Extraordinary Virtual

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Regulatory experience with using regulatory tool of remote assessments and hybrid inspections

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Challenges, Experiences and Sustainable solutions

Challenges

March 2020: COVID-19 pandemic halted routine on-site inspections
April 2020: Remote and hybrid 'routine' inspections commenced

We continued:

- Prioritised onsite inspections for critical follow-up, licensing need or COVID-19 support, where necessary, with a focused inspection scope.
- Emergency approvals & conditional MA (including overseas sites)

We paused:

- Routine overseas inspections
- National Health Service (NHS) sites (e.g. hospital aseptic compounding, blood banks) unless critical, to enable essential COVID-19 work to continue
- Assessment of highly complex processes unless critical

Technological challenges

- Ability to access all eSystems – accounts / passwords!
- Hybrid systems
- Technical capability of sites impacts remote interactions
- Data protection considerations
- Size of e-files and time to download
- Camera restrictions in some areas/ countries
- Connection issues….!

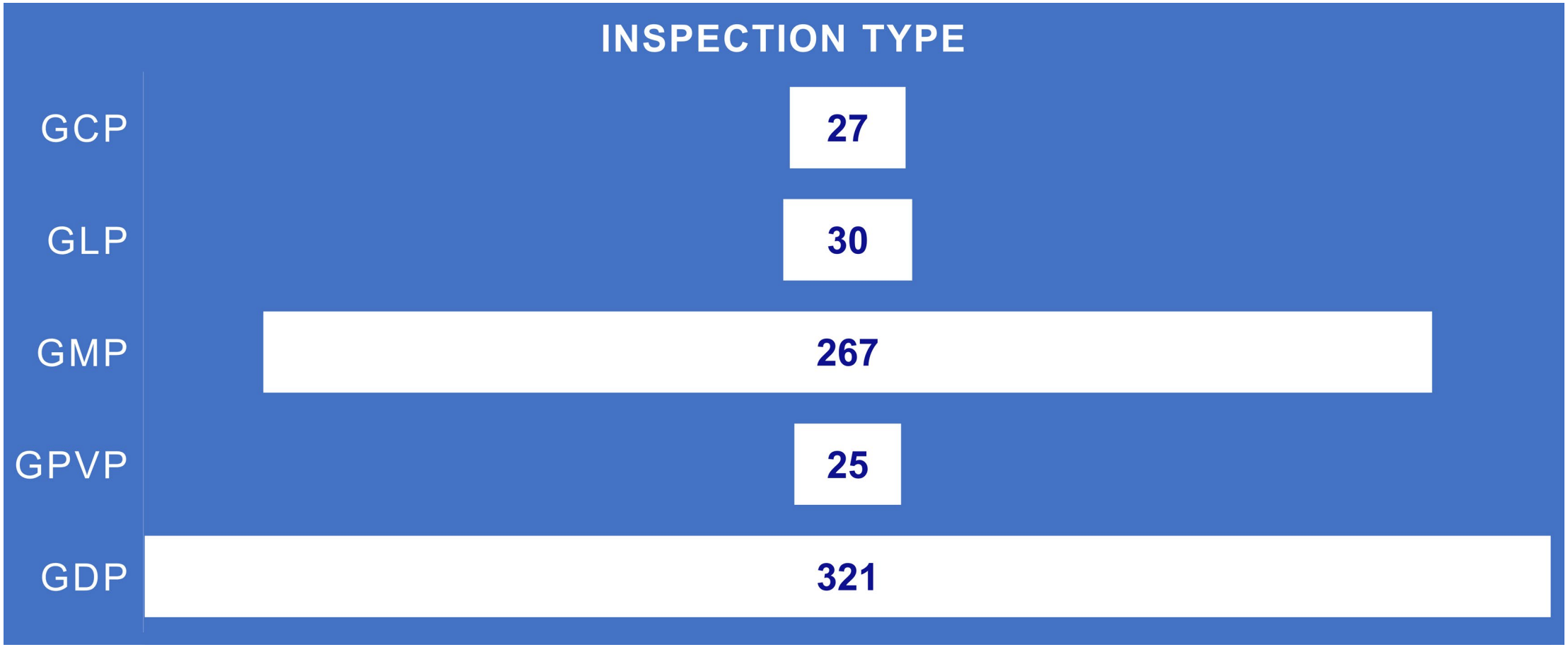
Logistical Challenges

- Assessments take longer
- Delays in receipt of requested documents
- Inability to ask ‘real-time’ Qs
- Constant video calls
- Inability to easily assess state of premises/ equipment/ facilities

- Distractions!

Experiences

Remote Inspections Conducted 1st Apr 20- 31st Jan 21
Total 670 inspections

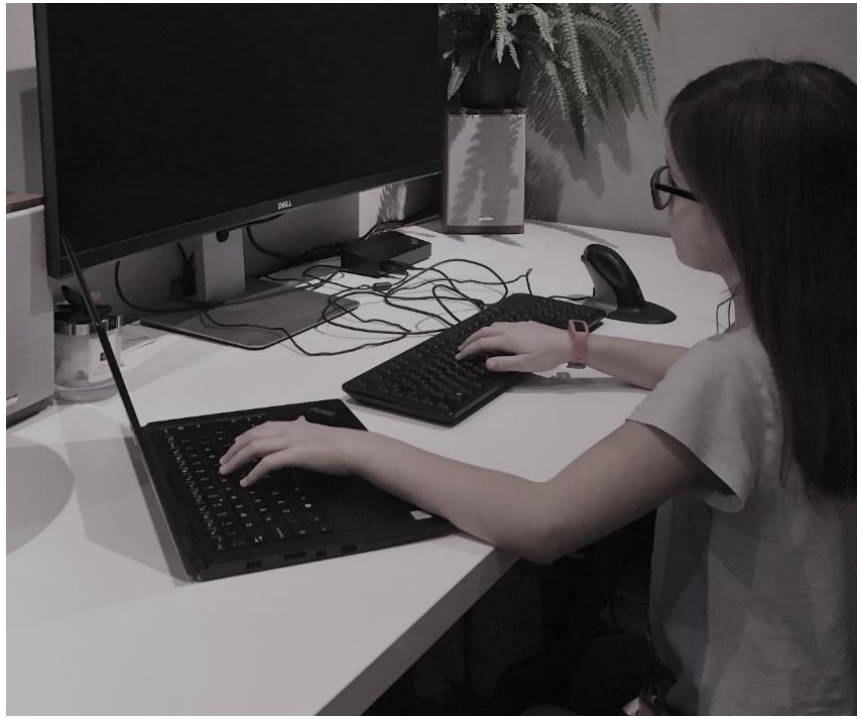


Sustainable solutions

- Organisations notified as normal (unless triggered short-notice)
- Any pre-inspection documents requested & reviewed as normal
- Modified requests & dossiers ensuring needs of inspection scope are met
- Inspection scope often narrower than on-site, but directed by risk
- ICMRA Digital Transformation of GCP & GMP Inspections:
  - ‘Deep-dive’ presentation to ICMRA Policy Group in Oct 2020
  - Reflection paper in development on remote inspection approaches

Practical considerations

- TC and Video conference for opening/ closing meetings; interviews and screen share
- Use of file sharing technology
- Email
- Livestreaming of documents
- Remote access to eSystems such as eTMF, eCRF etc.



Regulation Flexibilities

- Measures taken to support:
  - Healthcare products supply chain
  - Wider pandemic response
- Areas of focus:
  - Clinical trials
  - Marketing authorisations
  - Pharmacovigilance
  - Inspections and good practice
  - Blood components for transfusion
  - Medical devices

- https://www.gov.uk/guidance/mhra-regulatory-flexibilities-resulting-from-coronavirus-covid-19

Pre-pandemic remote inspection approaches

MHRA

MHRA
Regulating Medicines and Medical Devices

GOOD MANUFACTURING PRACTICE
PRE-INSPECTION COMPLIANCE REPORT AND INTERIM COMPLIANCE REPORT
GUIDELINES FOR COMPLETION AND SUBMISSION

Processes/ Products

1	Have there been any changes in the types or numbers of products manufactured / handled. This should include re-introduction of a product after a period in excess of one year without manufacture and any products subject to shortages in supply. *Although changes to types of products would be picked up through the licensing process it may be that a site has re-introduced a product type after a lengthy period without manufacture. Increase in demand for products may have resulted in increased volumes – this is particularly significant where shift patterns are changed to accommodate or staff are recruited, transferred or made redundant.*
2	Please populate the table for all actives handled on site - regardless of market or commercial status (this can be attached as a separate table)

Active	PDE (µg/day)	Facility / Building	Manufacturing area (s)	Filling line (if different)	Primary Packing line	Dedicated (√)	
						Facility	Equipment

Please advise if the site handles any product types that would potentially be a hazard to specific individual inspectors e.g. beta-lactams, hormones etc.
The table can be taken out of the report format and appended to it if this is easier to prepare outside of the report.
PDE values should be determined via a Health Based Exposure Limit (HBEL) determination by a toxicologist. If HBEL assessments have not yet been completed, please report the Active but enter 'not determined' or ND against PDE.

3	Have there been any outsourcing activities or bringing back in-house previously outsourced activities directly related to production or Quality Control?
4	Have any GMP compliance issues been identified with any API sources that would lead to the conclusion that the source was not or may not be GMP compliant e.g. critical or numerous major findings in an audit of the API site, recurring failures on incoming goods testing of the API?
5	Have there been any Sterility test failures since the last inspection? *If so, please specify the date and product details*
6	Has there been any Media fill failures resulting in re-validation in accordance with guidelines in annex 1of the EU GMP Guide? *If so, Please give date, process/line detail and indication of products affected.*

[Microsoft Word - GMP_Compliance_Report_Guidelines_V_7.0 (publishing.service.gov.uk)]

Critical medicines - further afield..

Reg 174 vaccine approval

- Human Medicines Regulations 2012, Regulation 174:

  "The prohibitions in regulation 46 (requirement for authorisation) do not apply where the sale or supply of a medicinal product is authorised by the licensing authority on a temporary basis in response to the suspected or confirmed spread of … (a)pathogenic agents … which may cause harm to human beings."

- Flows from EU Directive 2001/83/EC Article 5 (2)

  "Member States may temporarily authorise the distribution of an unauthorised medicinal product in response to the suspected or confirmed spread of pathogenic agents, toxins, chemical agents or nuclear radiation any of which could cause harm."

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Regulating Medicines and Medical Devices

Thank you

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