

PERSPECTIVE

Cross-company collaboration to leverage analytics for clinical quality and accelerate drug development: The IMPALA industry group

Quality functions from pharmaceutical sponsor companies aim to increase the use of analytics in their oversight of Good Clinical Practices and Pharmacovigilance activities. To leverage and accelerate progress, several companies decided to establish a collaborative model. The goals of this collaboration span the sharing of knowledge and ideas, the sharing of analytics methods, discussion of talent upskilling and technology adoption strategies, and collaborative discussion on these potential changes with global Health Authorities.

Quality Assurance (QA) teams from pharmaceutical sponsor companies conduct activities to assess compliance to Good Clinical Practices (GCP) and Good Pharmacovigilance Practices (GVP) regulated activities.^{1,2} These activities encompass the set-up and management of a Quality Management System (QMS), including training, Standard Operating Procedures (SOPs), and Quality Strategic Activities (QSAs) such as audits. These activities follow well-defined processes and have been implemented for over 25 years (at least since the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use—Good Clinical Practice [ICH-GCP] in 1996) and involve a high volume of manual work. This is a reactive process in that audits are executed based on risk assessed from past data (from several months up to a year). For large and medium sized companies, auditing the entire “universe” of clinical trials sites on an annual basis is generally infeasible due to sheer volume, placing an even greater emphasis on a sound and timely risk assessment strategy to ensure QA activities are prioritized to assess the identified risks contemporaneously.

Moreover, the increasing number of clinical trials and the growing complexity of study designs and of pharmacovigilance (PV) processes make it challenging to detect and identify clinical quality issues timely. As a consequence,

late detection of quality issues can lead to delayed filing, delayed approval, and to delayed patient access to innovative therapies.^{3–5}

The industry has recently been leveraging developments in data management and IT systems that facilitate the cross-analysis of clinical studies and PV processes. Several companies that have implemented analytics solutions for QA decided to establish a collaboration.

THE IMPALA INDUSTRY GROUP

In July 2019, we set up a cross pharmaceutical industry group with the initial goals to share knowledge and better understand opportunities in applying advanced analytics for QA: the Inter coMPany quALity Analytics (IMPALA) Industry Group. To date, seven companies are represented in this group: F. Hoffmann-La Roche (Roche), Merck (MSD), Johnson & Johnson (J&J), GlaxoSmithKline (GSK), Pfizer, Boehringer Ingelheim (BI), and Biogen. Core members are functional heads of quality analytics/data science organizations, ad hoc members are quality and/or data analytics professionals.

SHARING KNOWLEDGE AND BEST PRACTICES

The IMPALA industry group meets on a periodic basis to share knowledge and discuss best practices related to the use of advanced data analytics for QA. Members of the group share individual approaches to embedding data analytics within the QA process and explore the best strategies for facilitating the adoption of analytics solutions both within internal quality processes and by external stakeholders. The group discusses what capabilities, hiring strategies, and training curriculum are necessary to achieve their goals and ways in which

*IMPALA industry group members are present in the Acknowledgements.

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to enhance the skills of QA staff. Members also share discrete use cases being implemented within quality data analytics. Identification and deliberation of potential use cases has also helped the member companies advance, ranging from high-level discussion on value/benefits to deeper-dive presentations with project teams and data scientists. The group discusses the challenges and progress that is made on these individual use cases and brings ideas for new use cases. This allows for best practices to be surfaced and new analytics solutions to be implemented across the member organizations leading to standardization and optimization of QA analytics within the industry. The group is looking to advance information sharing with additional meetings in 2021 open to broader audiences at the member companies. See Table 1 for examples of best practices and knowledge sharing.

CROSS-COMPANY DATA SHARING

One of the challenges associated with the use of analytics for QA purposes is to develop approaches with broad applicability and high use value across a diverse pharmaceutical industry. Local approaches have been developed, validated, and used with success. However, their acceptance across the industry and with regulators as a reliable, standardized QA tool to augment or replace audits will be limited as the number of solutions and assumptions will be as diverse as the companies. To address this issue, a cross-company data sharing project is proposed.⁶ This would enable companies to aggregate data across different study phases, designs, therapeutic areas, etc. With larger and diverse data sets, data can be partitioned into modeling and validating data sets where assumptions can be assessed and ultimately confirmed through predefined processes. The validated models could be accessed by member companies to drive a more efficient clinical site audit program. The efficiency would result in a holistic, real time assessment of all sites throughout the duration of a study and drive the selection of only the critical few sites for face-to-face audits.⁶ In addition, companies assessing items, such as innovative trial designs or new geographies, may be able to put mitigations in place because historical models demonstrate site performance issues when compared to baseline performance (Table 1).

CO-DEVELOPMENT OF QA ANALYTICS TOOLS

A first use case for shared experience across member companies relies on a bootstrap resampling open source package initially developed and deployed within one of the member companies.⁷ This method uses a resampling methodology

to predict adverse event under-reporting at clinical trial sites, including assessment of potential regional trends (see the Supplementary Material document for the complete method and code). In order for the method to be deployed within other member companies, some level of data mapping and harmonization must first be completed. The method can then be run, and results compared across members. This process will begin to inform the group about potential cross-company variability (for example, application of the same method in different companies who have different areas of therapeutic focus, and thus distinct profiles for trial design and data flow). This feedback loop should increase the strength of the model in terms of broad applicability. The goal of this exercise would be implementation across sponsors and a harmonized approach for monitoring clinical safety reporting that increases the power of quality oversight of this process while reducing the manual workload that exists today.

As a next step in co-development of analytics tools, the group will seek additional use cases where a method can be deployed and value-tested across companies. An additional area of development could be in the deployment of data science methods that speed the step of data harmonization and preparation, allowing more nimble installation and testing of methods across companies and public data sets (Table 1).

FUTURE PROSPECTS

As a way of sharing best practices, the team collaborates on cross-company presentations at leading congress venues both in the QA area and the wider pharmaceutical industry. Recognizing that use of data analytics to guide quality related decision making is an innovation, the group seeks to present information appealing to companies in all stages of uptake of this emerging trend. For example, to encourage companies who may only have a first idea about quality data analytics, the IMPALA group has presented on how to get started sharing information about the basic requirements of systems, tools, and other infrastructural elements to successfully launch such an initiative. At the other end of the spectrum, the group also presents complex analytic models for those companies who are further along in their adoption of this industry trend, perhaps inspiring new ideas or even leading to increased membership in the IMPALA group to expand the collaboration opportunities.^{8,9}

It is also important for the group to engage with Health Authorities (HAs) and with inspector working groups to gain their feedback and perspective on the proposals for specific methodological approaches to quality risk management using data analytics. The IMPALA group seeks to operationalize the aspiration for adoption of risk based approaches to asset development and management that

TABLE 1 Areas of focus, current and future projects for the IMPALA group (as of June 2021).

Area	Scope	Expected outcome(s)	Tentative timelines
Sharing knowledge and best practices	Data science capabilities for QA organizations Trainings on data analytics for QA staff	Further define skills and capabilities needed for the quality professional of the future Enabled open-access to tailored training (e.g., the Data Analytics University ¹⁰) for QA staff	Currently ongoing, expected to continue throughout 2022 The Data Analytics University program ¹⁰ has been rolled out on April 2021
Sharing knowledge and best practices	Use of NLP – value proposition, applications, and deployment	Shared NLP applications for QA (e.g., to improve CAPA processes) Continuous improvement of NLP models, by learning from the experience of the IMPALA member companies	Currently ongoing, expected to continue throughout 2022
Sharing knowledge and best practices	Data privacy	Explore applications of QA analytics tools to strengthen data privacy – if relevant, share externally any learnings Learn from the IMPALA members	To be started by 2022
Sharing knowledge and best practices	Cybersecurity	Explore applications of QA analytics tools to strengthen cybersecurity – if relevant, share externally any learnings Learn from the IMPALA members	To be started by 2022
Sharing knowledge and best practices	External engagement through industry conference and peer-reviewed publications	Engage with industry peers, regulators, inspectors to define acceptable standards for the use of advanced analytics in QA Transparency, validation and reproducibility of co-developed models (see also co-development of analytics tools)	June 2021 – Presentation at the Drug Information Association Annual conference 2022 and beyond – peer-reviewed publications (e.g., co-developed analytics tools, data sharing)
Data sharing	Platform and mechanism to share aggregated QA data	Enable data sharing across the IMPALA members; aggregated data could be used for: <ul style="list-style-type: none"> • co-development of QA analytics models; • development of QA analytics when internal data are limited and/or not available 	Ongoing, first data-sharing experiments to start in 2022
Data sharing	Validation (i.e., model verification) of advanced analytics models	Provide additional evidence for the verification of QA statistical models (i.e., testing statistical models on “external” data)	Ongoing, first data-sharing experiments to start in 2022
Co-development of QA analytics tools	Study Quality Risk assessment using statistical modeling	Develop a common model and approach to assess quality risks for clinical trials ⁶ – see also engagement with HA and inspector working groups	Testing phase and implementation by end 2021
Co-development of QA analytics tools	AEs under-reporting detection using a Bootstrap resampling statistical method	Develop a common model and approach to detect AE under-reporting ⁷ – see also engagement with HA and inspector working groups	Testing phase and implementation by end 2021

(Continues)

TABLE 1 (Continued)

Area	Scope	Expected outcome(s)	Tentative timelines
Future prospects	Engagement with HA and inspector working groups	Ensuring adoption by all relevant parties of new QA approaches and QA analytics tool, to improve and accelerate pre-approval inspections timelines	From 2022 and onward
Future prospects	Engagement with industry peers (not yet members of the IMPALA group)	Strengthen the diversity of the IMPALA group by inviting an additional 3 to 5 pharmaceutical companies to join	Four new members to join by mid 2021
Future prospects	Alignment and collaboration with other QA industry group	Ensuring QA analytics efforts driven by the IMPALA group are aligned with other cross-industry QA initiatives	Currently ongoing, expected to continue throughout 2022
Future prospects	Analysis on efficiency and impact of QA analytics	Further demonstrate the value proposition of QA analytics and quantify the return on investment	To be started by 2022

Abbreviations: AE, adverse event; IMPALA, Inter coMPany quALity Analytics; NLP, Natural Language Processing; QA, quality assurance.

have been laid out for the Industry in Regulations, the GVP Modules, and ICH-GCP E6 R2.^{1,2} By developing and testing risk models across different companies, the group is laying the foundation for establishing the validity of analytical methods for identification, assessments, and monitoring of risks to patient safety and data integrity. Once the first joint collaboration analytical models have demonstrated consistency across different pharmaceutical companies, the IMPALA group will use this as a basis for reaching out to key external stakeholders (e.g., HA). See also Table 1 for further details on future prospects.

CONCLUSION

One of the primary benefits of this group continues to be the discussion, collaboration, and debate on best practices across the member companies. Beyond this collaborative knowledge exchange, goals have been established to shift the QA paradigm via advanced analytics for clinical quality oversight of clinical sites and clinical trials, and to facilitate adoption by internal (e.g., quality professionals) and external stakeholders (e.g., HA inspectors). These goals include sharing of method development and potential sharing of data or results. Approaching this collaboratively can both accelerate overall transformation of these capabilities for the industry as well as increase acceptance of new methods by HAs.

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CONFLICTS OF INTEREST

At the time this paper was written: T.M. was employed by Roche. K.Y. was employed by Merck. L.S. was employed by GSK. J.E. was employed by Boehringer-Ingelheim. R.S. was employed by Johnson & Johnson. L.S. was employed by Biogen.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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