**1st meeting of the** **CIOMS Working Group WG XIV on
Artificial Intelligence in Pharmacovigilance**

**18-19 May 2022, Geneva, Switzerland, hybrid meeting**

**Meeting Minutes**

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Summary

**The CIOMS Working Group (WG) XIV on Artificial Intelligence in Pharmacovigilance held its 1st meeting with participants attending both in-person and virtually on 18-19 May 2022.**

**The WG discussed the background, scope, and target audience of the report. Two subgroups were formed to independently draft the table of contents of the future report, which will be merged during the next full WG meeting.**

Minutes of discussion

Day 1

# Opening and welcome

Hervé le Louët, CIOMS President, welcomed the members to the 1st Meeting of CIOMS WG XIV on Artificial Intelligence (AI) in Pharmacovigilance (PV).

Lembit Rägo, CIOMS Secretary General, added his words of welcome and opened the meeting as Chairman for the two days (for a list of participants see [**Annex 1**](#_Annex_1:_List)**).**

The meeting is the first partially in-person meeting after the pause imposed by COVID-19 pandemics. Lembit introduced the CIOMS working groups and [CIOMS](https://cioms.ch/) in general. The CIOMS quarterly newsletter is available on the CIOMS website for all to read and subscribe to.

Sue Le Roux, CIOMS Administrative Assistant, explained logistics for the two-day meeting. The meeting was held in a hybrid form with several members joining via Zoom.

Tour de Table: all participants introduced themselves to the group.

The meeting agenda was adopted.

Kateriina was rapporteur.

# Background, scope, and target audience of the future report

## Scope

The WG members raised the following discussion points:

* Include definitions and develop practical recommendations and ideas on how organisations can implement AI and Machine Learning (ML).
* The scope of the future report should be narrow to remain focused and provide tangible recommendations, while maintaining a broader awareness of the areas that the report could impact.
* Indicate the scope of the document in the introduction. The discussion on scope could include possible future directions of AI in PV and acknowledge their potential importance.
* A vision for the future should be added to the report, as ML and AI will reshape the field of PV to a certain extent.
* Regarding AI and ML, the public is either very sceptical or overly enthusiastic. There is an obvious need for CIOMS to provide a consensus position and provide more clarity among the different stakeholders.
* We need to be careful not to stifle innovation while ensuring that systems work appropriately.
* Address technical and operational considerations as well as regulatory decisions related to AI and ML. e.g.
	+ What are the technical possibilities we can apply?
	+ How can the workload accompanying automation be managed?
	+ How can we rethink PV through the use of data mining and ML as there is much faster access to a vast amount of data?
* How can the needs of industry be addressed within the applicability of ML? How can one benefit from it and maintain quality? How can you inspect something that is potentially a 'black box'?
* Are the solutions offered by AI and ML permanent and worth the investment?
* Reliability must not be compromised and the challenges of needing additional AI and ML skills within organisations must be addressed. There are brilliant developers and medical scientists, but very few who can work in both fields.
* The field of PV is known for its increased wish for preciseness. It is about a balance between innovation and acceptable risk that would be recognised by all health authorities worldwide.
* The goal is for the entire PV system to function as a tangible, validated system that provides accurate information, rather than focusing on an individual component performing to the highest level.
* Address translation issues. It is not just a PV issue and examples/tools can be sought and used from other areas.
* Include discussions on searching information in free text, as searching for keywords in source documents or narratives is not sufficient to find information. Address semantic search strategies.
* Provide recommendations for validation and discuss ways to validate and train the machines, including the benefit-risk considerations.
* Address machine coding when faced with different regulations, timelines and requirements that are difficult to align globally.
* One of the challenges is being constrained to a single platform as vendors may not be experts in AI / ML components. There are specialists who have more advanced solutions, but it is difficult to integrate them. The aim would be a more open platform to integrate the different components.
* Address touchless approaches and provide guidance.
* As technology continues to evolve, so do the tools that enable ML. We should keep this document as a living and forward-looking document that we can add to, keeping in mind the future implications of less structured data from devices.
* Include discussions on devices and consider them not in comparison to vaccines or medicines, but from the aspects of AI and ML, as there may be similarities in some cases.
* Address the implementation of a ML-based systems, e.g. what are the unique contributions, what are the issues and challenges to be considered, and provide practical aspects that can be used by stakeholders and examples to demonstrate different points.
* Several members of the WG suggested creating a framework / reference document to evaluate the appropriateness of the different tools and how they can be implemented, trained, validated and maintained. The consensus document should be provided as a set of principles that would contribute to alignment between regulators and industry.
* The possible constraining effect of relying on templates should be considered. We should remain cautious and encourage others to do so. The final report should clearly state that the principles presented are not an exhaustive set of criteria for effective use of ML. Different stakeholders will look at the list of principles from different viewpoints.
* Yusuke shared an initiative from [TransCelerate](https://www.transceleratebiopharmainc.com/assets/intelligent-automation-opportunities-pharmacovigilance-solutions/) regarding the types of technologies available in PV and the level of implementation of each technology in the Individual Case Safety Report (ICSR) process.
* Agree on the key performance indicators for a well-functioning AI-enabled PV system.
* Focus on spontaneous reports from any source.
* The inclusion of labelling would be appreciated by all stakeholders.
* [IMI WEB-RADR](https://www.imi.europa.eu/projects-results/project-factsheets/web-radr) has already dealt extensively with social media in PV, so perhaps this area should not be included in the report.
* The pre-marketing phase should be included as well as the post-marketing phase.
* In the context of clinical trials, a safety report produced as part of a clinical trial that goes into the safety databases falls within the scope, but the actual systematic surveillance, unsupervised pattern recognition of clinical trials or meta-analyses would fall outside the scope.
* Address critical areas that should be considered when implementing or validating quality regardless of source.
* Rather than developing a linear scope for the report, create a matrix of data streams and technologies, and from there determine the issues to be addressed.

## Target audience

The WG discussed the target audience of the report and raised the following issues:

* The primary audience comprises industry regulators and academic colleagues working in the field. The WG should also address the issue of general interest in AI and its application to PV.
* Some WG members suggested involving the public as an interested stakeholder. This would be an opportunity to build trust in the industry and the health care systems of the respective countries. At the same time, concerns were expressed that the scope of the report could become too broad, leading to only high-level descriptions of AI.
* Communicating with the public should not mean oversimplifying and writing in layman's terms. We can expect a certain level of expertise from the public in this context.
* Walter agreed with the interest in focusing on the public, but we should not underestimate the challenge in communication to enhance public trust. He shared a [CIOMS guide to vaccine safety communication](https://cioms.ch/wp-content/uploads/2019/05/WEB-CIOMS-Communication-Guide-2018.pdf) (2018) as a source document.
* Should we add healthcare providers as a target audience, as PV data is increasingly provided from all healthcare settings? Patient support programmes and all social media platforms also provide much more PV information nowadays and could also be considered as conduits to a target audience and a stakeholder group.
* We can consider patients in the future recommendations without including them as a target audience.
* Walter shared an article by Jokinen et al., [“Industry Assessment of the Contribution of Patient Support Programs, Market Research Programs, and Social Media to Patient Safety”](https://link.springer.com/content/pdf/10.1177/2168479019877384.pdf) (2019) as relevant to the discussions.
* Include vendors as a target audience.
* Identify and involve stakeholders who are the sources of data and provide them access to tools that provide good quality data and the opportunity to benefit from it through the use of AI.
* [CIOMS WG XI: Patient involvement in the development, regulation and safe use of medicines is](https://cioms.ch/working-groups/working-group-xi-patient-involvement/) addressing some of the issues on processing patient data and the report will be published this year.
* If human review is required in all areas when implementing a ML solution, then ML is clearly not useful. We need to provide recommendations and agree on what is appropriate and what is not.
* The traditional human process still emphasises the principle of oversight, and the same principle can be applied to ML / AI, depending on the type of programme used and the nature of the cases. There could be a group of touchless cases, but also a group of significant cases set as a threshold.
* Setting thresholds for a number of use cases will be a major challenge. We may have to scale back expectations, especially for tasks where people themselves disagree. We need to emphasise that machines can only perform to a point.
* Lembit suggested the WG consider adding an appendix to the future report that would provide more high-level information on key points about AI and ML in PV. This approach has previously been opted for by some CIOMS WGs.

## Data

* The amount of data may not be large enough to train models. In the case of federated learning, security is critical for organisations.
* Avoid restricting ourselves to a specific area, e.g. case processing.
* ML enables capabilities that cannot be achieved with purely rule-based solutions.
* Safety data and spontaneous reports as well as case processing are the areas to focus on. The entire lifecycle of medicine must be taken into account.
* The aspect of what number of training data is needed is crucial. The aim would be to achieve concrete recommendations.
* Address data issues, e.g. data sources, training data, data sharing, spontaneous data vs. observational data.
* Include spontaneous reports and solicited reports as data sources.
* Consider including Statistical Process Control (SPC).
* Establish reporting requirements that provide guidance on how we do or report science. For example, how do you report what the training data was? What was the nature of the training data?
* When it comes to automation, the focus should not be on the efficiency of multiple new sources. This should be treated as an opportunity to actually improve data and include recommendations.
* The COVID-19 pandemic has amplified the challenges and lessons of data management and offers several experiences with case reporting that would be worth addressing.
* There are several sources of signal detection, e.g. clinical trials, reports, social media, etc. Not everything can be included. Do we focus on simpler automation when considering AI or more complex systems? Do we consider external or internal processing? ML can be employed as part of the signal validation process.
* Causality assessment at the Individual Case Safety Report (ICSR) level needs further guidance.
* There is a conflict between data sharing / ownership and commercial interests. Third parties may not be able to access the data, which in turn could hinder the development of AI technologies and undermine open innovation. The WG needs to discuss the aspects of accessing data for commercial purposes versus non-commercial or academic purposes.
* Discussions on different types of technologies and approaches will change depending on the type of data involved.
* The focus of the report will not be on data per se, but on the appropriate use of data in ML.
* Discuss the inclusion of claims analysis and social media.
* Adding too many data sources could result in a large number of recommendations. Consider keeping the recommendations generic.
* As the development of ML is a significant investment, the WG can make recommendations on what adds value, which in turn would be a good indicator to narrow the scope in terms of including discussions on data.

## Involving vendors/service providers

The WG discussed possibilities for involving vendors as representatives from two companies who are expected to join the discussion the next day.

The WG agreed to include vendors not as core members but in the form of an advisory group. Several titles for the group were suggested, with the titles Technical Advisory Group and Technical Reference Group gaining the most support. Some members suggested calling the group the Developer Advisory Group and suggested including members from academia too. The following discussion points summarise the messages and recommendations from the WG members. The minutes refer to the future group as the Advisory Group, as the name of the group will be decided at a later date.

* The technical expertise and experience of the Advisory Group will be valuable for providing guidance in the AI field and will lend the needed credibility to the WG. Vendors who have made progress in the field would be a valuable addition to advise and progress the WG.
* The Advisory Group will be formed of volunteers and the final decision on their inclusion will remain with CIOMS. They will not be involved in the drafting of the WG’s report.
* Consider involving vendors not only from the PV sector but also from other fields of healthcare.
* Recommendations to the CIOMS Secretariat regarding additional members to invite to the Advisory Group are welcome.
* The WG might consider signing a confidentiality agreement as well as a conflict of interest statement declaration with the members of the Advisory Group.
* Clear Terms of Reference will be drawn up to facilitate transparent and open interaction with the Advisory Group. They will not participate in the WG meetings in full but will work independently and in parallel with the WG, joining the WG meetings for an agreed time. Nevertheless, it should be ensured that the two groups are moving in the same direction.
* In addition to including vendors as an Advisory Group, the WG’s report can be made available for public consultation to allow all interested parties to comment.
* The Advisory Group is urged to engage in discussions within their group to obtain more consolidated views.
* A group of volunteers (Andrew, Dieter, Elizabeth, Jesper, Justyna, Luisa, Nicolas, and Phil) will draft the Terms of Reference to facilitate interaction with the advisory group and share them with the WG for feedback.
* Information on the process of including members in the advisory group will be made available on the CIOMS website along with the Terms of Reference to ensure transparency for all interested parties.

# Other initiatives relevant to the CIOMS WG XIV

WG members involved in initiatives discussing AI are invited to inform the members to share knowledge and avoid possible overlaps between the work of parallel groups. CIOMS WGs have previously invited guest speakers from different initiatives for the WG with the aim of mutually benefitting from the experience.

* Jesper is involved in the Heads of Medicines Agency (HMA) / European Medicines Agency (EMA) Steering Group with work related to AI in medicine regulation. The aim of the group is not to provide a guidance document but a discussion paper to be finalised towards the end of the year. Work is currently ongoing between the national competent authorities in Europe and the EMA. The discussions could be relevant to the WG.
* Andrew is involved with TransCelerate, a non-profit organisation that collaborates across the global biopharmaceutical research and development community. He sits on the [Pharmacovigilance Steering Committee](https://www.transceleratebiopharmainc.com/our-mission/meet-the-people/) and is involved in a workstream on [Intelligent Automation Opportunities in Pharmacovigilance](https://www.transceleratebiopharmainc.com/initiatives/intelligent-automation-opportunities-pharmacovigilance-2/).
* He also co-edited a special issue of Drug Safety on the [Role of Artificial Intelligence and Machine Learning in Pharmacovigilance](https://link.springer.com/journal/40264/volumes-and-issues/45-5), published in May 2022.
* The [Office for Human Research Protections](https://www.hhs.gov/ohrp/index.html) (OHRP) is the lead agency in protecting the rights, welfare and health of human subjects involved in research conducted or supported by the U.S. Department of Health and Human Services (HHS). OHRP also supports the Secretary's Advisory Committee on Human Research Protections (SACHRP), which advises the HHS Secretary on various issues, including the use of AI and research. Stephen Rosenfeld chairs the working group and has agreed to share relevant documents on the WG agenda with members.

# Involving additional expertise

To balance and strengthen the WG, all are welcome to propose additional members from academia, including ethicists working in the field of ethics and AI. Any suggestions are welcome and to be emailed to Lembit.

# Breakout groups to draft the TOC of the future WG report.

## Two subgroups were formed from the members participating in-person with a task to draft their initial thoughts on the major topics to be included in the future WG report. Please see [Annex 2](#_Annex_2:_Draft) for the draft Table of Contents (TOC) of both subgroups.

## Subgroup 1: Hua, Andrew, Dieter, Justyne, Phil, and Luisa.

## Subgroup 2: Jesper, Nicolas, Niklas, John, Elizabeth, and Hans-Jörg.

## The subgroups presented their initial thoughts on the major topics to be covered in the future report. The following represents the discussion points after Subgroup 1 presented their draft TOC.

* Lembit suggested referencing [UNESCO’s Recommendation on the ethics of Artificial Intelligence](https://unesdoc.unesco.org/ark%3A/48223/pf0000381137) (2022) as one of the recent publications addressing AI and ethics.
* Andrew mentioned an example of training a ML algorithm based on a particular set of spontaneous reports, where problems can arise when a request to remove a case report is received. Should such case reports that are then invalidated be excluded from the model? How can we demonstrate how the ML algorithm worked before the report was removed?
* We need to consider the broader implications of the work of the WG on the scientific field in relation to AI and its appropriate and safe use.
* Several existing ML algorithms are patented. An investigation into the owners of the patents and the possible uses is one of the issues to consider.
* Address the lack of accountability: if the machines make wrong decisions, how can they be held accountable?
* Consider the possibilities and characteristics of AI and address the limitations.
* Include a section on public trust. Stephen offered to circulate documents on the work ahead.
* Panos suggested all members inform the WG members about initiatives that have developed or are in the process of developing ethical guidelines for AI, even if they are not in the field of PV. These would serve as valuable references when drafting the chapters.
* Lembit suggested that the members from the regulatory agencies consult among themselves on the inspectors who should be invited to participate in the WG to include their experience in the quality management of the systems and email him the suggestions.

## Terminology

* The WG agreed that addressing the basic terms is an essential task of the report. The CIOMS Cumulative Pharmacovigilance Glossary is available on the CIOMS website and compiles terms and definitions from published CIOMS PV reports. The WG is welcome to consult it as a resource when considering its terms, definitions and sources.
* Taxiarchis shared an article by Robert Pall and Gerald dal Pan (2022) [““Artificial Intelligence” for Pharmacovigilance: Ready for Prime Time?”](https://link.springer.com/article/10.1007/s40264-022-01157-4) which could serve as a starting point for the discussion on definitions.

## Ethics

* The WG is welcome to consider a separate section, chapter or an appendix addressing ethics or other issues considered necessary within the framework of the report.
* Include discussions on success from the perspective of not only technology but also people. Address the expectations.
* Discuss the approaches used to process data and remain in the regulatory framework and legal responsibilities to narrow the scope.
* Roli shared a WHO guideline she was involved in creating: [“Ethics and governance of artificial intelligence for health”](https://www.who.int/publications/i/item/9789240029200).
* The future report must be in compliance with the existing policies and international requirements related to health data.
* Roli would be interested in working with a smaller subgroup and focus on the ethics aspect of the report.

**The following represents the discussion points after Subgroup 2 presented their draft TOC.**

* Work towards creating a document that can be endorsed by both regulators and industry, and that is a set of tools rather than a guidance.
* Recommendations developed jointly by industry, regulators and academia are of great value as they allow for broader applicability of the tools.
* Exercise caution when addressing benchmarking as the case intake approach will vary greatly. Free text compared to a structured form requires very different technologies for processing and therefore different considerations. This is one of the areas where some guidance would be needed.
* Consider the entire lifecycle of the medicine. Address signal processing.
* If a particular AI methodology can be applicable to multiple use cases, then we need to consider the performance of that particular methodology.
* The aim of the future report is to create an understanding between regulators, academia and industry about what AI means and what some of its best practises are. Using translation as an example, what is done by AI is fundamentally different from what a human can do, but it is still "good enough". Would it be useful to agree on what "good enough" means in order to develop a common understanding?
* When we compare AI with human performance, we need to remember that the two must not necessarily be at the same level. AI has advantages, e.g. timeliness, as its systems process data much faster. The overall system with a human component will later compensate for a possible imbalance.

**Including rule-based AI**

* The WG supported the idea of not including rule-based AI in the report, but perhaps the use of rules in addition to AI / ML approaches needs to be examined to ensure they work effectively.
* We should be careful not to completely exclude systems that employ rules as part of them. There are several reports on specific use cases. The reports could be researched as they describe specific use cases and offer explanations of how automation may support them.
* The hybrid systems that use rules will be included in the report. The way to include them would be not to look at ML in isolation, but to focus on how ML supports the system and on the interaction between the rule-based AI and ML. There is a need for guidance in this area.

**DAY 2**

Lembit summarised the Day 1 discussions and opened the Day 2 discussions.

Bruce Palsulich from Oracle and Eric Sandor from Genpact virtually joined the meeting to discuss their involvement in the WG’s work and Lembit updated them on the previous WG discussions and agreement on forming an Advisory Group and creating Terms of Reference to facilitate interaction.

The following includes discussion points raised by Bruce and Eric:

* Balance the complexity of involving vendors and service providers, and the value of accessing additional perspectives.
* Clarify the involvement expected from the Advisory Group. Establish clear Terms of Reference and define the scope and mechanisms for future input.
* Establish the role of medical evaluation in individual cases or in aggregate reviews, and the ways in which automation or AI can replace or enhance it.
* Address current human accuracy – automation is often expected to achieve 99-100% accuracy, which in many cases would far exceed current human accuracy.
* Discuss the possibilities of establishing open datasets for training and evaluating, and the potential of federated learning opportunities that could also protect privacy. Discuss ways to share data or have common datasets to allow the same problem to be tackled by multiple parties but with a standardised method of evaluation.
* Research for legal advice to avoid possible concern of collusion. The advisory group meetings would need to be well documented and observed by parties other than the advisory group members.

Cooperation is beneficial for all parties and WG members are invited to suggest additional members to the advisory group who possess experience and expertise in the field.

Regarding the future work, the vision is to organise common sessions where all parties have the possibility for open discussions.

**Subgroups presentations**

The two subgroups continued discussing the scope and goal of the future WG report and drafting the future TOC.

The initial thoughts drafted as TOCs will be added to the minutes and made public in the CIOMS webpage, but in order to reach wider visibility, the WG members are also welcome to use the material created to publish in scientific journals.

The subgroups will continue their discussions and will draft the future TOC with additional members joining during the virtual meetings planned for June. Kateriina will send Doodle polls to agree on the dates and set up virtual meetings.

The following summarises the discussion points following the subgroups presentations.

* Consider and list the issues that should be excluded from the future report.
* There are systems that have a strong ML component but at the same time incorporate other technologies, e.g. processing information from text narrative is performed by natural language processing (NLP) and rule-based systems. Meanwhile, the systems have been enhanced with ML and other technologies. Should we exclude these systems from the scope of the report?
* Focus on the tools and processes of the system that include at least one component of ML. If the system is not solely based on ML, focus on the interaction between ML and the rule-based system, or what the ML element requires of a system.
* Include the disproportionality score based element of a system, but the disproportionality score itself, and how to interpret it, will not be addressed in detail. The focus will be on novel elements.
* The purpose of the report is not to review existing models and algorithms, but to create the guideline in a model-agnostic way, so that it can be transferable to other models.
* Provide guidance to vendors regarding the development of open AI versus proprietary AI, particularly in the area of PV, so that new technologies can be substituted to achieve better performance than proprietary technologies supported only by the platform vendor.
* Not to focus extensively on individual AI algorithms, as it is a rapidly evolving field, which in turn may hinder the sustainability of the report. Opting for a model-agnostic approach to creating a guideline would provide greater benefits.
* One of the tensions in the field of PV is between the pursuit of scientific innovation and progress, and compliance with regulatory expectations. One of the barriers to the implementation of these technologies is concern that companies may be reluctant to support innovation due to uncertainty around whether these innovations will meet regulatory expectations.
* Articulate agreement between all parties on training, validation, quality and the risk that the parties are willing to accept in developing and implementing the technologies. The inspector's perspective is also vital.
* Discuss issues related to medical review from the perspective that it is not to be replaced or eliminated, but that it is a paradigm shift.
* Discuss the level of accuracy we are aiming for the AI and ML, and how we can measure and demonstrate this. Start the document with a fundamental statement or paragraph describing ML and AI and continue by describing the differences.

# Way of working

Lembit explained a few practical matters about the CIOMS WGs in general:

* Each CIOMS group finalises a guideline, usually in 2-4 years, which will be both in electronic and print formats. All CIOMS reports are free to be downloaded from the CIOMS website.
* The draft minutes from meetings will always be provided to the members to review and approve before being uploaded to the public WG page on the CIOMS website.
* Where WG members consent to meetings being recorded for the purposes for taking minutes, the recordings will not be used for any other purpose and will be deleted as soon as possible.
* The CIOMS Secretariat will help with setting up Zoom meetings, writing minutes, and will assist with general communications.
* Each WG has its own section on the CIOMS website where the WG documents are available. Some content is open to the public e.g. the Concept Note and full WG meeting minutes, and other content is available only to the WG members behind password-protection e.g. working documents and publications of outstanding importance shared among the WG members.
* CIOMS reports are usually finalised by an editorial team composed of five to six WG members. A near-final draft would be brought back to the full WG at a possible final meeting.
* A simultaneous text editing platform that would be accessible to all WG members does not seem to exist, mostly due to security reasons, and CIOMS does not wish to exclude any WG members. Going forward, the WG members are welcome to suggest platforms or ways of working that would include all members.

# Any other business

The WG members are welcome to share relevant publications among the WG members via the CIOMS Secretariat. They will then be posted to the WG’s password-protected area of CIOMS’ website. If possible, brief descriptions about the relevance of the article would be helpful, as members come from different fields of expertise.

Niklas enquired whether the WG should draft a project dissemination plan and set the timelines including the early deliverables, e.g. in the form of a declaration of intent. Lembit emphasised the importance of agreeing on the TOC at the next full WG meeting and deciding what should be included in each section. Following this, the leads of the future chapter groups of the report will be appointed and the chapter groups are then able to set the timelines for drafting.

Members are welcome to present the work of the WG at other meetings and conferences but are kindly invited to inform the WG and the CIOMS Secretariat in advance, as several people may wish to raise similar issues at the same conference.

###

# Next steps / next meeting

* The next full WG meeting will take place in Geneva, and the dates will be researched for mid-September – mid-October 2022.
* The aim of the next full WG, in-person meeting is to merge the two proposed TOCs, and subgroups will be assigned to start drafting the agreed sections of the future report.
* If the WG decides to hold a virtual meeting instead of an in-person meeting, the CIOMS Secretariat will assist with organising it. Several CIOMS WGs have opted for three-hour meetings (during one day) to progress their work. Virtual meetings are an occasion to agree on what has been drafted to move forwards.

# Closing remarks

Hervé and Lembit thanked the WG members for joining in-person and virtually, and for the productive discussions.

#  Annex 1: List of participants

**Attending in person**

Justyna Amelio (AbbVie), Luisa Barrios (Merck Sharp & Dohme), Andrew Bate (GlaxoSmithKline), Hua Carroll (Biogen), Stephen Heaton\* (CIOMS) Dieter Kempf (Genentech, Roche), Jesper Kjær (Danish Medicines Agency), Hervé Le Louët (CIOMS), Niklas Norén (World Health Organization / Uppsala Monitoring Centre), Nicolas Perez (Swissmedic), John Reinhard Pietzsch\* (Bayer), Kateriina Rannula (CIOMS), Lembit Rägo (CIOMS), Hans-Jörg Römming (Merck Group), Elizabeth Savage (Johnson & Johnson), and Phil Tregunno (The Medicines and Healthcare Products Regulatory Agency, UK).

**Attending virtually**

Robert Ball (US FDA), Arvind Bellur (Sanofi), Taxiarchis Botsis (Johns Hopkins University School of Medicine, US), Flávia Moreira Cruz (ANVISA, Brazil), Kirsten Egebjerg Juul\* (Danish Medicines Agency), Piero Francesco Franco (Pfizer), Benny Ling (Health Canada), Harumi Maniwa\* (Pharmaceuticals and Medical Devices Agency, Japan), Roli Mathur (India Council Medical Research), Yusuke Matsunuga (Pharmaceuticals and Medical Devices Agency, Japan), Richard McAteer\* (Health Canada), Ravi Patel, (Unither), Stephen Rosenfeld (North Star Review Board), Walter Straus (Moderna), and Panos Tsintis (CIOMS Senior Adviser).

\*Alternate

**Attending Day 2 hybrid session only:**

Bruce Palsulich (Oracle) and Eric Sandor (Genpact).

**Apologies**

Russ Altman (Stanford University, US), Denny Lorenz (Bayer), and Vineet Singh (Novartis).

#  Annex 2: Initial thoughts on the draft Table of Contents

Subgroup 1

1. Background and current state of Machine Learning in Pharmacovigilance. ML in PV.
2. Value areas or opportunities in PV lifecycle (short overview).
3. General best practice (training data; the data sets; possible required retraining; reacting to changes in the companies´ product portfolios and its impact on the models and training requirements; sources of data; validation data sets; general expectations of how these technologies would perform, including acceptance criteria or performance and ways of measuring the processes; the skill profile of the staff.
4. Expectations setting, limitations.
5. Implementation of specific components –case studies and technologies applied, assessment of risk, level of human interaction. Recommendations on all aspects.
6. Maintenance aspects (more on best practices).
7. Future vision.
8. Glossary.

Subgroup 2

1. Definitions (AI, scope).
2. Current state (general PV guidances, key publications, references).
3. Scope – data capture and ICSR processing.
4. Individual problem statements – structuring from different angles (industry, academia, etc), commonalities and synthesising.
5. How to appropriately implement and maintain ML along the lifecycle within quality framework.

Model training, model deployment, model in production in different dimensions - description of the models, data description, model performance measures.

People dimensions: human-computer interaction, touchless case processing, and aspects related to quality control and quality assurance.

1. Theoretical quality framework for specific use cases (e.g. languages).
2. Transferring the framework to other areas along the PV lifecycle, towards later ends of the PV lifecycle in signal management and benefit-risk management.
3. Outlook to the future, additional research needs, development of reference data set (for benchmarking).