







EPR EUROPEAN PHARMACEUTICAL REVIEW | PHARMA HORIZONS REPORT

Artificial Intelligence



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AI – what's on the horizon for pharma?

This report is dedicated to exploring some of the latest advances in artificial intelligence (AI) and machine learning (ML) for drug development, pharmaceutical manufacturing and quality control.

AI/ML are predicted to be the top technology investment for 60 percent of life sciences companies over the next two years, according to a recent survey from the Pistoia Alliance.[1]

Additionally, the global AI pharmaceutical market size is projected to grow from $908 million to $11.8 billion by 2032, based on data from Precedence Research.[2]

On page 9 we speak to Dr Feng Ren, Chief Scientific Officer and Head of R&D at Insilico Medicine, about its novel AI-generated drug for idiopathic pulmonary fibrosis, which became the first in the world to enter Phase II trials in June 2023.

We also interview Dr Andrew Hopkins, founder of Exscientia, a company that brought four AI-generated drugs into the clinic in 2023, on page 12. Predicting that "all drugs will be designed by AI by 2030," Hopkins outlines areas he believes can benefit most from the technology, including personalised medicine and trial design.

Continuing, on page 15 we delve deeper into how AI can support clinical trials with UCB's Tero Laulajainen, who believes the greatest benefit of AI is "its potential to improve clinical trials through data collection and analytics." Laulajainen elaborates on challenges facing the application of AI/ML technology, including data limitations and how they may be overcome through collaborations.

Regulation and governance of AI within the pharmaceutical industry are at an early stage. In a review on page 4 Catherine Eckford summarises some of the recent regulatory developments in the AI space, including activities by the European Medicines Agency, World Health Organization and the UK Government. Additionally, on page 19 legal expert Vincenzo Salvatore of BonelliErede looks at the European Commission's proposed AI Act and the potential opportunities and challenges for pharma amid this transformative landscape.

In an article on page 22 Sanofi explains how it is embracing digital technologies, including AI/ML, to simplify, standardise and transform its manufacturing operations.

On page 25 renowned microbiology expert Dr Tim Sandle discusses how AI/ML is shaping the future of pharmaceutical microbiology.

Finally, on page 30 we hear how generative AI can enhance various aspects of a qualified person's (QP's) role - from learning and development to automation of routine tasks, and from aiding in deviation investigations to enhancing quality risk assessments.

We hope you enjoy this report and welcome your feedback.



Caroline Peachey
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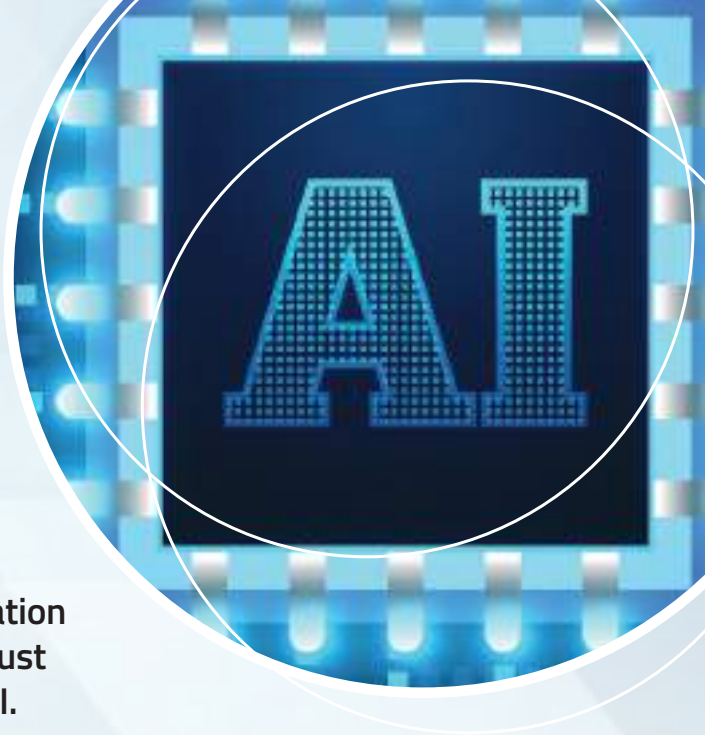

Recent developments in artificial intelligence

Demonstrating the revolutionary potential that artificial intelligence (AI) can offer the pharmaceutical industry, *EPR's* Catherine Eckford reviews recent research from drug formulation through to clinical development. Insight from key industry leaders also emphasises how robust regulations are fundamental to giving the industry a safe and prosperous future alongside AI.

The biotech and pharmaceutical industries are in a transformative era driven by a convergence of science, data and tech.[1]

Meanwhile, the cost of bringing new drugs to market and to patients has become prohibitively expensive. Recognising these headwinds, AI/ machine learning (ML) techniques are appealing to the pharmaceutical industry due to their automated nature, predictive capabilities, and the consequent expected increase in efficiency.[2]

Preliminary data from CPHI Annual Report 2023, released in September 2023, showed that AI is anticipated to transform every area of the industry, from drug discovery through to drug development, within the next 24 months.[3]

Currently, there is great focus on AI as an innovative tool in drug discovery. In March 2023, a major advancement was announced by the UK Government, revealing plans for a new supercomputer for industry. Part of a £900 million investment to upgrade the UK's next-generation computer capacity, the supercomputer will be "one of the most powerful for AI in Europe", according to the UK Government.[4]

> *"In clinical development, AI has potential in greatly improving the planning and outcomes of clinical trials"*

Additionally, in June 2023, BioMed X, a German independent research institute, began its first collaborative research project with Sanofi: Next Generation Virtual Patient Engine for Clinical Translation of Drug Candidates (VPE). By developing a computational platform that can predict the efficacy of first- or best-in-class drug candidates in virtual patient populations with unprecedented accuracy, the project aims to overcome "one of the most critical bottlenecks of the pharmaceutical industry": the 90 percent failure rate of new drug candidates during clinical development.[5]

However, recognition of AI's potential in later stages of development is also rapidly increasing.

In clinical development, AI has potential in greatly improving the planning and outcomes of clinical trials, eg, trial design and promoting greater adoption of decentralised/remote trials. AI streamlines data collection and management in clinical trials, accelerating the process.[6]

AI/ML can also support data recording and analyses for submission to regulators in marketing-authorisation procedures. At the marketing-authorisation stage, AI applications include tools to draft, compile, translate, or review data to be included in the product information of a medicine.[6]

In the post-authorisation phase, these tools can effectively support, for example, pharmacovigilance activities including adverse event report management and signal detection.[6]

AI also offers opportunity to enhance other areas, such as manufacturing. For example, it could optimise continuous manufacturing operations. AI algorithms will make pharmaceutical manufacture uniform and efficient via data analysis and feedback. It will also analyse large amounts of data to inform regulatory decisions and assist regulatory bodies in speeding up medication approval and improving safety.[7]



Overcoming sustainability implications of AI

A 2023 research paper published in *Nature Electronics* reported on the development of a new nanoelectronic device that can perform tasks using AI without requiring connection to the cloud to execute analyses.

Key benefits of this technology include its positive implications in relation to data privacy protection, as well as environmental sustainability:

"Artificial intelligence tools are consuming an increasing fraction of the power grid," Northwestern University's Mark Hersam, the study's senior author, remarked: "It is an unsustainable path if we continue relying on conventional computer hardware."

While devised to analyse an individual's personal medical data, the research demonstrates the highly efficient potential of AI for the future.

According to the initial data from the CPHI Annual Report 2023, when looking three years ahead, AI's role in manufacturing optimisation was the most chosen application by 52 percent of the 250 global pharmaceutical companies that responded to the research survey. Almost 43 percent of respondents predicted it will support in building base regulatory submissions.[3]

AI in industry – regulator and agency perspectives

In July 2023, the European Medicines Agency (EMA) published its draft reflection paper on the use of AI. Positively, the paper addressed the application of this technology across the entire medicine lifecycle, from

drug discovery to post-authorisation, as a tool for safe and effective development, regulation and medicine use.

"With this paper, we are opening a dialogue with developers, academics, and other regulators, to discuss ways forward, ensuring that the full potential of these innovations can be realised," Peter Arlett, EMA's Head of Data Analytics and Methods, co-chair of the Big Data Steering Group (BDSG), explained at the time of the publication's release.

The EMA and the Heads of Medicines Agencies (HMAs) also published a workplan, which sets out a "collaborative and coordinated strategy" to maximise the benefits of artificial intelligence in regulation.

The workplan, which runs until 2028, will help the European medicines regulatory network (EMRN) embrace the opportunities of AI for personal productivity, automating processes and systems, increasing insights into data and supporting more robust decision-making to benefit public and animal health.

The plan was prepared by the BDSG, a joint initiative between HMA and EMA. The goal of this steering group is to ensure the EMRN "remains at the forefront in benefitting from AI in medicines regulation."

WHO

On 19 October 2023, the World Health Organization (WHO) published its fundamental considerations for the regulation of artificial intelligence (AI), examining what is needed to make AI systems safe and effective as a tool for health.

To "support countries to regulate AI effectively, to harness its potential, [eg, in treating cancer], while minimising the risks", according to Dr Tedros Adhanom Ghebreyesus, WHO Director-General, the paper outlined six areas of focus:

- Transparency and documentation
- Risk management
- Data validation and intended use
- Data quality
- Privacy and data protection
- Collaboration.

"Artificial intelligence holds great promise for health, but also comes with serious challenges, including unethical data collection, cybersecurity threats and amplifying biases or misinformation," commented Dr Adhanom Ghebreyesus.

Exploring the regulation of this developing technology, WHO's paper addressed the challenges posed by "important, complex regulations" such as the General Data Protection Regulation (GDPR) in Europe, and emphasised the importance of "understanding the scope of jurisdiction and consent requirements, in service of privacy and data protection", further appealing that AI models should be "made as simple as possible".

To facilitate regulatory compliance with AI, the paper underlined the importance of collaboration between regulators and

Optimising drug formulation

In May 2023, *EPR* reported on research from MIT's School of Engineering and Takeda's (MIT-Takeda) programme on developing new ML/AI approaches to drug development.[9] A novel ML algorithm that can extract the particle size distribution (PSD) of a pharmaceutical powder surface from its laser speckle was discussed.

Recent advances in ML have demonstrated successful imaging via scattering media and speckle suppression, according to the authors of the paper, although "the speckle pattern is treated as an unwanted disturbance".

In their paper published in March 2023, Zhang *et al.* wrote that, to their knowledge, there are no real-time online monitoring methods that can detect early on and prevent such abnormal particle size changes for wet powder drying.

However, the authors highlighted that free-space propagation equations allowed them to relate the ensemble-averaged spatial-integral autocorrelation function to the statistics of powder surface, eg, the PSD.

Zhang *et al.* concluded: "Especially for densely concentrated wet powders, this method is the first in-line measurement, and it is easily deployable in the industrial instrument" – thus is therefore suitable for processes such as blending and milling in pharmaceutical manufacturing.

parties such as industry representatives and government partners.

Regulating artificial intelligence – industry response

Speaking in an interview with *EPR* in November 2023, Stephen Ward, Chief Manufacturing Officer for Cell and Gene Therapy Catapult, stated that global regulators are saying that biopharma needs to be embracing this technology. "I do think there is a big opportunity and people often say the regulators are a block." He considered regulators to be "very innovative and they want to engage." Ultimately, it is up to industry to give regulators the right level of certainty that it is in control and that manufacturers know what they are doing, he explained.

In October 2023, the UK industry responded to UK Prime Minister Rishi Sunak's speech on AI through the CBI, which speaks on behalf of 170,000 businesses of all sizes and sectors.

"We welcome the Prime Minister's confirmation [in his speech] that the UK [will not] 'rush to regulate' AI.

> *"While the often-mentioned existential risks from AI are certainly not imminent, it makes sense to already start considering a regulatory framework, that must be international as well as national"*

"Government must however balance the UK taking a global leadership role on 'frontier' challenges with support for immediate effective governance and adoption of AI, particularly when recent CBI analysis shows AI adoption could add £38 billion to UK GVA by 2030," Benjamin Reid, CBI Technology & Innovation Director, commented.

Dr Jonathan Aitken, an expert in AI at the University of Sheffield, urged: "We need to ensure that our education system gives people the skills they need to understand AI and also utilise the technology, so the UK develops a strong workforce who are at the cutting edge of the industry."

However, elaborating on the regulation of AI in industry, Dr Nicole Wheeler, Birmingham Fellow, Institute of Microbiology and Infection, School of Computer Science at the University of Birmingham and Turing Fellow, shared: "The speech did surface an important question – how can we regulate something we do not fully understand? This is a core challenge underpinning efforts to develop safeguards for broadly capable, continually evolving technologies. We will need mechanisms in place that move faster than government policy-making or a way to update what compliance with AI safety policy looks like in practice as technology evolves.

"While the often-mentioned existential risks from AI are certainly not imminent, it certainly makes sense to already start considering a regulatory framework, that must be international as well as national. Such a framework will be complex and require difficult-to-achieve agreements at

Digitalisation in the laboratory

"Connectivity between the laboratory and manufacturing facility is growing, and the use of digital tools will continue to build that integration. I think we'll see our labs change significantly over the next five to 10 years," Miriam Guest, former Principal Microbiologist at AstraZeneca, commented in *EPR's* article on microbiology trends in January 2023.

In terms of applying AI in pharmaceutical laboratories, Guest predicted: "We will see more guidance provided on the application of machine learning and artificial intelligence. I think it will be important that we work with our regulators to ensure activities are executed within the framework of clear guidance."

Coinciding with the UK Prime Minister's speech on AI in October 2023, a report on the capabilities and risks of frontier AI, published by the UK Government's Department for Science, Innovation and Technology, stated: "Existing frontier AI models have some ability to design and troubleshoot laboratory experiments… [however] significant barriers remain for novel laboratory work… Some of these barriers could be reduced by near-future advances in frontier AI and associated advances in laboratory automation."

Embracing AI/ML to improve manufacturing efficiency

In this short video, Anil Andrade, Vice President Global Sales, ACG World, shares examples of how ACG has been embracing cloud-based platforms and machine learning to improve operational efficiency and product quality.



Anil Andrade, Vice President Global Sales, ACG World

a global scale, so the time to start such negotiations is now," Anthony Cohn, Professor of Automated Reasoning, University of Leeds and Foundational Models Theme lead at the Alan Turing Institute, added.

"The EU [is] being much more forward-leaning in [its] approach to AI safety, and [its] regulations may well become the de facto standard that AI developers need to meet if they want to reach a global market. The UK, in contrast, [is] applying a very light-touch approach to AI governance," Dr Wheeler continued.

The UK Government's discussion paper on the capabilities and risks of frontier AI, concluded with rational optimism: "There are many opportunities from [recent developments in AI], and these can only be realised if the risks are mitigated..." Further response from Dr Wheeler on the UK Prime Minister's speech warned: "The risk landscape is going to change substantially in the coming years". Yet, the government's report *'Capabilities and risks from frontier AI'* paper affirmed: "Addressing [the risks], however, will allow us to seize the opportunity, and realise their transformative benefits."

AI's future in pharma

While AI presents exciting possibilities, it is important to recognise that challenges related to data quality, regulatory frameworks and ethical guidelines will need to be addressed for the full realisation of AI's potential in pharmaceutical product development. However, with continued advancements and collaborations between industry, academia and regulatory bodies, AI-driven innovations have the potential to revolutionise the pharmaceutical industry and improve patient outcomes in the years to come.[8]

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Entering an era of *in silico* drug development



Dr Feng Ren, Chief Scientific Officer and Head of R&D, Insilico Medicine, discusses the transformative role of AI in pharmaceutical drug development, sharing his company's journey to license an AI-produced drug candidate for idiopathic pulmonary fibrosis.

What is AI's current role in the pharmaceutical industry?

We have seen a real shift recently where pharma companies who were once resistant to using AI and machine learning are beginning to embrace these technologies. When Insilico Medicine was founded, it was a difficult task to convince pharma executives that AI could improve their processes – adding speed and efficiency to novel target discovery, providing a deeper understanding of disease and biology, and designing new potentially best-in-class therapies with optimised characteristics.

But we are in a new era with a number of AI-designed drugs progressing through later stage clinical trials and most pharma companies have adopted AI capabilities into their R&D operations. Many are still just testing the waters with these technologies, adding AI to their existing methods rather than really incorporating it end to end, but they clearly have greater confidence in its capabilities and are eager to apply it. Of course, there are a number of pharma companies that have made AI a core part of their strategy – including Sanofi, with whom we signed a strategic research collaboration last year worth up to $1.2 billion to advance drug development candidates for up to six new targets.[1]

What is the significance of the world's first AI-generated drug (INS018_055) entering Phase II trials?

Across the industry, everyone is waiting to see the first AI drug approved and on the market. Making it to Phase II is a big step in that direction. Generative AI as a technology has been around since 2020, but now there is much broader awareness of its capabilities and real validation with a several AI-produced drug candidates in clinical trials.

As this idiopathic pulmonary fibrosis (IPF) drug advances, and has begun Phase II trials

with patients, we are in the critical final stages of demonstrating that this method of finding and developing new drugs works – and it can do the work faster, better and cheaper than ever imagined. The success of this drug would mean that not only patients suffering from IPF, but from other diseases, can have new hope that AI can help speed new cures. We have 31 AI-designed drugs in our pipeline and four in human clinical trials.

Can you provide an update on the clinical development of INS018_055?

To our knowledge, Insilico's lead drug for IPF – INS018-055 - is the first drug for an AI-discovered target and designed by generative AI to reach Phase II clinical trials with patients.

AI was used in every stage of the process. Insilico Medicine used its AI target-discovery engine to process large amounts of data – including omics data samples, compounds and biologics, patents, grants, clinical trials, and publications – to discover a new target (called "Target X") relevant for a broad range of fibrosis indications. We then used this newly discovered target as the basis for the design of a potentially first-in-class novel small-molecule inhibitor using its generative AI drug design platform.

Insilico's molecule – INS018_055 – demonstrated highly promising results in multiple pre-clinical studies, including *in vitro* biological studies, pharmacokinetic and safety studies. The compound improved myofibroblast activation, a contributor to the development of fibrosis, with a novel mechanism and was shown to have potential relevance in a broad range of fibrotic indications, not just IPF.

> *"To our knowledge, Insilico's lead drug for IPF – INS018-055 - is the first drug for an AI-discovered target and designed by generative AI to reach Phase II clinical trials with patients. AI was used in every stage of the process."*

The current Phase II study is a randomised, double-blind, placebo-controlled trial to assess the safety, tolerability, pharmacokinetics and preliminary efficacy of 12-week oral INS018_055 dosage in subjects with IPF divided into four parallel cohorts.[2] To further evaluate the candidate in wider populations, the company plans to recruit 60 subjects with IPF at about 40 sites in both the US and China.

If our Phase IIa study is successful, the drug will then go to Phase IIb with a larger cohort. This is also the stage where our primary objective would be to determine whether there is significant response to the drug. The drug will go on to be evaluated in a much larger group of patients – typically hundreds – in Phase III studies to confirm safety and effectiveness before it can be approved by the US Food and Drug Administration (FDA) as a new treatment for patients with that condition. We expect to have results from the current Phase II trials in 2024.

Three areas AI can play a role

1. **Protein target identification in cancer and other diseases.** Systems are available for target identification using multiple data types. Now there is a 10x increase in data compared to what was previously available.
2. **Acceleration in the time it takes to generate novel molecules to validate these targets in disease-relevant models quickly.** It is now possible to go from a protein target with a structure to an IND-ready molecule in less than a year and to synthesise the molecules very quickly. In addition to quickly generating promising new molecules, we also have an AI-powered robotics lab that can autonomously perform experiments and help validate these molecules.
3. **Knowledge discovery and hypothesis generation.** We used about $1.7 trillion in government grants over the past 25 years as our core data source linked to everything else – including biological and chemical data and data from clinical trials and published studies. Thanks to our AI algorithms, our platform can find hidden connections between diseases and biological pathways that human scientists might miss.

What has been the biggest challenge Insilico has faced in using AI for drug development?

The biggest challenge remains overcoming remaining industry scepticism and also advocating for pharma partnerships earlier in the drug development process. We are able to produce optimised, high-quality molecules at a much faster rate and ideally want to partner early on these molecules to leverage the disease and clinical trial expertise of pharma to advance more therapies to patients in need faster.

In traditional drug discovery, it takes over 10 years and costs around $2 billion to bring one drug to market – and 90 percent of drug candidates fail during human trials. This high cost and lengthy timeline are preventing new life-saving medications from reaching patients.

> *"The biggest challenge remains overcoming remaining industry scepticism and also advocating for pharma partnerships earlier in the drug development process"*

What solutions hold most potential?

In terms of potential, technology is rapidly evolving. We believe that it will be possible to continue to integrate AI more fully into the end-to-end drug discovery and development process across the industry and to hasten personalised medicine using AI advances, from giving us a better understanding of a patient's disease risk, to identifying likely drug interactions and recommending best treatment options for a particular patient.

What does the future hold for AI as a tool for drug development?

We are continuing to incorporate the latest technological advances into our drug discovery platform to increase speed and accuracy – including AlphaFold, large language models and quantum computing. In January 2023 Insilico published a study using AlphaFold and Pharma.AI to accelerate the design of a novel drug for hepatocellular carcinoma, the most common primary type of liver cancer. It is the first successful application of AlphaFold to the hit identification process in drug discovery. The study was led by a team of international researchers and published in the journal *Chemical Science*.[3] We see great potential for continued use of the predicted protein database with our platform.

And in another international collaboration, Insilico also published a study combining quantum computing with generative chemistry to generate new molecules. It is the first step in what we believe will be the future of drug discovery and was published in the *Journal of Chemical Information and Modeling*.[4]

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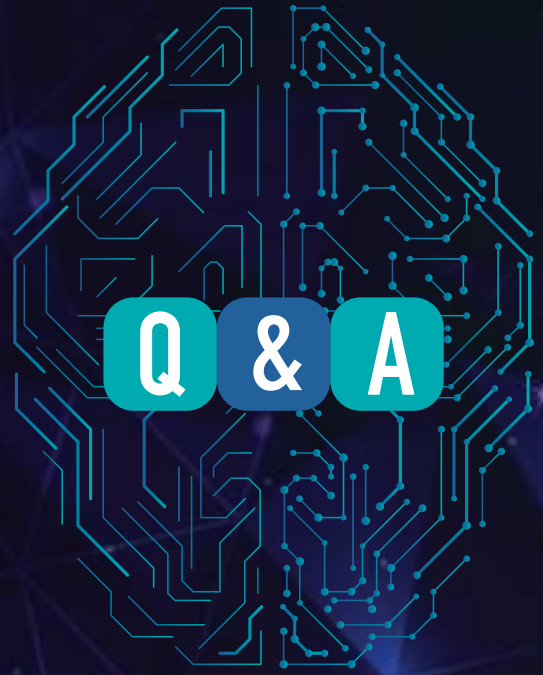
Feng Ren, PhD

Dr Feng Ren is Chief Scientific Officer, Executive Director and Co-CEO of Insilico Medicine. He received his PhD degree in chemistry from Harvard University in 2007. He then spent 11 years in the discovery and development of small molecule innovative drugs at GlaxoSmithKline (GSK), where he served as the principal scientist, programme leader, director and head of chemistry of Neurodegeneration DPU, a global drug R&D unit in neurosciences in GSK. In 2018, Dr Ren joined Medicilon, a contract research organisation (CRO) as Senior Vice President and head of the drug R&D service business of the Chemistry Department and Biology Department with over 600 chemists and biologists.

Exchanging trial and error for transformative technology



Using key findings from the UK Government's interim report on AI, one of the report's contributors, Andrew Hopkins, Founder and Chief Executive of Exscientia, envisions how artificial intelligence could shape drug development in the rapidly transforming pharmaceutical industry.

What was the most significant finding from the UK House of Commons Science, Innovation and Technology Committee's interim report on the governance of AI? How could this impact the pharmaceutical industry?

First, it is significant that a report of this nature – comprehensively outlining the potential of artificial intelligence (AI) and the most significant challenges related to its governance – has come to fruition.

In terms of the Committee's findings published in *The governance of artificial intelligence: interim report*,[1] I'm pleased that it recognises AI's potential to reduce drug development costs and bring personalised medicine closer to patients. As I shared during my testimony to the House of Commons Science and Technology Committee in March, if we as a society do not embrace AI now – ie, the possibility of better decision-making and better information it brings – we are choosing to lock ourselves into outdated ways of working. The biopharma industry has historically used a risky and costly process of trial and error, in which it often takes 10 to 15 years to develop new drug candidates, most of which fail in the latest, most expensive stages of development. AI offers a way to develop better drugs, faster, and the time to do this for patients is long overdue.

> *"AI is powerful and as its use grows, access to large datasets will be an obstacle for some"*

Another significant finding, from my perspective, is the report's recognition that "access to data" represents a key challenge to the future of AI. AI is powerful and as its use grows, access to large datasets will be an obstacle for some.

The Committee used this report to inform the UK AI Safety Summit in November 2023, so I anticipate it will be a foundational document that will guide the field and the UK in setting up frameworks that allow AI to benefit our society.

How is the rise of AI affecting the current market?

Over the past few years, we have seen the industry embrace AI and machine learning (ML) technologies in ways it never has before. Overall, this is positive for the industry. To shed light on how monumental a shift this is, when Exscientia began its work in 2012, there was significant scepticism in the biopharma industry about the disruptive nature of AI and ML. The technologies went largely unadopted at the time. However, now many – if not most – companies are embracing AI in some capacity to inform research and development (R&D). With this new enthusiasm, we are seeing more and more drug candidates come to the clinic for study in humans; for example, Exscientia itself brought four to clinical stage this year, which means we are closer to realising the promise of AI.

That said, there are numerous obstacles for the pharmaceutical industry to overcome to fully embrace AI. One of the biggest challenges is the industry's overly narrow view of this innovative technology. Many companies focus solely on the potential of AI to speed up drug R&D. This is an important benefit of AI and a win for patients who do not have 10 to 15 years to wait for new therapies. Yet AI – if applied more comprehensively as part of an end-to-end platform and integrated with automation – is more than that.

Additionally, with a few exceptions, many companies are applying 'add-on' AI technologies to discrete aspects of their drug discovery and development work. So, while industry's adoption of AI is exciting and welcomed, an end-to-end approach ultimately is needed to disrupt the landscape of drug development.



> *"Many companies focus solely on the potential of AI to speed up drug R&D. Yet an end-to-end approach ultimately is needed to disrupt the landscape of drug development"*

What is the most exciting potential use for AI in late-stage drug development?

At present, most AI-designed candidates are in early to mid-stage trials. For example, at Exscientia, our own wholly or partially owned candidates are currently in Phase I/II trials.

However, there are several key areas with exciting potential in late-stage development.

First, because of AI, we can now reach later-stage trials more quickly and increase the probability that they succeed. The current failure rate in drug development is 96 percent and that failure often takes place in late-stage trials.[2]



It is also important to note that as perhaps our nearest-term potential, AI offers the possibility of making personalised medicine a reality.

At Exscientia, we are currently working to explore the validity of our precision medicine platform in other tumours, aiming to strengthen trial design for our prospective later stage trials as well as to ultimately bring new innovative treatment options to those patients who may benefit most from these future therapies.

What role do you predict AI will have in the industry in ten years?

We see 2023 as a formative year in the industry's journey to adopting AI and its role in the discovery and development of the next generation of medicines. At Exscientia, we predict that all drugs will be designed by AI by 2030 and we are energised by witnessing the field already moving in this direction and embracing AI as an increasingly critical tool.

At Exscientia, we will be complementing AI with automation, so we can bring discovery and laboratory studies closer in sync.

We want to not only increase the probability of success, but also accelerate the time needed to turn science into medicines and to lower costs. Our strategy is to shift the investment return curve of new drugs and reset the industry's economic model.

We are just scratching the surface of what AI can do. By pioneering a new approach to medicine creation using AI, the best ideas of science can rapidly become the best medicines for patients.



Andrew Hopkins

Andrew Hopkins is the Founder and Chief Executive of Exscientia plc, a precision medicine company pioneering the use of artificial intelligence (AI) and machine learning (ML) to design new drug candidates. In this role, he led the teams that discovered the first AI-designed drugs to enter human clinical trials.

Andrew holds an honorary professorship at the University of Dundee, where he previously held the Chairs of Medicinal Informatics and Translational Biology. He served as Director of the Scottish Universities Life Science Alliance and co-founded the European Lead Factory. Prior to the University of Dundee, he spent a decade at Pfizer leading various informatics groups. Andrew received his DPhil in biophysics from the University of Oxford and LLD from the University of Dundee.

In 2023, Andrew was elected for life as a Fellow of the Royal Society, as well as a Fellow of the UK Academy of Medical Sciences in recognition of "exceptional contributions to science." Also in 2023, Andrew featured on the inaugural TIME100 AI list of most influential people in AI.

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Augmenting clinical trials with AI: from design to data analysis



Artificial intelligence can help transform efficiency and effectiveness of clinical trials. Yet as Tero Laulajainen, Vice President at UCB, elucidates here, human expertise remains essential in this process.

Q & A

What are the main benefits of AI for late-stage drug development?

AI brings several benefits to the table in late-stage drug development, the most prominent of which is its potential to improve clinical trials through data collection and analytics.

Specific enhancements include overall efficiency and effectiveness of the clinical trial process, given that AI can be used to analyse patient data, predict patient responses, and quickly identify patterns. This aids in participant selection, outcome prediction, and real-time treatment monitoring, expediting trials and enhancing accuracy while reducing errors.

Additionally, AI can automate data collection in large clinical trials. This allows for continuous and real-time monitoring of patients, leading to the generation of more accurate and comprehensive datasets. AI algorithms, especially machine learning and deep learning models, can analyse vast amounts of data more quickly and accurately than traditional statistical methods. They can identify patterns and correlations in the data that might not be apparent to human analysts, thereby improving the accuracy of predictions about a drug's efficacy and tolerability.

It is my view that to be able to better understand the full benefits of AI, we need to partner with leading technology companies. A good example was our Microsoft collaboration. Within our partnership, we were able to benefit from Microsoft's expertise and learned how to better leverage the benefits of AI. The pharmaceutical industry needs to not only invest in AI technologies but also continue to build partnerships with those who are at the forefront of AI developments. As an industry, it

is also up to us to address challenges related to data privacy and security to ensure the quality and diversity of the data used for AI training.

Are there current drawbacks of AI in late-stage drug development? How can the pharma industry work to make them advantageous?

While AI offers numerous advantages, as with any rapidly developing technology, it poses some challenges as well:

- **Understanding the complexity of a task:** AI may need support from scientific experts to fully understand the complexity of certain tasks, despite advanced tools, requiring ongoing improvement. We should collaborate with AI, combining human expertise with its foundation to accelerate goal achievement. We should aim to develop better AI models for predicting human responses and invest in richer human data like real-world evidence for AI training.
- **Data challenges/limitations:** One of the drawbacks of using AI in late-stage drug development is the challenge with data. The scale, growth and diversity of the data can pose a problem. AI algorithms require large amounts of high-quality, diverse and well-labelled data to train effectively. However, such data may not always be available or easily accessible due to privacy concerns, proprietary restrictions, or simply the lack of such data in specific areas.

Moving forwards, we must invest in simplifying the technology for end users. We need to create user-friendly interfaces that can make complex AI tools accessible to a broader audience, including those who are not currently confident in their technological prowess.

Collaborating with large tech companies can also help in bridging the gap between technology and pharmaceutical companies, ensuring a patient-centric approach. It will also enhance data collection and annotation, as well as develop advanced AI models for



Can AI help improve clinical trials diversity?

Historically, certain demographics such as ethnic minorities or the elderly have been underrepresented in clinical trials. However, the integration of AI can play a crucial role in tackling this disparity, according to UCB Pharma's Chief Medical Officer Iris Loew-Friedrich.

Notably, AI has the potential to identify gaps in representation and offer strategies to promote diverse participation. By incorporating a more comprehensive range of individuals in clinical trials, researchers can obtain valuable insights into the efficacy and safety of drugs across various populations. Using real-world data and social media content, AI can identify eligible participants from diverse populations, considering factors like demographics, health records and genetic information.

Click or scan the QR code to read our full interview with Iris Loew-Friedrich:

better predictions. Together we can collect richer human data like real-world evidence for AI training.

What is the best approach for using AI to enhance pharmaceutical data selection and validation?

The best approach is to combine the power of AI with human expertise. While AI can process vast amounts of data quickly and identify patterns, the human element is essential for understanding the nuances and making final decisions.

Successful implementation of AI in drug development requires careful attention to data management, algorithm training and validation, and predictive modelling, all of which requires human input.

For instance, when selecting investigator sites, AI can provide a list of potential investigators, but human judgment is crucial to read between the lines and make the final selection.

Collaboration with tech leaders in the AI field can also help refine algorithms and ensure they are tailored to industry-specific needs.

What do you predict the next technology disruptor for the pharmaceutical industry will be in ten years?

There are lots of exciting and new technologies that are entering the pharmaceutical industry, from quantum computing to 3D printing

Seven ways AI is impacting R&D within the pharmaceutical industry

The integration of AI is significantly impacting research and development in many different and diverse ways, with the greatest impact being made in several key areas:

CLICK TO VIEW 1

ACCELERATING DRUG DISCOVERY

AI and machine learning algorithms can sift through vast amounts of data, including genetic information and compounds, to identify potential drug candidates quicker than traditional methods.

CLICK TO VIEW 2

INFORMING FUTURE RESEARCH

By analysing past and present trial data, AI can provide insights for future research and suggest better study designs. Additionally, machine learning algorithms can learn from existing data to predict outcomes and inform decision-making.

CLICK TO VIEW 3

IMPROVING SUCCESS RATES

The drug development process is notoriously risky, with many potential drugs failing in clinical trials. AI has the potential to improve success rates by using predictive models to identify likely outcomes based on preclinical and clinical data.

CLICK TO VIEW 4

ENHANCING EFFICIENCY AND SPEED

AI has the ability to shorten drug development timelines and cut costs by streamlining discovery, enhancing clinical trial efficiency, and speeding up patient recruitment.

CLICK TO VIEW 5

IMPROVING PATIENT MONITORING

AI algorithms can continuously monitor patient data, which helps identify potential issues at an early stage. This should in turn lead to better patient safety and more efficient drug development.

CLICK TO VIEW 6

PREDICTING DRUG EFFECTS

AI can be used to predict the effects of drugs on the human body, including potential side effects. This can help researchers to identify and mitigate risks earlier in the drug development process.

CLICK TO VIEW 7

LOCATING TARGETED PATIENT POOLS

AI can analyse large amounts of disease and region-specific healthcare data to locate targeted patient pools for clinical trials. This makes patient recruitment more efficient and accurate.



AI can provide a list of potential clinical trial sites, but human judgment remains crucial.

and digitalising biology at the molecular level. All have the potential to disrupt the pharmaceutical industry.

In terms of AI, we still have a lot more to gain from this technology. Its potential for further development and advancement is immense. As technology evolves, more data becomes available, and our own knowledge of diseases and biology grows, I expect AI models will become more sophisticated and accurate, leading to even greater advancements and disruption for the industry.

Additionally, two evolving technologies that have the potential to disrupt the pharmaceutical industry are 'blockchain' and 'tokenization'. Blockchain can provide secure, transparent and efficient methods for tracking and verifying drug supply chains, ensuring data integrity and managing clinical trials. Tokenization has emerged as a valuable solution to accurately link real-world patient data while maintaining patient privacy.

Predicting the exact trajectory of technological disruption for pharma is challenging; several potential developments could significantly impact the industry and beyond. However, when we look into the future, I would like to see a blend of automation, digitalisation and AI-driven processes complemented by human expertise; particularly in areas requiring personal interactions, like patient groups and investigator interactions. This blend of technology and human touch will ensure that our approach remains patient-centric, fostering innovation and strengthening continuous partnerships across the board.



Tero Laulajainen

In his current role, as Head of Global Clinical Science and Operations at UCB, Tero provides leadership for clinical programme delivery, clinical project management, medical writing, strategic clinical partnering, site and patient engagement, as well as clinical data and innovation teams.

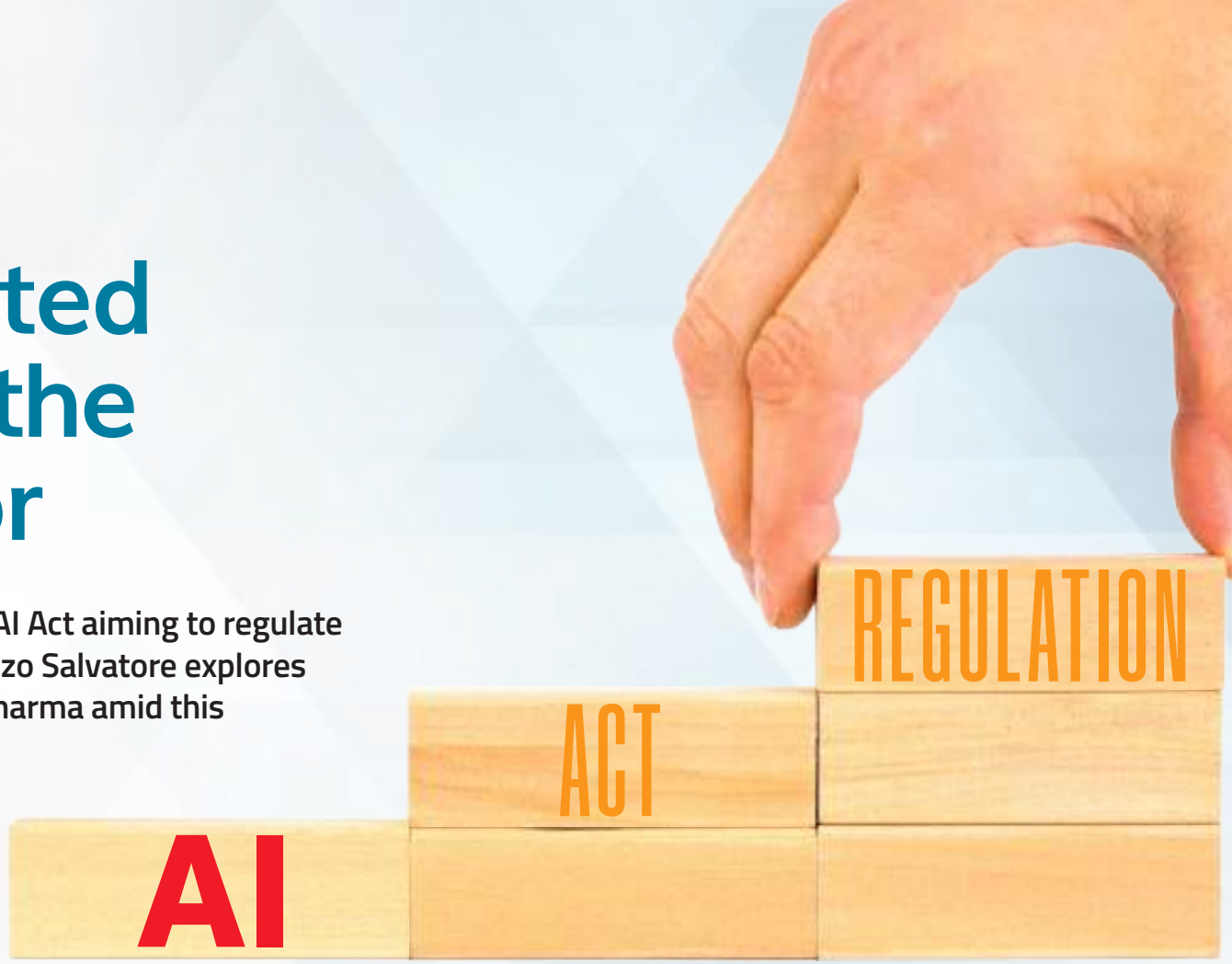


Iris Loew-Friedrich

Iris is Chief Medical Officer for UCB Pharma, a member of the company's executive committee and head of development solutions. She provides strategic global leadership for worldwide clinical development, medical affairs, regulatory affairs, quality assurance, statistical innovation, real-world evidence and patient safety/pharmacovigilance.

Facing AI-related challenges in the pharma sector

With the European Commission's proposed AI Act aiming to regulate artificial intelligence use, legal expert Vincenzo Salvatore explores potential opportunities and challenges for pharma amid this transformative landscape.



The EU's ambition to play a leading role in setting trustworthy regulatory standards and to ensure excellence in the use of artificial intelligence (AI) led the European Commission to propose, on 21 April 2021, the adoption of a regulation laying down harmonised rules on AI applicable throughout the 27 EU Member States (AI Act).[1]

Now that the age of AI appears to be on the cusp of launching, the Commission's proposal has garnered newfound attention.

The proposal addresses the risks generated by certain uses of AI through a set of complementary, proportionate and flexible rules. More specifically, the proposed legal framework lays down:

(a) harmonised rules for the placing on the market, the putting into service and the use of AI systems in the EU
(b) prohibitions on certain AI practices
(c) specific requirements for high-risk AI systems and obligations on their operators
(d) harmonised transparency rules for AI systems intended to interact with natural persons, emotion recognition systems and biometric categorisation systems, and AI systems used to generate or manipulate image, audio or video content
(e) rules on market monitoring and surveillance.

The proposal takes a clear, easy-to-understand approach based on four different risk levels: unacceptable risk, high risk, limited risk and minimal risk.

AI systems that present unacceptable risks would be prohibited. A wide range of high-risk AI systems would be authorised but would be subject to a set of requirements and obligations in order to gain access to the EU market. The list of prohibited practices comprises all AI systems whose use is considered unacceptable for contravening EU values, for instance by violating fundamental rights.

The prohibitions cover practices that have a significant potential to manipulate people through subliminal techniques beyond their consciousness or exploit vulnerabilities of specific vulnerable groups, such as children or people with disabilities, in order to materially distort their behaviour in a manner that is likely to cause them or another person psychological or physical harm. Other manipulative or exploitative practices affecting adults that might be facilitated by AI systems could be covered by existing data protection, consumer protection and digital service legislation that guarantee people are properly informed and have free choice not to be subject to profiling or other practices that might affect their behaviour. Only AI systems that present a limited risk would be subject to very light transparency obligations.

Opportunities for AI in the medicines industry

Once adopted, the proposed regulation will be applicable across the board – ie, not only to the health sector but also to any other industrial/business sector.

Nevertheless, AI's impact on the health sector is expected to be massive, if not revolutionary.

> *"The benefits stemming from the use of AI have been highlighted across the entire lifecycle of medicinal product development"*

Indeed, opportunities to apply AI occur at all stages of a medicinal product's lifecycle, and AI systems and machine learning technologies (which constitute part of AI) can be widely used to diagnose, treat, prevent and monitor medical conditions and diseases.

AI increases the potential for healthcare professionals to better understand their patients' patterns and symptoms because it offers access to broader datasets; it therefore provides better feedback, guidance and support to healthcare professionals and caregivers.

The benefits stemming from the use of AI have been highlighted across the entire lifecycle of medicinal product development – from target validation to identification of biomarkers, annotation and analysis of clinical data in trials, pharmacovigilance activities, and clinical use optimisation.

AI also could conceivably enable treatments and medicinal product development to be tailored to specific patient needs, not to mention enhance engagement with healthcare stakeholders and users.

Finally, AI systems have the potential not only to relieve healthcare systems – especially medical staff – by supporting routine tasks such as patient transport and medication reminders for patients, but also to address the challenges posed by rapidly ageing populations.

Potential regulatory challenges, as highlighted by ICMRA

As highlighted by the International Coalition of Medicines Regulatory Authorities (ICMRA), this range of applications brings with it regulatory challenges, including the transparency of algorithms and their meaning, the risks associated with AI failures and the wider impact those would have on AI's uptake in pharmaceutical development and ultimately on patients' health.[2]

Another factor to consider is that, in principle, AI systems appear suitable for the detection of safety signals.

The added value of AI-assisted pharmacovigilance compared to traditional

safety monitoring activities is that AI uses sophisticated algorithms to extract useful information from the huge amount of real-world healthcare data, dramatically improving data collection and assessment speed and accuracy thanks to its learning and intrinsic self-correcting capability. In fact, it has been noted that the current signal detection and management tools have a heavy manual component that may be hard to sustain in the future, partly due to the growing data from increased adverse drug reactions reported worldwide.

The challenge in implementing AI solutions will lie in striking the right balance between AI and human oversight of signal detection and management, which may vary according to the risk associated with the medicinal product(s) concerned. In any case, such AI use has the potential to discover safety signals that are more difficult to detect with current methods, such as drug-drug interactions, drug-disease interactions, medication errors, secondary malignancies, changes in frequency and severity of known events, patterns of use in medications, and misuse.

Regulatory guidelines should be developed to ensure a transparent and trustworthy environment for AI development and use in the healthcare sector and to address and govern several sensitive issues, including data provenance, reliability, comprehension and validity (construct, content, external, etc), pharmacovigilance purposes, real-world performance and monitoring.

Regulatory authorities indeed appear to be going in this direction and pursuing this goal, as evidenced by the European Medicines Agency's recent (draft) reflection paper on the use of AI in the medicinal product lifecycle,[3] the US Food and Drug Administration's discussion paper on AI in drug development,[4] and the World Health Organization's recent publication listing key regulatory considerations on AI for health.[5] Expected feedback from different stakeholders will certainly help better determine and fine-tune the applicable legal framework.

The impact of the EU AI Act

Despite some hiccups in the EU legislative process currently involving the European Parliament and the Council – indeed, the difficulties of reaching a final agreement on the proposed text are evidenced by the request for a code of conduct that would allow companies to self-regulate rather than abide by a previously proposed tiered recognition model, not to mention the divergences on the proposed approach for foundation models – the EU AI Act is likely to be adopted in the next few months.

Its entry into force will require both pharmaceutical companies and regulators to further adjust their working methods in order to keep pace with revolutionary AI technologies. It will take the best efforts of all parties to strike the right balance between human intelligence and AI in order to obtain the greatest possible benefit for patients' health.

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Vincenzo Salvatore

Vincenzo Salvatore is of counsel and leader of BonelliErede's Healthcare and Life Sciences Focus Team.
He joined the firm in 2015, bringing with him unrivalled regulatory and compliance expertise in clinical trials, marketing authorisation procedures, pharmacovigilance, promotion and marketing of medical devices, inspections and enforcement.
Vincenzo is also Full Professor of European Union Law at the University of Insubria and was Head of Legal Service at the EMA from 2004 to 2012.

Simplify, standardise, digitalise to transform manufacturing

Here, Sanofi's Brendan O'Callaghan explores how advances in digital technology, partnerships and new ways of working are supporting manufacture and delivery of medicines for patients across the globe.



With over 90,000 employees across the globe, Sanofi supplies over 5 billion doses of medicines and vaccines every year, supporting the health needs of millions of patients in more than 170 countries. The company's ambition is to build a modern, industry-leading manufacturing network, by bringing together talented people and cutting-edge processes, technologies and data to reliably deliver high quality, affordable and sustainable medicines and vaccines to patients.

Simplify

In a global company built from many mergers and acquisitions (M&As) over the years, Sanofi has inherited many different legacies, including mindsets, ways of working and a wide variety of systems, applications and processes. On the data front, we have successfully generated and collected data from numerous applications; however, we have fallen short on sharing data across the organisation and deriving insights. We have had many different and incompatible data solutions, adding a technical complexity to the equation.

To address this, we're focused on two aspects: mindset and tools. First, we are adopting an agile mindset across the business: in 2021, we upskilled over 16,000 Sanofi employees – with courses offered for different levels, with an emphasis on an agile mindset, not just the methodology. This new shared knowledge is what allows us to innovate faster today. Second, we developed with a partner a mobile application called Plai, that displays our key performance indicators (KPIs) across the company, from research to manufacturing to commercial. Plai has been

a driving force to glean the relevant and important data, embrace data transparency and become a more data-driven organisation adept at generating and analysing the wealth of data at our fingertips. We have created an environment where we can celebrate successes and discuss areas of improvement across the board, without functional silos. We even incorporated a layer of gamification to motivate our leaders to improve KPIs.

While the technical solution behind Plai is relatively straightforward – albeit involving a lot of work – catalysing the cultural shift, a key driver for collective success, is not as straightforward. While there was some initial reluctance about sharing KPIs across the company – some employees were concerned about a loss in autonomy and an increase in top-down monitoring – our employees soon began to see data transparency as an opportunity. For example, a manufacturing site leader can see positive trends at another site, connect with peers and apply the learnings to improve his/her own team's performance. Each site is strong, but our network is even stronger once we collaborate and work together with a 'One Sanofi' mindset and common datasets.

Standardise

Sanofi is also partnering with the McLaren Formula One team to help standardise processes, streamline performance and advance our ability to innovate. Through this close collaboration between the McLaren team and our digital, manufacturing and supply teams, we are accelerating the efficiency and performance of our global network to attain world-class standards of manufacturing excellence. By embracing its racing spirit, McLaren brings experience in precision engineering and data analytics to help us optimise performance for better throughput and capacity utilisation.

Another example, the deployment of electronic batch records enabling



> *"In the future, predictive artificial intelligence (AI) will monitor every step in our manufacturing processes"*

computer-assisted batch reviews, has led to a decrease in batch review cycle times from 10 to two days. With such improvements, we can be more reliable, efficient and effective suppliers, maximising the reach of our medicines and vaccines to patients.

Digitalise

This is only the beginning – our ambition is much bolder. In the future, predictive artificial intelligence (AI) will monitor every step in our manufacturing processes. Through machine learning (ML) it will feed back into the system and simultaneously adjust or improve based on real-time data inputs. We will build self-healing processes where data and algorithms can influence and optimise our operations in real time without human intervention. Collecting precise data will be key in producing optimum yield, avoiding potential disruptions, and producing more of our medicines, faster, more reliably and at higher quality for the benefit of patients.

Data generated in our plants serves more than just our manufacturing operations. We share this data with the wider organisation through our internal, AI-driven search engine called OneSearch. This enables employees from across the company to tap into manufacturing and other relevant datasets, enabling smarter, data-driven decision making, to ensure the best actions are taken for all activities of our value chain, from R&D to commercial.

Democratising data – from accessibility to insights to automated action – has been a key step in our digital transformation, creating a successful digital organisation that enables us to do more for patients.

We are applying the same digital and data transformation across the board.

For example, in R&D we use data and AI to find new targets; design new molecules, messenger RNA (mRNA) sequences and lipid nanoparticles (LNPs); automate several processes based on sophisticated image recognition; and leverage digital twins to design, implement, qualify and operate modular operating lines at our Evolutive Facilities (EVF) in France and Singapore.

> *"Democratising data – from accessibility to insights to automated action – has been a key step in our digital transformation"*

As another example, we have standardised our key commercial applications across the globe – a Herculean task. We are now able to innovate at speed and at scale, using data and AI to suggest the best content on the best communication channel to our healthcare professionals (HCPs), have a real-time, 360 view of HCP engagement, and find new HCPs that have patients that could benefit from our treatments.

The digital transformation journey is not an easy one. We are taking ambitious steps to simplify, standardise and digitalise a large multinational company working in a highly regulated industry. Moving from an individual to collaborative mindset within an organisation built on a history of M&As provides an added challenge.

As an industry, we have an obligation to do the best by all the patients we serve. To achieve this, we will continue to collaborate openly across our digital and manufacturing teams to build a data-driven network that is constantly improving.



Brendan O'Callaghan

Brendan leads Sanofi's international network of manufacturing sites. His ambition is to enable successful commercialisation of Sanofi's diverse pipeline, to build world-class standards of manufacturing and supply chain excellence and to future-proof Sanofi's manufacturing network, leveraging the latest digital, process and technology solutions, to ensure the continued reliable supply of essential, high-quality medicines and vaccines to patients worldwide.

Footnote

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Enhancing contamination control methods: how AI is shaping microbiology and QP oversight

Modern microbiological methods and contamination control approaches are being enhanced by artificial intelligence (machine learning in particular). The aim is to speed up analysis; increase accuracy; avoid error and introduce a level of automation. Examples include tracking contamination, verifying cleaning and disinfection, microscopy, colony counting, and microbial characterisation and matching, many of which are based on improvements in image analysis. Bio Products Laboratory's Dr Tim Sandle explores further.

Artificial intelligence (AI), or more specifically machine learning (ML), is used in many aspects of microbiology, including microbial classification problems, studying the interaction between microorganisms and the surrounding environment, and for microscopy. This article reviews some recent developments in this emerging field. While more progress has been made in the clinical microbiology space, these emerging technologies have the potential to re-shape aspects of rapid microbiology within the pharmaceutical and healthcare sectors too and assist with enhancing qualified person (QP) oversight of pharmaceutical manufacturing.

Machine learning

The subject of ML often has an air of mystery, given the concept of an 'intelligent' computer. While ML is fast and a well-designed and trained algorithm capable of delivering new insights; the concept can more easily be viewed as a "thing labeller; taking your description of something and telling you what label it should get".[1] Through this, instead of the classic computing approach of providing explicit instructions, the user programs an algorithm with examples and the algorithm proceeds to find patterns in the data; transforming these into information and instructions that

the user would likely not have found themself. The process is advanced in the initial stages by users guiding the algorithm as it learns what is correct and incorrect.

Machine learning is applied to microbiology at various stages of the development curve, including sample processing (pre-analytical, analytical and post-analytical process management), sample tracking, image acquisitions systems, smart incubation and workstation operation. There have also been advances with earlier detection of growth in broth and with headspace analysis, which require rapid accuracy, precision, and limit of detection analyses. Many of these have been designed to address issues of human error that arise from fatigue, high work volume that needs to be processed in a short time, and task repetition;[2] thus overcoming some of the data integrity concerns that affect microbiology. Another area of application is drug development, especially with the design of new antimicrobials where ML can help to progress computationally intense problems such as predicting drug targets against specific microorganisms.

Contamination control

Artificial intelligence has the ability to gather more data about the manufacturing process, and contamination control measures in particular, and such data can help to increase assurance for the QP that contamination control steps have been followed. This includes using algorithm-powered hand sanitisation stations to prompt when personnel should disinfect their gloved hands and also record when this is undertaken and for how long. Such information can be used to support important parts of the batch record, such as with aseptic processing. More sophisticated tools can be used to undertake risk assessments of the flow of personnel and materials through the facility, where data inputs such as removing layers of wrapping can be inputted, and computer software used to identify any gaps thereby enabling the contamination control strategy to become enhanced.[3]

> *"Machine learning is applied to microbiology at various stages of the development curve, including sample processing, sample tracking, image acquisitions systems, smart incubation and workstation operation"*

Characterisation and classification

In recent years, microbial sequencing has advanced through high-throughput sequencing technology, which has served to generate massive quantities of microbial data. While the majority of microbial methods performed in microbiology laboratories are phenotypic (biochemical or proteomic based), genotypic methods can prove useful for assessing sterility test and media fill failures, and for tracking the route of contamination as part of a contamination control strategy. Generally, but not exclusively, this is an outsourced activity (an 'as a service' concept provided over a network). However the task is undertaken, the ability of ML to find patterns has the potential to make a significant contribution to understanding types of microbial contaminants, their origins, and the relationship between organisms isolated in different areas or from different sources.[4] This requires a mixture of supervised (for classification) and unsupervised (for pattern clustering) approaches to ML. An example is random forest, which combines the output of multiple decision trees to reach a single result.

The advantage of ML is rapid detailed pattern analysis that cannot be easily achieved using conventional databases or spreadsheets.[5] An example of the ML approach is the placement of microorganisms into operational classification units such as grouping microorganisms according to the similarity of their DNA sequences. For contamination considerations and understanding batch release risks, the main goal is to determine whether an unknown microorganism belongs to a specific species or not and whether two or more unknown organisms are related (or where an unknown organism is related to an organism previously characterised). This may reveal, for example, that microbial



> *Microscopes enhanced with AI have the potential to aid microbiologists' examination of organisms and use the collected data for diagnosis or root cause analysis*

isolate A found on a machine bed within a Grade A zone matches microbial isolate B found from the finger plate of the operator who set up the filling line, and perhaps that the same operator recently recovered the same matched organism from an exit gown plate.

A different approach considers microbial interactions, such as predicting co-operative and competitive relationships within the same microbial population. Understanding the likelihood of interactions centred on neutralism, commensalism, synergism, mutualism, competition, amensalism, parasitism and predation,[6] can indicate the likelihood of biofilm formation within a water system, for example, and help to predict the frequency of preventative treatments like sanitisation.

As well as genotypic identification, ML also has the potential to advance the analysis of matrix-assisted laser desorption-ionisation/time of flight mass spectrometry (MALDI-TOF) data, thereby applying AI to improve phenotypic characterisation.[7]

> *The advantage of ML is rapid detailed pattern analysis that cannot be easily achieved using conventional databases or spreadsheets*

Microscopy

Microscopes enhanced with AI have the potential to aid microbiologists' examination of organisms and use the collected data for diagnosis or root cause analysis. In a study, microbiologists at Beth Israel Deaconess Medical Centre have demonstrated that an automated AI-enhanced microscope system is "highly adept" at identifying images of bacteria quickly and accurately.[8]

The process involved using an automated microscope designed to collect high resolution image data from microscopic slides. The researchers trained a convolutional neural

network (CNN) for the assessment. A CNN is a class of artificial intelligence modelled on the mammalian visual cortex. The CNN was used to analyse visual data and categorise bacteria based on their shape and distribution. The characteristics assessed represented common bacterial morphologies, including rod-shaped bacteria and coccoidal, the round clusters indicative of *Staphylococcus* species and the pairs or chains indicating *Streptococcus* species.

> *"Advances in visual assessments of images using ML have led to new image systems with higher sensitivity"*

The process of training was gradual, involving multiple images. This began with an unschooled neural network that reviewed more than 25,000 images from samples. By cropping these images, where the bacteria had previously been identified by human microbiologists, the research team generated more than 100,000 training images. Over time, the machine intelligence learned how to sort the images into the three categories of bacteria (rod-shaped, round clusters and round chains or pairs). At the end of the exercise, almost 95 percent accuracy was achieved.

For the subsequent phase of the study, the researchers challenged the algorithm to sort new images from 189 slides without human intervention. Overall, the algorithm achieved a 93 percent accuracy across all three categories. With further development and training, it is hoped this form of AI-enhanced platform could be used as a fully automated classification system in the future.

As additional functionality, the images can be sent remotely for microbiologists located in other parts of the world or shared directly with the QP.



Colony counting

Colony counting may sometimes appear straightforward, but evidence shows that errors can happen either through failing to spot colonies due to their appearance, or fatigue.[9] Advances in visual assessments of images using ML have led to new image systems with higher sensitivity. Such high resolution image analysis systems can detect small and mixed colonies, which a human eye cannot.

An effective, automatic and AI-driven colony counter should be capable of the following functionality:[10]

- Standardised and accurate results. Accuracy is important since colony counting can be affected by numerous parameters related to the physical properties of the colony: size, shape, contrast and overlapping colonies. Achieving this requires automatic colony separation (for when colonies are positioned close to each other)
- Counting colonies within appropriate parameters (such as down to 50 microns and measuring zones accurately to 0.5mm, within detection limits of 0.1mm)
- A good optical response performance (sufficient control of the background noise, contrast, resolution, etc) of the image acquisition tools

- Effective image resolution, file size/ data management, sample lighting and instrument uniformity
- Ability to visualise white light and fluorescent colonies
- The ability to differentiate between chromatic and achromatic images and thus deal with both colour and clear media
- Ability to separate aggregated colonies
- Ability to count the entire plate or sectors of the plate
- Obtain results within one second per plate
- The display of real-time full-colour on screen images
- Zoom function for looking at smaller colonies
- Software to allow for data collection and analysis. Data should ideally be transferrable to a laboratory information management system (LIMS).

Machine learning applications for colony counting are not completely reliable, although technology is progressing. The main obstacles are low image resolution; high CFU density; background noise; artifacts on the dish's boundary; and CFUs located close to the boundary of a Petri dish.[11] These issues are being addressed through repeated patterns of learning. The ML approach can also be used for other types of image analysis including cell staining.

Summary

Applying ML to microbiological analyses can make tasks quicker and more accurate. In conjunction with automation, this can also lead to rapid microbiological methods that can help to overcome tedious, slow and error prone process. There will be barriers to the use of some of the technologies, necessitating conversations with regulators and addressing the concerns of laboratory analysts who are used to doing things in certain ways and with making certain decisions. Microbiologists and QPs may need to better understand perception, know-how and infrastructure relating to all aspects of data handling. While these issues must be addressed, they are not insurmountable challenges. ML will be driven by access to data; in particular, accessing large, structured, interoperable and interconnected datasets. This article has presented a few examples of the ML applications that are further advanced. Ideally, in a few years' time, these methods will be established and new technologies presented.

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Leveraging generative AI in quality control: a paradigm shift in the pharmaceutical industry

Phoebe Clough, an experienced Qualified Person, discusses some of the main ways generative artificial intelligence can help support pharmaceutical quality control.

The integration of generative artificial intelligence (AI) in quality control (QC) marks a transformative era in the pharmaceutical industry. This technological leap represents a fundamental shift in QC processes, where innovation is no longer optional but essential. Generative AI's versatile

applications extend from learning and development, standardisation, automation, laboratory design and layout, as well as real-time process monitoring and risk management, embodying a new era of efficiency and accuracy. This article delves into these applications, emphasising the importance of robust validation and regulatory compliance to ensure AI implementations meet operational standards of excellence.



Learning and development

QC analysts are the backbone of the pharmaceutical industry, ensuring the safety and efficacy of products. Traditional training methods, while effective, can be time-consuming and resource intensive. Generative AI can revolutionise this aspect by creating personalised training modules. These AI-driven programs can adapt to the learning pace and style of each analyst, making the training process more efficient and effective. Furthermore, AI can simulate complex analytical methods, allowing analysts to gain hands-on experience in a virtual environment. This dynamic approach not only accelerates the learning curve, equipping QC personnel with both theoretical knowledge and practical skills to reduce the risk of errors in a real laboratory setting, it also helps foster a competent and agile workforce ready to tackle the challenges of the evolving QC landscape.



Standardisation and automation of routine tasks

Routine tasks, such as data entry, analysis, audit trail assessment, trend analysis and report generation, are integral yet time-consuming aspects of quality control. Generative AI can automate these tasks, bringing increased efficiency and accuracy. This automation also enhances data integrity, reduces human errors and delivers more consistent QC operations, allowing quality control professionals to focus on more complex and value-added activities, ultimately enhancing the unit's overall productivity and effectiveness.



Laboratory and OOS investigations

In the event of laboratory investigations and out-of-specification (OOS) results, rapid and accurate investigations are crucial. Generative AI can assist by quickly analysing vast datasets to identify potential causes of OOS results. It can also suggest corrective and preventative actions based on historical data trends, thereby reducing the time taken to resolve such issues and minimising their recurrence.



Quality risk assessments

Quality risk management (QRM) is a critical component of quality control, requiring the careful analysis of potential risks and their impacts. Generative AI can revolutionise this process by providing predictive analytics to identify potential risk areas that might not be evident through traditional methods. This proactive approach ensures better preparedness, better-informed decision making and more robust risk mitigation strategies.



Analytical method validation and analytical instructions

Developing and validating analytical methods is a cornerstone of quality control. AI has the potential to streamline method validation by simulating various scenarios and predicting outcomes. This allows QC teams to assess

methods' robustness, accuracy and precision effectively. AI-generated instructions ensure clear, error-reducing guidance.



Analytical method transfer

Method transfer between different analysts and sites is a challenge for many organisations, often leading to inconsistencies and delays. AI can play a pivotal role in standardising and streamlining this process. By analysing data from different analysts and sites, AI can identify key parameters and conditions that must be standardised for successful method transfer. It can also generate step-by-step guides and checklists customised for each site, ensuring a smooth and efficient transfer process. This standardisation is crucial in maintaining the consistency and integrity of the methods across different locations.



Knowledge management

Generative AI's role in knowledge management is transformative. It can serve as a central repository for an organisation's collective knowledge. By aggregating data from various sources and making it accessible, AI enhances the decision-making process. This comprehensive knowledge management capability ensures that all decisions are informed by the most current and comprehensive data available.



Continuous process monitoring

Generative AI significantly enhances continuous process monitoring in QC. By constantly analysing process data in real time, AI systems can provide immediate trend alerts, identifying both process and analytical trends. This real-time monitoring capability enables early detection of deviations or anomalies, allowing for prompt corrective action. AI-driven trend analysis not only improves the accuracy of monitoring but also enables predictive maintenance, reducing downtime and improving overall process efficiency.



Laboratory design and layout

n the realm of laboratory design and layout, generative AI has the potential to revolutionise how spaces are planned and utilised. By analysing workflow patterns, equipment usage and safety protocols, AI can suggest optimal laboratory layouts that enhance operational efficiency and safety. This intelligent design approach can lead to significant improvements in workflow, reducing bottlenecks and improving overall productivity. AI can also assist in predicting future space needs based on projected growth or changes in technology, ensuring that laboratory designs remain flexible and adaptable.



Validation and compliance

The integration of AI into QC requires a multifaceted approach to validation and compliance. This involves developing and implementing detailed validation protocols that test the AI system's accuracy, reliability and consistency over time. Validation should include rigorous testing against known datasets to ensure the AI's decision-making aligns with industry standards and regulatory expectations.

In addition to initial validation, continuous monitoring and revalidation are crucial. As AI systems learn and adapt, their outputs can change. Therefore, ongoing assessment is necessary to ensure that these systems remain

within the bounds of regulatory compliance and continue to meet the high standards expected in QC.

Moreover, documentation and traceability are vital components of compliance. AI decisions and processes should be transparent and auditable, with clear records maintained to demonstrate compliance with regulatory requirements. This transparency is crucial for both internal quality assurance and regulatory inspections.



Engaging with regulatory agencies

A crucial aspect of implementing AI in QC is proactive engagement with regulatory agencies. This engagement is multi-dimensional:

- **Early and transparent communication:** It's vital to establish an open dialogue with regulatory bodies from the early stages of AI implementation. Transparent communication about the role of AI, its capabilities and limitations fosters a collaborative environment.
- **Alignment with regulatory standards:** Organisations must ensure that AI systems align with existing regulatory standards and guidelines. This includes understanding how AI decisions are made and ensuring they comply with industry-specific regulations.
- **Joint development of guidelines:** Collaborating with regulatory agencies to develop AI-specific guidelines is beneficial. This collaboration can help shape the regulatory landscape, ensuring that guidelines are practical, achievable and reflective of the latest technological advancements.
- **Continuous reporting and feedback loop:** Regular updates and feedback to regulatory agencies are essential. This includes sharing performance data, any challenges faced, and the steps taken to mitigate risks. Continuous reporting ensures that regulators are kept informed of the AI system's performance and its impact on QC processes.

Conclusion

The integration of generative AI into quality control signifies a major advancement for the pharmaceutical industry. Its applications extend from enhancing training and development to refining analytical methods, improving risk assessments, and revolutionising real-time process monitoring and laboratory design. The successful implementation of AI in QC hinges on thorough validation, regulatory compliance and a proactive engagement with regulatory bodies. By addressing these challenges, QC units can fully harness AI's potential, driving efficiency, accuracy and innovation in pharmaceutical quality control.



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