Industry 4.0 and Regulatory Challenges

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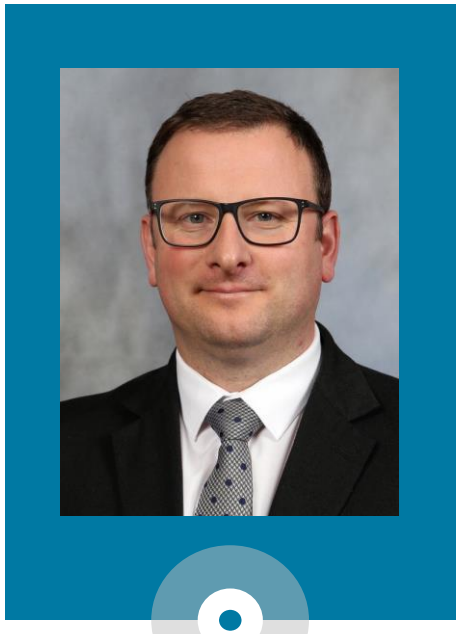


EXPERIENCE

- 17 years at MHRA, roles including:
  - Deputy Director Inspection, Enforcement & Standards Division
  - Head of MHRA Inspectorate and Process Licensing (over 75 GXP inspectors in team)
  - Group Manager Medical Device Safety & Surveillance
  - Senior GMP & GDP Inspector prior to holding leadership roles
- Executive Bureau member of the Pharmaceutical Inspection Co-operation Scheme (PIC/S)
- Eligible Qualified Person since 2003
- 10 years at GSK, roles including Technology Transfer, Supplier Audits and R&D QA

AREA EXPERTISE

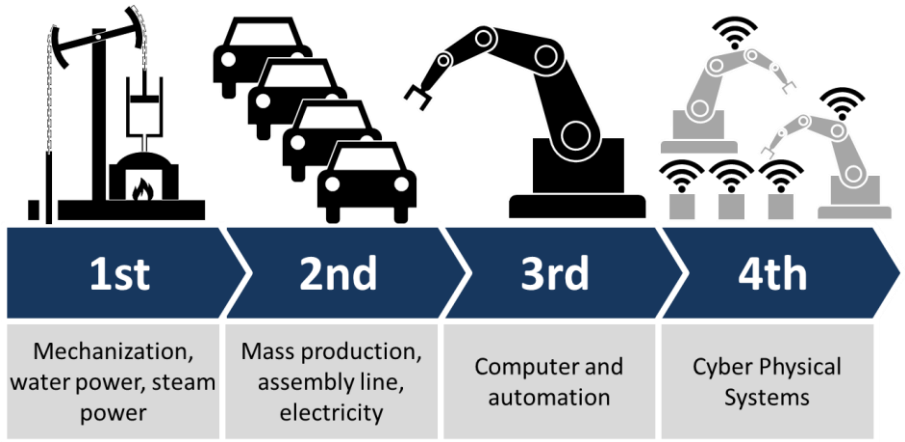
- GMP inspections of manufacturers of investigational drugs, finished drug products, active ingredients, excipients and packaging materials
- Regulatory risk-based inspection programs and approaches, including desk-based assessments
- New innovative technologies and processes; and associated regulatory thinking in these areas
- Developing training programs and conferences for international regulators and industry
- Regulatory crisis management (e.g. H1N1/09 Pandemic, Heparin)

EDUCATION

- University of Hertfordshire, BSc (Hons) Chemistry with Chemical Technology, 1996
- University of Greenwich, MSc Pharmaceutical Science, 2002
- University of Warwick, MBA, 2020

Industry 4.0

- The Fourth Industrial Revolution is expected to create up to $3.7 trillion in value by 2025
- WEF/McKinsey Global Lighthouse Network
  - 2018: >1,000 production facilities examined
  - 16 companies were recognized as Fourth Industrial Revolution leaders
  - 28 new sites added in 2019



Christoph Roser at AllAboutLean.com

mckinsey.com

GSK in Ware, UK	This pharmaceutical site has applied Fourth Industrial Revolution technologies across its manufacturing operation, exploiting advanced analytics and neural networks to use existing datasets. It has improved line speed by 21%, reduced downtime and increased yield, delivering an OEE improvement of 10%.	Advanced analytics-based machine performance improvement	↑ 10% OEE
		Deep learning image recognition to detect quality defects	↑ … Cost avoidance
		Artificial intelligence-guided machine throughput optimization	↑ 21% Throughput
		Digital twin planning	↑ 13% Capacity
		Cycle time monitoring and visualization digital tool	↓ 9% Cycle time

mckinsey.com

Industry 4.0

Factory of the future and a Regulatory ‘awaking’

- Augmented reality
  - Operator interfaces
  - Digital batch records
- Virtual reality
  - Training
  - Partnering with suppliers
- Artificial intelligence and machine learning
  - Predictive quality
  - Digital twin
- Blockchain capabilities
  - Documentation
  - Supply chain management
- Knowledge management throughout lifecycle
  - Stopping the data loss
  - R&D through to manufacturing
- Connected facility
  - IOT
  - Connected systems

The issues
(and they are not new)

The problem – all industries

- Nesta's 2012 'The Impact of Regulation on Innovation' report highlighted that
  - **"…policies to improve the regulatory framework conditions relevant for innovation or even setting regulation with the explicit objective to promote innovation are becoming more important."**

[Blind, K, 2012. The Impact of Regulation on Innovation, Nesta Working Paper No. 12/02]

- The Department for Business, Energy & Industrial Strategy identified in their policy Paper on Regulation for the Fourth Industrial Revolution that:
  - **"Regulation has a powerful impact on innovation.**
    - **It can stimulate ideas and can block their implementation**
    - **It can increase or reduce investment risk – and steer funding towards valuable R&D or tick-box compliance**
    - **It can influence consumer confidence and demand – and determine whether firms enter or exit a market."**

[BEIS, 2019, Regulation for the Fourth Industrial Revolution]

The problem - pharmaceuticals

- Think about……
  - ICH Q8
  - Continuous manufacturing
  - Process analytical technology

- What would help
  - No dispute that industry & regulator collaboration happened
  - Levels of desire for change are there

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The keeping pace issue

Not a new issue

- UK Government in 2011
  - “…..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**.”

Gov.uk

- Strategy for UK life Sciences
  - Through the MHRA, we will work with industry and other international regulators to develop actions which will create a more enabling regulatory environment for the adoption of innovative manufacturing technology

Gov.uk

Current thinking on ‘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

- The WEF have proposed **7 principles of agile regulation**

WEF - 7 principles of agile regulation

- **Foresight and anticipatory outcome**, for example horizon scanning and early engagement
- **Outcome focused regulation**, by making regulations outcome focused with stretching outcomes that stimulate innovation
- **Experimental regulation**, support testing and trialling of innovation with regulatory sandboxes to provide supervision. Sandboxing was viewed like a clinical trial. Finance regulators looked to healthcare examples to help implement
- **Regtech and responsive regulation**, monitor outcomes in real time and adapt regulations accordingly. Use outcome focused triggers for review
- **Co-ordination and self-regulation**, by developing industry led self-regulation
- **Joined-up regulation**, through promoting joined up regulation across areas and use a primary co-ordinating authority
- **International regulatory co-operation**, unilateral adoption of international regulations and standards

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

- 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

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 – e.g. US and UK
  - 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

How do inspectors need to adapt

Challenges in regulating (inspector level)

- Is the inspector of today the inspector of tomorrow?
- Training – who to do / partnerships with leaders
- Complex IT systems - sample? / use own algorithms?
- Big data, blockchain, AI, black box – dedicated data inspector?
- Is new guidance needed
  - local / global?
  - greater harmonization as company systems become globally harmonized?
- Real-time regulatory oversight – can data be used to support
- An increased level of self regulation – partnerships and better communication

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Thank you

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