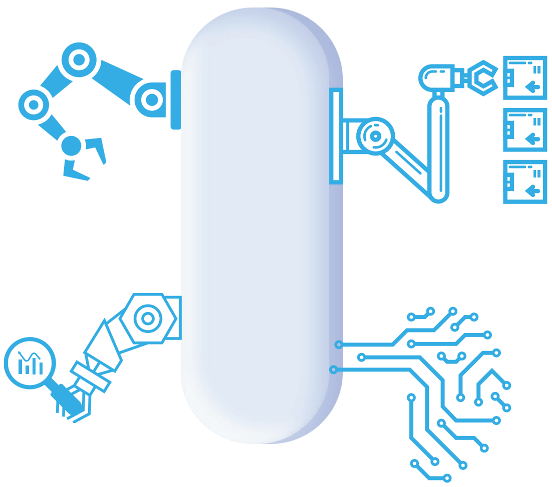
Fully optimized PV process deploying automating technologies where fit for purpose, leading to cost and process efficiency

Rule-Based Automation

PV process with most manual and repetitive tasks automated

Robotic Process Automation (RPA)

PV process with most manual and repetitive tasks automated, including system interfaces



Complementing Technologies, such as Optical Character Recognition (OCR)

PV process with innovative capabilities in automation

Artificial Intelligence

PV process incorporating AI models for process automation and provide a certain level of autonomy. AI models may evolve and improve over time.

Figure 1. Versatility of Automation in PV.

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At the core of automation within PV is rule-based automation[v]. This process relies on predefined instructions and logical conditional statements to operate. When specific conditions are met, actions are initiated automatically, negating the need for direct human intervention. A prime example is the implementation of auto-narratives for ICSRs. The system can automatically generate narratives by employing templates and rules for auto-populating safety case elements. This advancement expedites the case handling process, reduces errors, and reallocates human resources toward tasks requiring more critical judgment. The significance of this automation becomes even more pronounced as the volume of cases managed by a company increases, underscoring the impact on the PV department. However, because templates are used, auto-narratives may struggle with missing or extra data elements, resulting in poorly constructed text.

While rule-based automation serves as a robust foundation, the increasing complexity of PV processes and the diversity of software solutions have necessitated more sophisticated automation solutions, such as Robotic Process Automation (RPA). RPA mimics human tasks, enabling the automation of end-to-end processes and the integration of multiple systems [vi]. Although RPA builds on the principles of rule-based automation, its capability to accommodate complicated processes through a user-friendly development environment marks a significant advancement.

In PV, RPA can be utilized to automate the downloading of cases from a third-party website and having bots to populate the information into the safety database, streamlining the flow of safety information, reducing manual effort, and minimizing errors. However, RPA needs to be meticulously programmed for specific tasks and must ensure it is updated to handle changes in the source systems or processes. Thus, while RPA offers substantial advantages in automating repetitive tasks and enhancing productivity, it also demands careful planning, programming, and possibly substantial ongoing maintenance.

Integrating RPA with technologies such as Optical Character Recognition (OCR) enhances its ability to process and analyse unstructured data sources, a prevalent challenge in PV. As an example, OCR can be deployed in PV to automatically extract data from scanned documents and, together with RPA input handwritten or printed information from medical records into the PV database, improving data entry accuracy and efficiency. However, the versatility of RPA extends beyond pairing with OCR, allowing for potential coupling with various technological tools to meet the bespoke needs of PV operations.

The examples above show that rule-based automation and RPA are currently well established and broadly accepted technologies in PV, that can be supported by a large variety of vendors and tools. Current areas of exploration in PV automation include the deployment of AI. As AI begins to play a more prominent role in the PV space, new challenges are surfacing, such as ensuring data privacy, managing data ownership, validating AI models, and ensuring the predictability and reliability of AI outputs[vii,viii].

How can Artificial Intelligence be deployed in PV?

AI is driving innovation in many fields. As the European Union advances with the AI Act[ix], there is growing anticipation about the recommendations for incorporating AI technologies into PV practices to align with regulatory demands and bolster patient safety.

AI technology involves creating computer programs and algorithms that can perform tasks usually requiring human intelligence, such as making decisions, recognizing patterns, processing language, and learning from data without the need for reprogramming[x]. In PV, the potential of AI to improve how adverse events are detected, recorded, and analysed, is enormous[xi]. Therefore, AI technology is becoming an integral part of the PV toolbox.

One key AI technology is Natural Language Processing (NLP), which can decode and analyse large amounts of text (unstructured) data, such as electronic health records, patient narratives, and scientific articles, to identify and find important information about adverse events[xii,xiii]. This can speed up the detection of safety signals[xiv] and provide a more detailed understanding of safety of products during clinical trials and the post-marketing phase. Importantly, NLP also has the potential to translate case reports for a faster and more efficient workflow. Additionally, by leveraging NLP, AI could review complex documents, such as Pharmacovigilance Agreements (PVA) or Pharmacovigilance System Master Files (PSMF), bringing the most pertinent information to the reviewer in a more focused manner.

To enhance patient safety surveillance, a remarkable AI application is AI-powered data mining. AI can revolutionize data mining by introducing advanced techniques that greatly improve the extraction of meaningful insights from vast amounts of data[xv]. Key strengths of AI in this area include efficiently handling large datasets (scalability), detecting anomalies (data outliers), customizing data mining processes to individual needs, and improving decision-making with more accurate and comprehensive insights.

Another notable subset of AI is generative AI, which can create new content by learning patterns from existing data[xvi]. It uses models to generate realistic and original outputs, such as text, images, or synthetic data. One potential use case is the creation of synthetic datasets that maintain the statistical properties of real patient data without exposing patients to risk. This capability could be applied to enhancing predictive models and simulate how different demographics might react to a medication. Another application is the production of initial drafts of aggregate reports as a basis for the specialists to resume the document preparation. For example, generative AI could read through safety databases, electronic document management systems, and data warehouses to create summaries for different sections of the PSMF.

It has to be noted that AI amplifies rather than replaces human expertise. It is a tool in the toolbox of technologies or processes available to PV professionals. Armed with AI capabilities, PV professionals can now interrogate and utilize their data resources to uncover richer insights than previously possible. By leveraging the power of AI alongside other technologies, Pharmacovigilance could transcend traditional limitations through a data-driven shift from a reactive to a proactive stance, drastically reshaping the landscape of patient safety.

It is crucial, however, to recognize that AI does not come without risks. The technology comes with inherent challenges such as data protection, data ownership, and bias. There must be a fine balance between human critical thinking and AI to ensure the accuracy of PV outcomes and prioritization of patient safety. While regulations need to create a framework to untangle accountabilities among different stakeholders, such as the pharmaceutical companies and system providers.

Industry survey on the current landscape of Artificial Intelligence in PV

In previous sections, we have explored the main capabilities of automation and AI, as well as examples of their implementation in PV. We will now share the insights gathered from our industry survey.

Survey demographics

17 Respondents from 15 Pharmaceutical companies

NUMBER OF EMPLOYEES	
Large sized more than 25.000	5
Medium sized 5.001 to 25.000	6
Small sized less than 5.000	4

ANNUAL AVERAGE ICSR VOLUME	
High volume more than 100.000	7
Medium volume 10.001 to 100.000	6
Low volume less than 10.000	2

Among the companies that participated in the survey, all medium- to large-sized companies are currently exploring opportunities to deploy AI in PV, with about two-thirds already using AI. Larger companies, as expected, report prioritizing AI more when allocating their PV budget compared to smaller companies. Only one small-sized company reported using AI.

Current landscape and AI prioritization

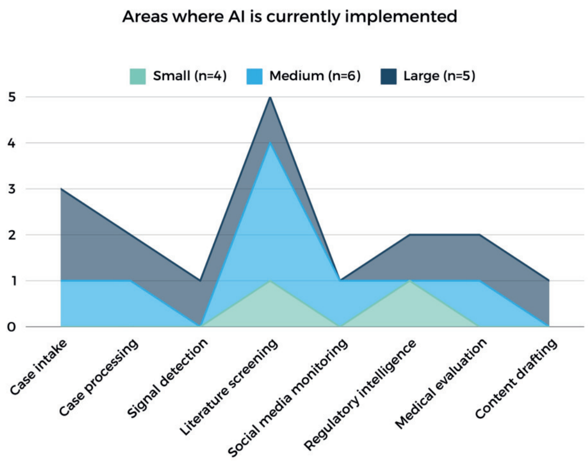

Figure 1. Areas of PV where companies are deploying AI.

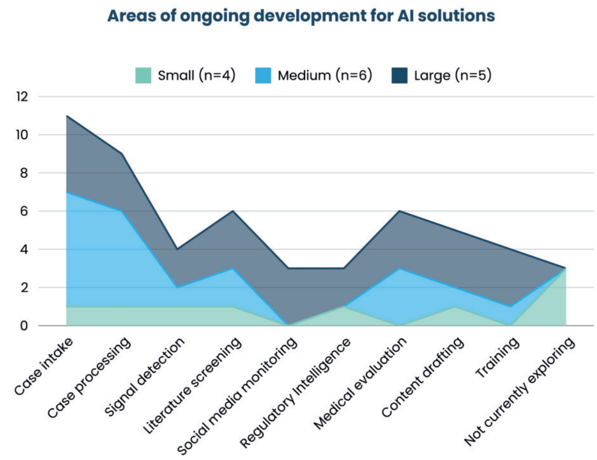

Figure 2. Areas of PV where companies are curently exploring deploying AI.

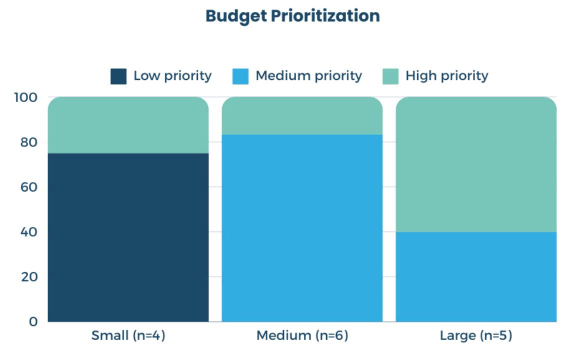

Figure 3. How much AI will be prioritized in the PV budget for the next fiscal year.

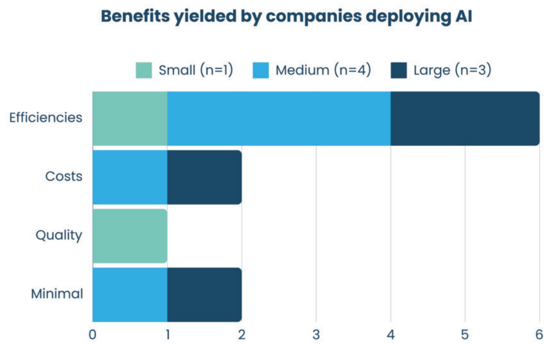

Figure 4. Benefits yielded by the companies currently deploying AI.

The predominant area where AI is being utilized in PV is literature screening, followed by case intake. The most reported benefits of AI are related to efficiency improvements, as cited by 6 out of 8 companies deploying AI in PV.

When asked what the biggest learnings are, companies that have already implemented AI refer the need for a detailed planning, change management expertise, and upfront management of team expectations. Respondents also highlight the importance of correctly understanding the technology capabilities for a robust estimate of return on investment and set realistic expectations on process improvements. To implement AI, companies require a strong internal knowledge of the process, even when relying on vendors, a strong understanding of how the technology functions and communication skills to manage the teams. Interestingly, to sustain AI, the most frequently mentioned skills are related to adapting to change and experimentation.

In terms of criteria driving AI implementation, the average annual number of ICSRs is identified by 80% of all respondents. Interestingly, companies with medium volumes are the ones spearheading AI deployment.

Influence of annual ICSR volume in AI deployment in PV

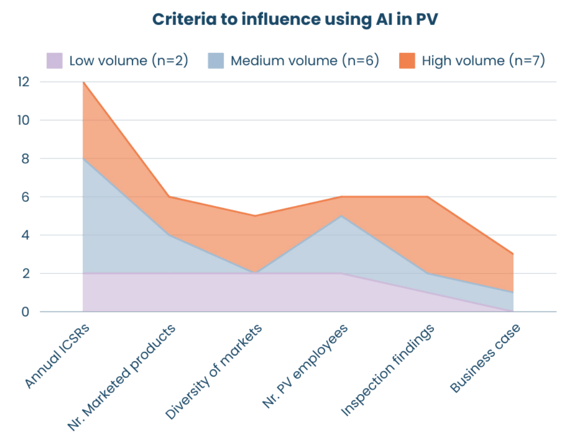

Figure 1. Criteria identified by respondents influencing the decision to use AI in PV.

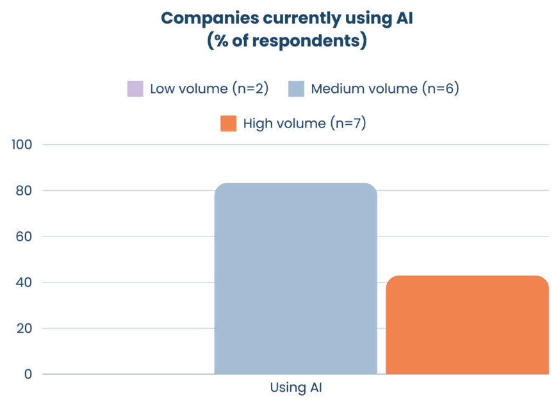

Figure 2. Percentage of companies using AI in PV based on their annual average ICSR volume.

Considering the respondents' roles, we observed that roles focusing on Safety Business are particularly concerned with the validation of AI models. Roles focusing on Safety Systems have a broader set of concerns, primarily focusing on Data Quality. Effective communication between these two groups is crucial for developing validation strategies and ensuring the data quality necessary for training AI models to achieve their perceived benefits of AI: automating manual tasks, and gains on efficiency and consistency.

Perception of risks and benefits

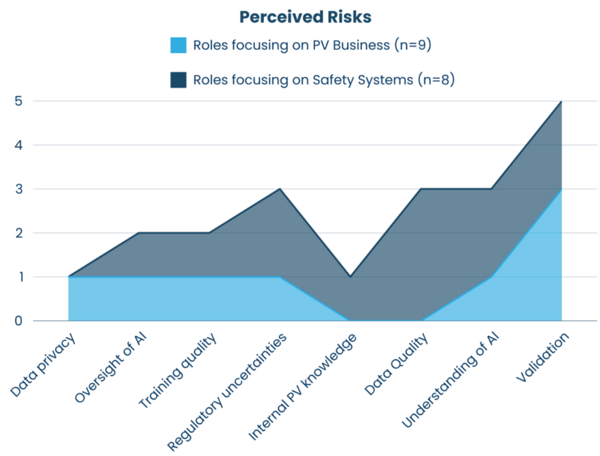

Figure 3. Risks of AI to PV anticipated by different roles.

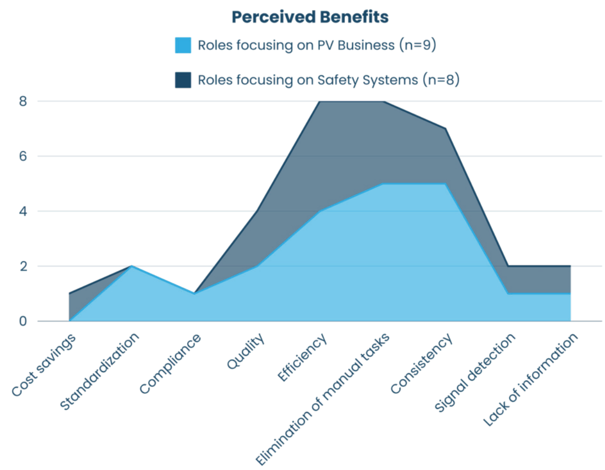

Figure 4. Benefits of AI to PV anticipated by different roles.

It is evident that there is an ongoing race to find AI applicability in PV, even though the benefits are still challenging to quantify. The strategies adopted by the companies vary depending on their size, with larger companies creating new roles to stay abreast of AI trends, and smaller companies reaching to external sources of information (e.g., industry experts and conferences).

Future outlook of AI in PV

The combination of AI and automation in PV extends beyond routine task automation, venturing into sophisticated domains like predictive analytics and deep learning. For instance, the employment of AI in literature screening, as reported in the survey, transforms the way adverse event reports are identified and processed. This combination enables the parsing of complex, unstructured data at an unprecedented speed and accuracy, potentially revealing safety insights that might escape conventional methods. Similarly, when AI is coupled with RPA for case compilation from databases such as EudraVigilance, the outcome is a highly efficient process that sifts through large volumes of incomplete or duplicative datasets, identifying new critical safety information ready for a human to assess.

This synergy is particularly potent when addressing the challenge of scalability and adaptability within PV. As new data sources emerge and reporting volumes increase, AI-driven automation can dynamically adjust to handle these changes, ensuring that safety monitoring remains robust and responsive.

The imperative for a stringent yet flexible validation framework for AI and automation technologies in PV cannot be overstated. This encompasses not just the technical accuracy of these systems but also their ability to integrate seamlessly into the existing regulatory ecosystem. Validation acts as a bridge between innovation and regulatory compliance, ensuring that advancements in AI and automation translate into tangible benefits for patient safety without compromising data integrity or oversight. Not surprisingly, validation was the major concern of the survey respondents.

The continuous evolution of AI models necessitates a validation process that is iterative, responsive, and case-specific. This involves routine checks for model drift, updates to incorporate new data sets, instructions to handle edge cases, and recalibrations in response to emerging safety signals or regulatory changes. Such a proactive approach to validation will be pivotal in maintaining the reliability and trustworthiness of AI-driven PV systems, ensuring inspection readiness. The guidelines being developed by CIOMS Working Group XIV could be the foundation for a standardized way to assess initiatives developing and/or deploying AI in PV.

Not to be undervalued, bridging the knowledge gap between AI developers and PV leaders is crucial for better technology adoption. AI developers need to understand PV requirements, while leaders must grasp AI's evolving capabilities and limitations.

Different players must be involved in this process; pharma companies, PV system vendors, and PV service providers. Improved communication and education can align expectations for smoother and consistent AI implementation. As pharma companies learn from their own explorations into AI, sharing this knowledge is crucial for the benefit of the whole PV industry.

PV continues to transform and adapt to new technologies, the current transformation is marked by the integration of AI and automation into core PV functions. This evolution requires today's PV professionals to keep developing skills in data science, AI, and regulatory science, as they need to navigate the complexities of modern drug safety monitoring. PV professionals will be key players in selecting, adapting, controlling, and evolving AI models. The development of Learning Data departments dedicated to the continuous improvement of AI algorithms and their alignment with safety goals could become a standard within the industry. This prediction is aligned with what the industry is already reporting, the need for human resources adaptable to change, highly experienced in the PV process, and even the creation of specialized roles by larger companies. Humans are here to stay, from correctly prompting AI, to making strategic operational and business decisions.

Simultaneously, regulatory bodies must evolve, offering clear guidance and frameworks to support the adoption of AI and automation in PV. Their role in establishing standards for validating and operating AI systems in drug safety monitoring will enable innovation, improve adoption by reducing the fear of failure, while safeguarding public health. The regulatory scope could potentially be expanded to include vendors that create these systems.

As the PV landscape changes, there will be a strategic shift in resource allocation and experience within pharmaceutical companies. Investments in internal resources will increasingly favour advanced signal detection capabilities, research initiatives, and risk management strategies rather than traditional data processing tasks which could be outsourced either by technology or to a data-processing vendor. This realignment highlights the potential of AI and automation to enhance operational efficiency and deepen our understanding of drug safety, ultimately leading to better patient outcomes.

Integrating AI and automation within PV presents a shift towards more efficient, insightful, and adaptable drug safety monitoring. The journey towards realizing this potential will be characterized by innovative solutions, rigorous validation, and a collaborative effort between pharmaceutical companies, regulatory authorities, software, and service providers.

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