Use of AI in Pharmaceutical Quality and Operations

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My interest in this topic

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LinkedIn

Experience

- Over 30 years of pharmaceutical industry experience, including 17 years at the UK Regulator (MHRA) and 25 years of performing both GMP/GDP audits and regulatory inspections
- Former Head of the MHRA GXP Inspectorate and Deputy Director, Inspection, Enforcement and Standards
- Led the creation of the risk-based inspection and compliance management principles at MHRA
- Headed up MHRA Digital Health team 2018-2019, including x-Government AI meetings
- Former PIC/S Executive Bureau member and PIC/S lead assessor (assessing various agencies including FDA and ANVISA)
- IRCA Principal Auditor PQMS - GMP Scheme and Eligible Qualified Person
- 10 years at GSK, roles including MSAT, Technology Transfer, Supplier Audits and R&D QA

Expertise

- GMP inspections of manufacturers of investigational drugs, finished sterile and non-sterile drug products, medical gases, active pharmaceutical ingredients, veterinary medicines, herbals, computerized systems, excipients, and packaging materials
- Deemed eligible by the MHRA to act as a Compliance Monitor (CM) in MHRA's compliance monitor programme for GMP/GDP remediation supervision activities
- Remediation and inspection responses to regulators, having sat as a regulator reviewing responses to regulatory action
- Regulatory risk-based inspection programs and approaches, including desk-based assessments
- New innovative technologies and processes; and associated regulatory thinking in these areas
- Developing training programs and conferences for international regulators and industry
- Regulatory crisis management (e.g. Pandemic, Heparin, drug shortages)

Education

- University of Hertfordshire, BSc (Hons) Chemistry with Chemical Technology
- University of Greenwich, MSc Pharmaceutical Science
- University of Warwick, MBA

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- Previously headed up MHRA digital Health Team and before that the MHRA GXP Inspectorate
- Attended cross UK government meetings on AI implementation
- MBA dissertation on “Adapting global pharmaceutical regulations in response to use of artificial intelligence, augmented reality and virtual reality by pharmaceutical manufacturers”
- Member of ISPE Pharma 4.0 working group

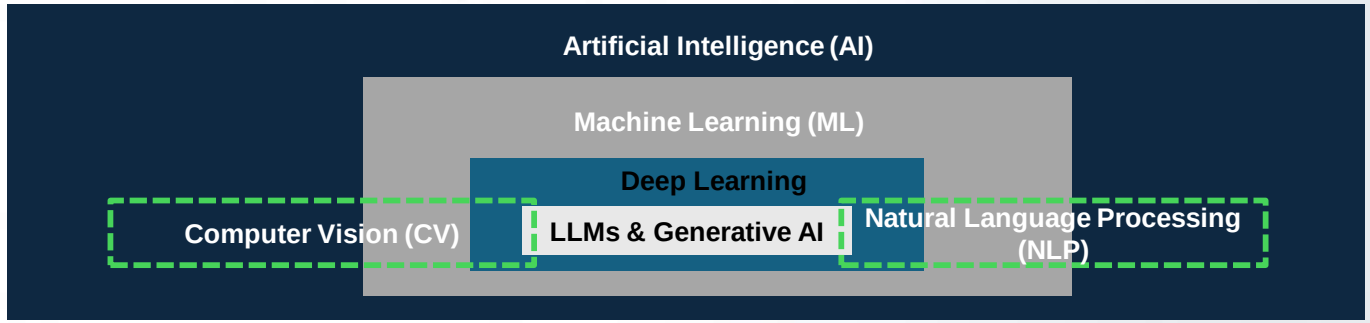
Agenda today

- Artificial Intelligence
  - Introduction
  - Level setting
- AI in Pharma Quality and Operations
  - Some key focus area
- Regulation of AI
  - Current Regulatory initiatives
  - The challenges for Regulators
- Wider AI and Digitization use
  - In Quality and Operations
  - Clinical Development
- The future of inspections
- Conclusion and key takeaways
- Questions

AI in Pharma Quality and Operations

- We are in an industry driven by an overarching need to meet Quality and Regulatory Standards, with a need for productivity and cost reduction.
- The adoption of AI in the pharmaceutical industry has the potential to revolutionize drug development, production, and quality control processes, ultimately improving patient outcomes and bringing medicines to market more efficiently
- By leveraging AI technologies, pharmaceutical quality assurance processes can be enhanced, leading to increased efficiency, improved detection of quality issues, and enhanced compliance with regulatory requirements

Level-setting on terminology:



Machine learning (ML):	**Deep learning**:	**Computer vision (CV):**	**Natural language processing (NLP)**:	**Large language models (LLMs)**:
•Ability to learn from data and improve performance as they identify patterns and make predictions. Traditional machine learning requires some human intervention to correct mistakes.	•Subset of machine learning that focuses on artificial neural networks to solve complex problems and discover intricate patterns in large datasets.	•Enhances a machine's ability to interpret and understand images or videos; can tap into machine learning or deep learning.	•Allows computer systems to interpret text and perform tasks including speech recognition, sentiment analysis, and automatic text summarization.	•Trained on massive datasets of text and codes to learn patterns in human languages and make predictions.

Artificial Intelligence (AI): Development of computer systems capable of performing tasks such as text/speech recognition, decision-making, problem-solving, and data analysis. While capable of streamlining processes and driving efficiencies, these algorithms often require human oversight.

Examples of AI in Pharma Quality

- **Automated data analysis:**
  - Analyze large volumes of data collected from various stages of the manufacturing process, including quality control tests, environmental monitoring, and batch records. By quickly identifying patterns or anomalies in the data, AI can help detect quality issues and deviations faster than traditional manual methods.
- **Real-time monitoring:**
  - Continuous monitoring of critical quality parameters in real-time, such as temperature, humidity, pressure, or pH levels, ensuring that they remain within acceptable ranges. Any deviations can trigger immediate alerts, allowing for prompt corrective actions to maintain product quality.
- **Image and pattern recognition:**
  - AI-powered computer vision systems can analyze images and identify defects in product appearances, labels, or packaging. This helps in identifying any quality issues and ensuring that products meet visual quality standards consistently.
- **Predictive analytics:**
  - By utilizing historical data, AI can create predictive models to forecast quality risks and identify potential issues early in the manufacturing process. This allows for proactive measures to be taken to prevent quality deviations and ensure consistent product quality

Examples of AI in Pharma Quality

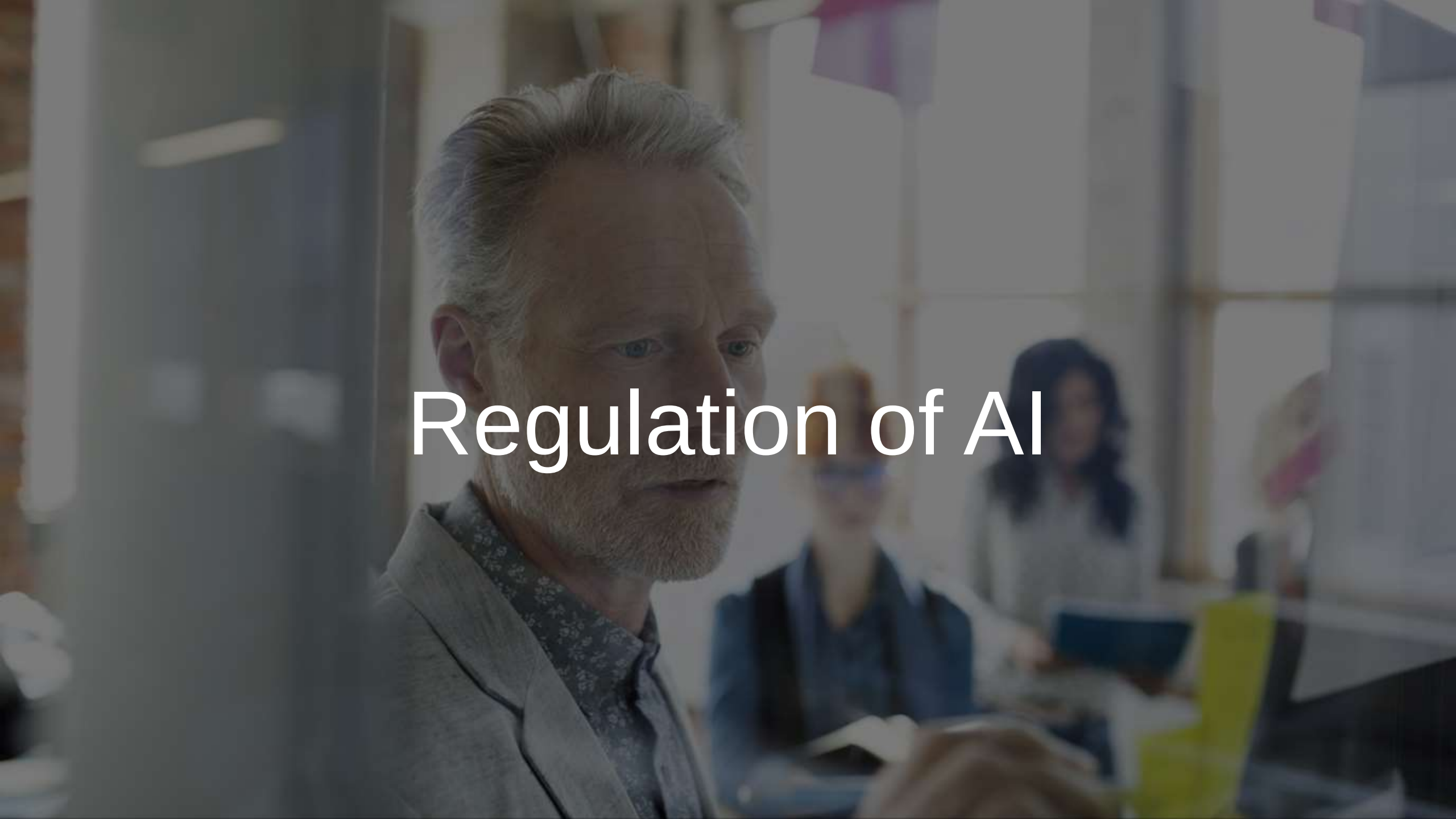
- **Root cause analysis:**
  - AI algorithms can perform root cause analysis by analyzing complex data sets to identify factors contributing to quality issues. This can help in identifying systemic problems and implementing corrective actions to improve processes and prevent quality deviations from recurring.
- **Quality documentation and compliance:**
  - Assist in ensuring accurate completion of quality-related documentation, such as batch records, deviations, and CAPAs (Corrective and Preventive Actions). It can also help in automating regulatory compliance checks, ensuring adherence to applicable guidelines and regulations.
- **Risk assessment:**
  - Perform risk assessments by analyzing a combination of data sources, including manufacturing data, quality control data, and adverse event reports. This helps in identifying potential quality risks, prioritizing resources, and implementing proactive quality assurance measures.
- **Deviation management:**
  - Analysis of ‘minor’ deviations to find trends and ‘themes’ worth investigating leaving more time to focus on critical and major issues

Examples of AI in Pharma Operations

- **Quality control and inspection:**
  - AI can automate the inspection process by analyzing images and data from various manufacturing steps, such as identifying defects in tablet coatings, and enhancing visual inspection of injectable products.
- **Predictive maintenance:**
  - Monitoring of equipment and machinery in real-time, identifying patterns and anomalies that can predict failures or maintenance needs. This helps to minimize downtime and optimize production efficiency.
- **Process optimization:**
  - Analyze large volumes of data collected during the manufacturing process to identify patterns and correlations that may improve production efficiency, reduce wastage, and enhance overall process optimization.
- **Predictive modeling:**
  - AI can utilize historical data to create predictive models for drug development and manufacturing processes, enabling pharmaceutical companies to forecast drug properties, stability, and shelf-life more accurately.

Examples of AI in Pharma Operations

- **Adaptive control:**
  - AI algorithms can continually monitor and adjust operational parameters in manufacturing processes, ensuring consistency, reducing human errors, and maintaining compliance with regulatory standards.
- **Regulatory compliance:**
  - AI can assist in regulatory compliance by analyzing vast amounts of data against regulatory guidelines, ensuring accuracy, reducing errors, and enhancing the efficiency of compliance processes.
- **Supply chain optimization:**
  - AI algorithms can optimize supply chains by forecasting demand, analyzing inventory levels, and predicting potential bottlenecks, thereby optimizing procurement, production, and distribution processes.
- **Drug discovery and formulation:**
  - Assist in identifying potential drug candidates by analyzing vast volumes of scientific literature, molecular structures, and pharmacological data, helping researchers to improve the efficiency and success rate of drug discovery.


Regulation of AI

Regulator perspectives on AI

Concerns with opacity, potential for bias and error, negative or harmful impacts in use

- Regulatory and legislative compliance needs to be engineered into AI app development pipeline from the outset
- Agencies seem set to take a risk-based approach
  - MHRA implementation paper for AI in regulation of medical products (April 2024)
  - FDA discussion paper (May 2023)
  - EMA draft reflection paper on AI in medicinal product development (July 2023)
- Lack of detail related to Pharmaceutical Quality and Operations use

Per MHRA: *"… the changes our customers make will not impact how we regulate."*

Per EMA: *"… the use of exceptionally great numbers of trainable parameters arranged in non-transparent model architectures introduces new risks that need to be mitigated both during model development and deployment to ensure the safety of patients and integrity of clinical study results. Also, as the overarching approach is inherently data-driven, active measures must be taken to avoid the integration of bias into AI/ML applications and promote AI trustworthiness ."*

Per FDA: *"There are also concerns with using algorithms that have a degree of opacity, or algorithms that may have internal operations that are not visible to users or other interested parties. This can lead to amplification of errors or preexisting biases in the data. We aim to prevent and remedy discrimination — including algorithmic discrimination, which occurs when automated systems favor one category of people over other(s) — to advance equity when using AI/ML techniques."*

Keeping up with innovation…

The ‘Pacing’ and ‘Co-ordination’ issue for Regulators

“…..a significant hurdle to the adoption of innovative technologies is that regulations and guidelines do not always keep pace with rapid developments in science

As a consequence, a new technology or innovative approach may need to be introduced where regulatory provisions do not exist or have not been sufficiently developed, or where there is a lack of understanding/knowledge of the new technology by the regulators.”

[BIS, 2011, Let’s Get Down To Buisness]

Further identified as an issue by the World Economic Forum’s Centre for the Fourth Industrial Revolution

- **Highlighted as an issue in conjunction with Regulatory co-ordination**
- **Packaged within ‘Agile Regulation’**

Agile Regulation

World Economic Forum (WEF)

Centre for the Fourth Industrial Revolution

2 distinct issues identified, a problem of **regulatory pacing** and a problem of **regulatory co-ordination**

- **Pacing** in that regulation often struggles to keep pace with the rapid emergence of new ideas, products and business models
- **Co-ordination** in that Regulators often struggle to respond to innovations in a joined-up way, as they frequently cut across administrative, sectoral and jurisdictional boundaries

What are regulators doing in this space

Current approaches

- Little regulatory guidance exists
- In a learning phase
- Very limited inspection protocols exist

Guidance applicability

- Divided opinion amongst regulators as to the adequacy of the GMP guide to support industry use of these technologies
- It was called out as lacking in this regard by industry

New approaches

- There is a consistent view between regulators and industry that new approaches are needed.
- The regulators called for this in several spaces:
    - Where there is a reliance on outsourced technology
    - In training, e.g. processing instructions
    - Validation, where there are large volumes of data needed to train systems and where performance metrics will be required

Wider awareness and applicability

- Very few regulators are aware of wider Government programs
- Industry view is relationships with regulator are there, but not fulling the required change

What could regulators do in this space

Enhance co-operation

- Establish a PIC/S regulators working group to bring greater consistency and levelling up of regulators globally
- Use those regulators with the greatest knowledge of this space to drive this forward
- Outcomes should embrace joined up regulation
- Co-ordinate any required regulatory guideline changes in a joined-up manner

Build partnerships

- Partner with industry leaders to understand better new technologies
- Foster transparent working relationships so regulatory hurdles can be surfaced
- Develop safe spaces for smaller, more agile, companies to work with regulators. In working with these companies through the regulatory pathway it will allow regulators to see first-hand any challenges, whilst also seeing cutting edge technology and learning in this area too

Regulatory relief

- Establish a tiered approach to compliance and innovation
- Identify manufacturers at the higher end of the compliance spectrum, where they consistently demonstrate regulatory knowledge and compliance, and, a mastery of Fourth Industrial Revolution technologies
- Allow these companies more relief to make innovative changes, linking in partnership principles so both parties learn, to start to normalise these technological advancements
- Provide an element of self-regulation through establishing triggers for reporting from these companies, in real time if possible. This allows regulators to be responsive when needed

Birse, M., 2020, “Adapting global pharmaceutical regulations in response to use of artificial intelligence, augmented reality and virtual reality by pharmaceutical manufacturers”, University of Warwick


Wider AI and Digitization
with Pharma

Quality & Operations

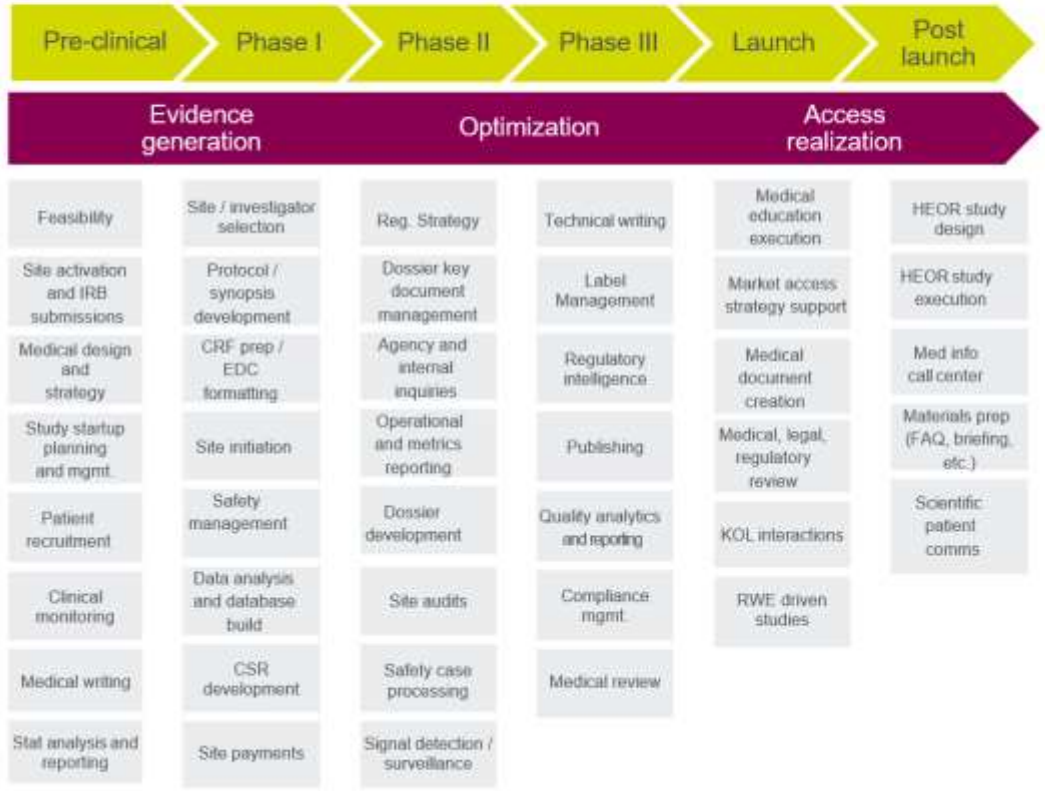
- Augmented reality
  - Operator interfaces
  - Engineering support
- Virtual reality
  - Training
  - Partnering with suppliers
- Robots/Cobots
  - Automating tasks
  - Providing consistency
- Digital batch records
  - Fully integrated
  - Data capture
- Blockchain capabilities
  - Documentation
  - Supply chain management
- Knowledge management throughout lifecycle
  - Stopping the data loss
  - R&D through to manufacturing
- Connected facility
  - IOT
  - Connected systems
- Platforms
  - 360 cameras and sharing

Clinical Development – an example

AI applications are set to accelerate clinical development

GenAI: Enabling next-gen search-and-retrieve and a step change in quality of content generation

- **ChatGPT and other LLMs are transforming the opportunity for AI/ML across the clinical development continuum**
- **Big bucket opportunities**
  - Search-and-retrieve
  - Content generation
  - Workflow automation
- **Considerations for businesses**
  - Access to talent with NLP skills
  - Need to re-engineer workflows
  - Staff training: selection of prompts (i.e., user queries) and need to check/confirm answers
  - User access to internal info and data assets via AI tooling
  - Regulatory and legislative compliance (emerging global legislation trends)



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The future of inspections

- Will the current inspection approach continue, or will it need to adapt?
- What levels of data access and oversight could be used?
  - Regulators having access to your dashboards?
- Is a new skill set of data focussed inspectors needed?
- What AI systems will be used on your data by regulators?

Key takeaways and conclusions

- The adoption of AI in the pharmaceutical industry has the potential to
  - improve patient outcomes, bringing medicines to market more efficiently
  - revolutionize Quality and Operations processes
  - lead to increased efficiency, improved detection of quality issues, and enhanced compliance with regulatory requirements
- New regulations are being developed and inspection strategies could change in the future
- Key that your Quality, Process, and Data SMEs work together.

THANK YOU

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