Inspections in a post COVID-19 world

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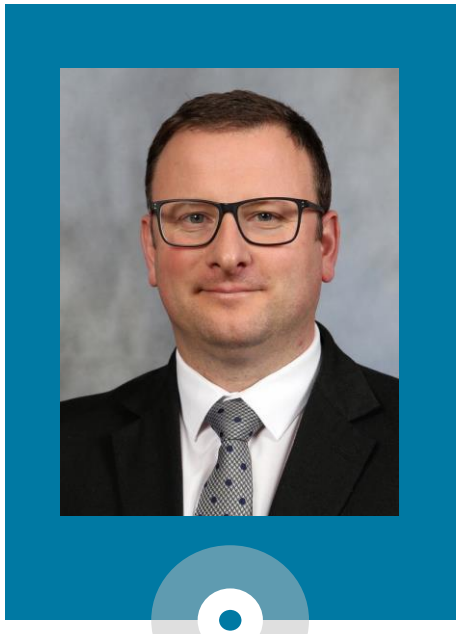


EXPERIENCE

- 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

Why inspect?

2019

- Assessing new facilities for GMP compliance
- Assessing a new drug product
- Follow-up on intelligence, from
  - an other National Competent Authority (NCA)
  - a patient
  - a whistleblower
- Follow-up of previous on-site inspection
  - Usually when poor compliance identified

How inspecting

2019

- Risk based models being used
- Some joined up inspections
- Use of MRAs and trade partnerships
  - Some well established
  - US/EU - whilst signed still developing in use
- Reliance initiatives in their infancy
  - PIC/S PI 048-1
- Some desk-based assessments happening
  - E.g. FDASIA 706

All change - COVID-19 impact

2020

- March 2020
  - US and EU regulators pause onsite inspections
- Some ‘critical’ inspections still occurring onsite
  - If associated with COVID-19 response
  - Where serious patient safety risk are present
  - Vast majority of onsite inspections are domestic and not overseas
- Some NCAs establish limited regulatory flexibilities
  - To support drug supply and availability
  - Increase in GMP certificate expiry date – EMA until end 2021

All change - COVID-19 impact

2020

- Regulators have pivoted their efforts towards COVID-19
  - Focus on therapies, vaccines and diagnostics
  - Greater need to spend time on communications with industry
- Assessment vs Inspection – an ongoing regulatory discussion
  - EMA finalizing EU guidance on this
- Inspection backlogs developing
- Agencies are ‘businesses’ too
  - Most shutting offices and staff home working – opening 2021?
  - Reduced support for enquiries

Remote Inspections

Some observations

What has Parexel observed so far...
Regulators

- Postponed inspections (PAI for applications vs surveillance)
- Domestic inspections are occurring onsite based on risk
- Document and Data requests with quick turnaround time for response
- Reliance on MRA inspection outcomes (some)
- Communications relating to impact on submission review due to inspection delay
- Use of technology – cameras and videos, video conferencing, data sharing platforms

What has Parexel observed so far...
Industry

- Firms need to protect staff, protect operations and protect patient supply
- This is leading to increased operational pressures
- Some facilities struggling to maintain a suitable level of quality oversight
- Increase in the number of deviations and data integrity issues being raised
- Companies being unprepared for remote inspections
- **Regulators will return** and remember…… GMP and data integrity are **not** optional

Post COVID-19 Inspections

Future possibilities

When regulators return

Inspectors will want to know

“What happened at your facility concerning quality during COVID-19?”

When regulators return

How will you demonstrate control when asked?

- Change Control
  - How managed
    - Open and dynamic vs one offs and closed
    - Any cumulative impact on quality
- Deviations
  - More? Less?
  - Expect closer review than before
- Regulatory flexibilities
  - Have they been used?
- Data Integrity
  - Can you confirm that you have control?
  - Fewer staff on-site
  - How you defined core roles
  - Challenges with maintaining a quality system and quality oversight
  - Access to documents and data
  - Pressures to maintain supply
- How did you maintain quality?
  - Can you explain everything done?

How will regulators assess facilities?

- More virtual inspections - A tool at a time of crisis / short term
- Longer term about balancing risk
  - More likely to be desk-top if there was a previous onsite inspection
    - Limitations: facilities, instrument/equipment operation and staff behaviors hard to assess remotely
  - “Hybrid” inspections – combination of desktop and reduced on-site presence.
  - Greater use of Mutual Recognition Agreement (MRA), cooperative agreements and confidentiality commitments with trusted allies.
  - Making risk-based facility classification decisions based on existing data.
- Balancing safety of medicines vs availability and avoidance of shortages
- If companies change supply models is there regulatory capacity to respond?

Future operational state? – but fundamentals don't change!

- **Within Regulators**
  - Hybrid – on-site / off-site – based on risk, knowledge and complexity.
    - Enhanced Real-time Communications (WebEx/Zoom etc.) to accomplish inspection goals
  - Don't expect "V" shaped trajectory for return to past practices.
  - Augmented regional inspection staffing
  - FDA - much more frequent use of "706" authorities and desk-top audits.
- **Quality Metrics or Benchmarking**
  - Modified risk-based site selection model.
- **Global Harmonization**
  - Greater reliance on mutual recognition and cooperative agreements.
  - Implementation of PIC/S inspection guidelines – ICH model.
  - User fee program for compliance – transparency, access and timelines.
  - Cloud based data/dossier globally available
- **Partnerships**
  - Third Party Qualified – low risk drugs and facilities (like device inspection process?)
  - Excipient CGMP model.

Post COVID-19 Inspections

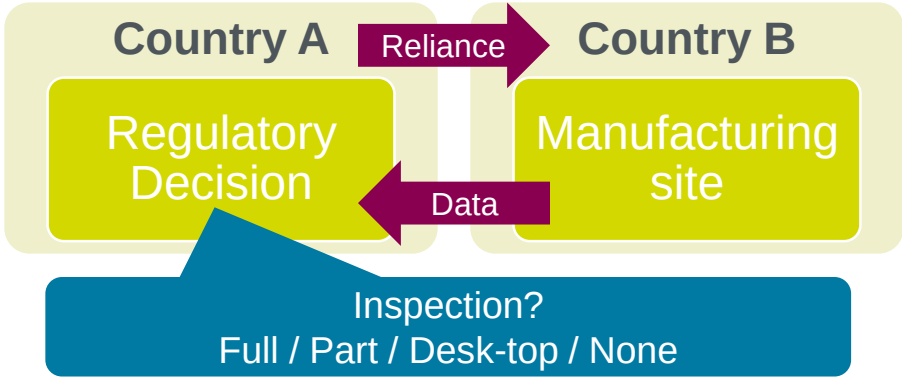
A need for greater collaboration

Knowledge Exchange
Regulators Sharing Inspection Outcomes

- How do they ‘trust’ each other?
  - Formal recognition
    - Trading blocks (EU / ASEAN)
    - MRAs
    - Frameworks
    - Underpinned by audits – JAP/JRP
  - Less formal reliance
    - PIC/S GMP Reliance initiative
- What are they doing with information?
  - Often nothing – just a tick box
    - Trust in the system
  - EU countries have well established systems for using MRAs
  - EUDRAGMDP database can be used
  - Gap analysis against own systems
  - Support decision making for historical cases of non-compliance
    - More likely to maintaining status quo
  - For FDA a much newer process.

PIC/S GMP Inspection Reliance Initiative (PI 048-1)

- The GMP Inspection Reliance Initiative supports
  - the better utilization of inspection resources by regulatory authorities enabling them to focus their attention on high risk issues domestically and abroad
  - a reduction in duplicate, same-scope inspections for industry and consequent cost savings



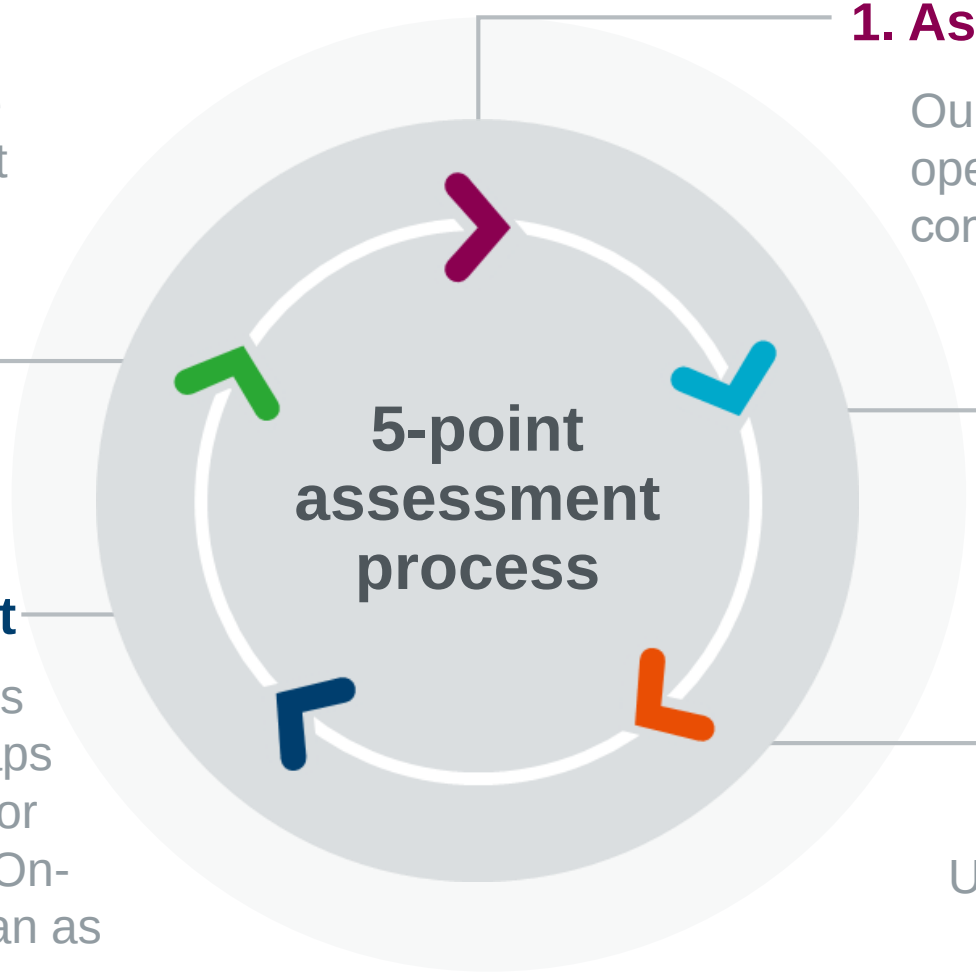
PIC/S GMP Inspection Reliance Initiative (PI 048-1)

- GMP compliance is confirmed by means of remote (desktop) inspections
  - A regulatory authority (the “requesting authority”) contacts the regulatory authority of the country in which the manufacturer is located (the “hosting authority”) to request specific information about the GMP status of the manufacturer in order to determine whether a remote (desktop) inspection can be relied upon.
  - The requesting authority will have established confidence in the competence and capabilities of the hosting authority through various means, e.g. membership of PIC/S
  - The information requested could be a GMP certificate / recent GMP inspection report.
  - Additional information may be requested from the manufacturing site (e.g. company’s CAPAs from the last inspection, outcome of inspections by other regulatory authorities, site master file, etc.) in order to complete the remote (desktop) inspection.
  - The requesting authority will inform the manufacturing site, and usually the hosting authority, of the outcome of the remote inspection.

Example: Parexel's remote desktop cGXP audits

Preparing for regulatory off-site compliance assessment

Making an informed evaluation of your needs



1. Assessment of the operations

Our experts will review your operations and assess your company's needs and end goals

2. Desktop review

We can assess products that are in your pipeline or are already approved

3. Videoconference and interviews

Using technology to meet your needs and deliver quality

4.Deliverables and onsite audit

Detailed reports and assessments which describe present cGMP gaps and provides recommendations for remediation, where appropriate. On-site audits can be performed on an as needed basis.

5. Regulatory dialogue

We can prepare you for a remote regulatory inspection and support your dialogue with regulators, both pre- and post-inspection

Parexel's remote desktop cGMP audits

Expert compliance assessment of all six quality systems;

- quality, facilities and
- equipment, production, laboratory controls,
- material, packaging & labeling

Assessment of pipeline and approved products and manufacturing strategy including, aseptic, biotech and non-sterile manufacturing

Evaluation of corporate policies and site procedures against regulatory requirements and industry best practices

Six-system evaluation | **Manufacturing strategy** | **Regulatory requirements**

Backed by 1000+ worldwide consultants including 80+ former regulators and inspectors

Thank you

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