Session 3: The Future of GCP Inspections

Joint US-FDA | MHRA-UK | Health Canada Good Clinical Practice & Pharmacovigilance Symposium
February 14, 2024 – 11:25 – 12:15 AM

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Remote Regulatory Assessment (RRA) for Marketing Application Review

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A Joint US-FDA | MHRA-UK | Health Canada Good Clinical Practice & Pharmacovigilance Compliance Workshop
February 13-15, 2024

Medicines & Healthcare products Regulatory Agency

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Disclaimer

The views and opinions presented here represent those of the speaker and should not be considered to represent advice or guidance of the U.S. Food and Drug Administration.

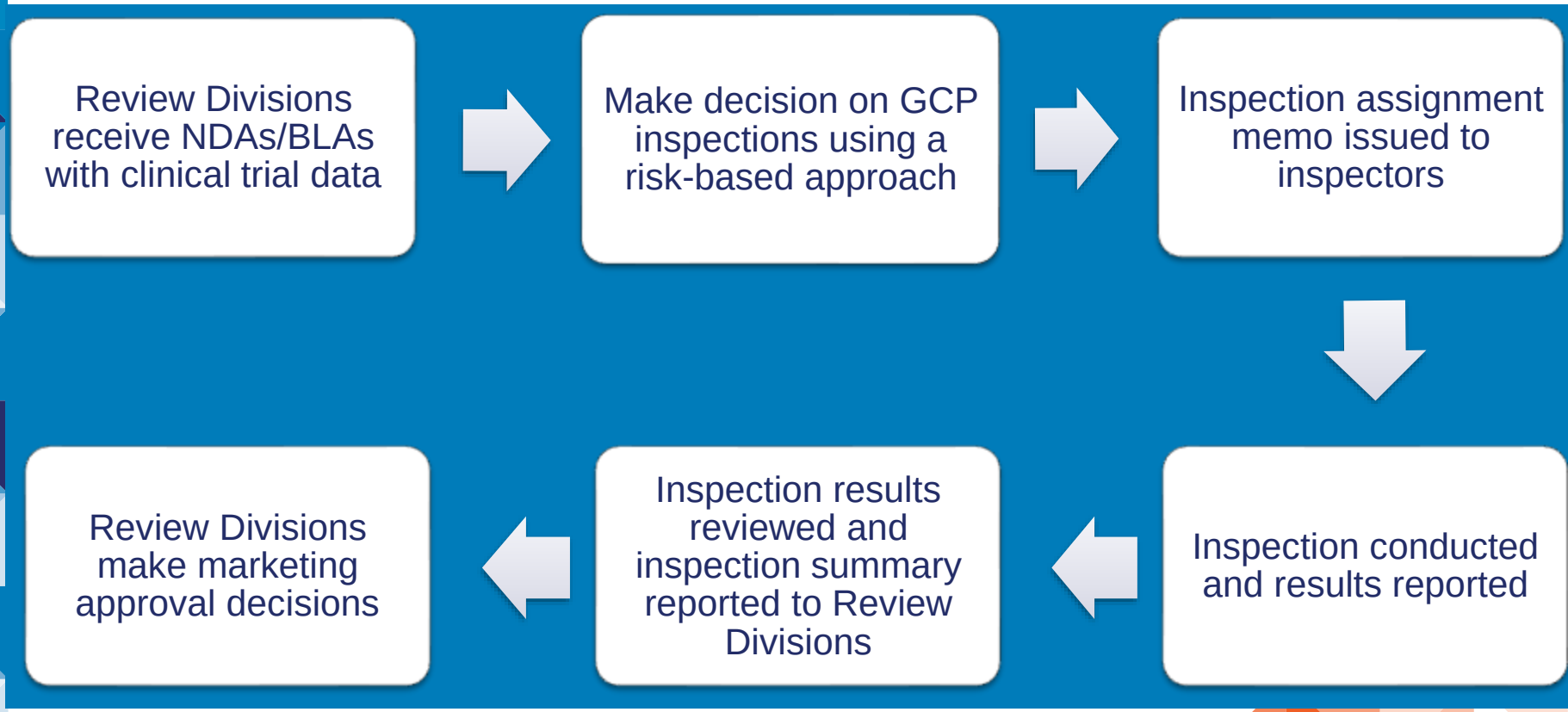
Overview

- Experience of remote regulatory assessment (RRA) during the pandemic
- Lessons learned from marketing application review
- Future use of RRAs

GCP Inspections for NDAs/BLAs

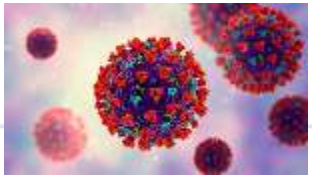
- Clinical Investigator (CI)
- Sponsor-investigator
- Sponsor
- Contract Research Organization (CRO)

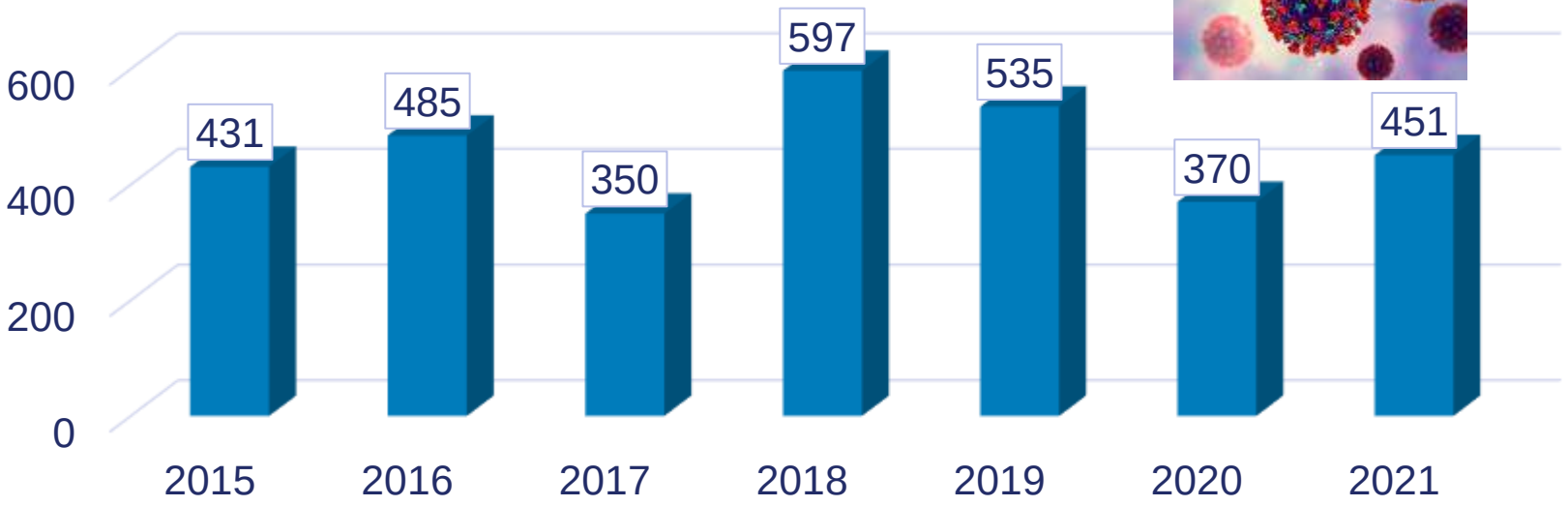
Compliance Review Process for NDAs/BLAs



Pandemic Impact on GCP Inspection

Number of Inspections by Fiscal Year





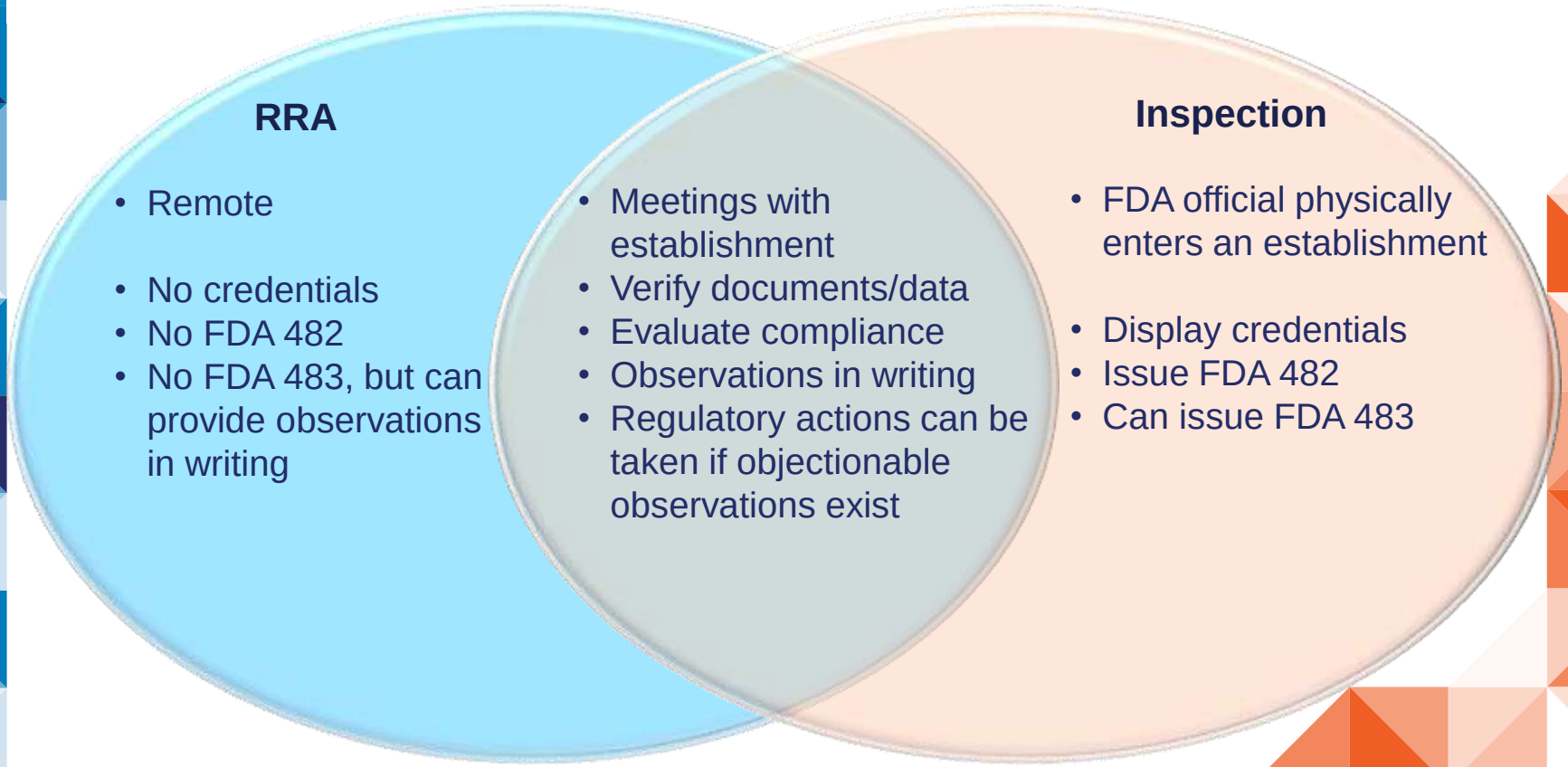
The yearly average
in FY2015-19: 481

FY2020: ↓ 23%
FY2021: ↓ 6%

Remote Regulatory Assessment (RRA)

- Remote examination of an FDA-regulated establishment and/or its records to evaluate compliance with applicable FDA requirements

Similarities and Differences Between GCP Inspection and RRA



RRAs During Pandemic FY20-21

FY20

- 39 RRAs
- Oncology and anti-viral

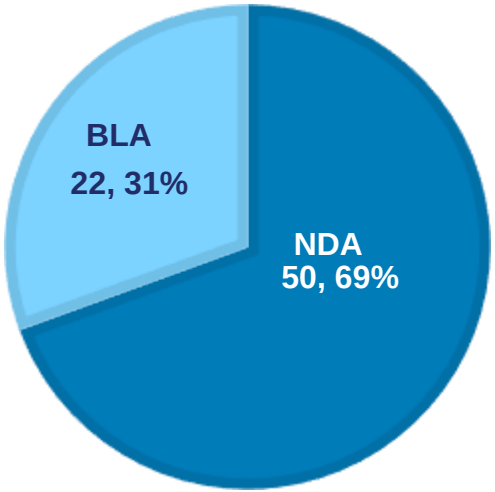
FY21

- 33 RRAs
- Oncology and rare diseases

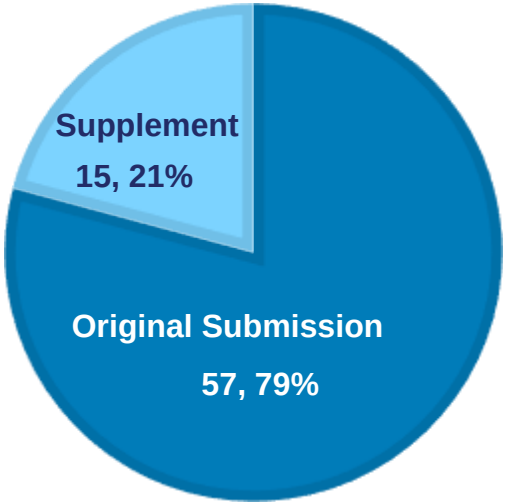
Total Number = 72

RRAs in FY20-21

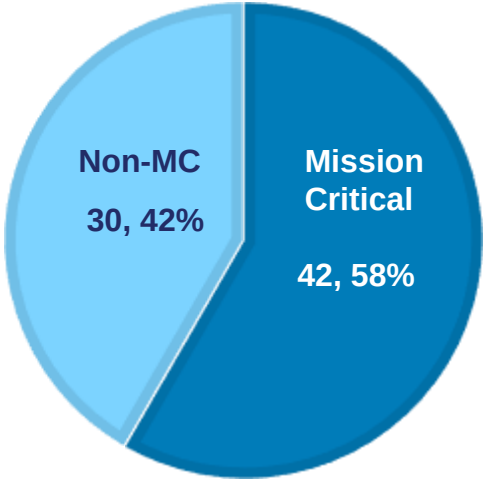
Application



Submission



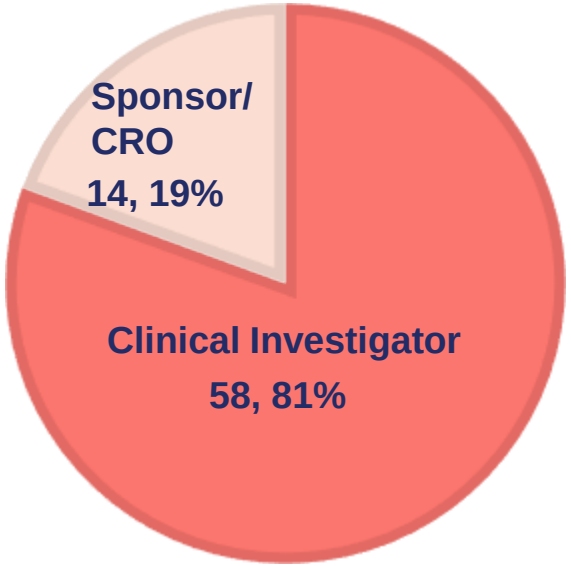
Mission Critical (MC)



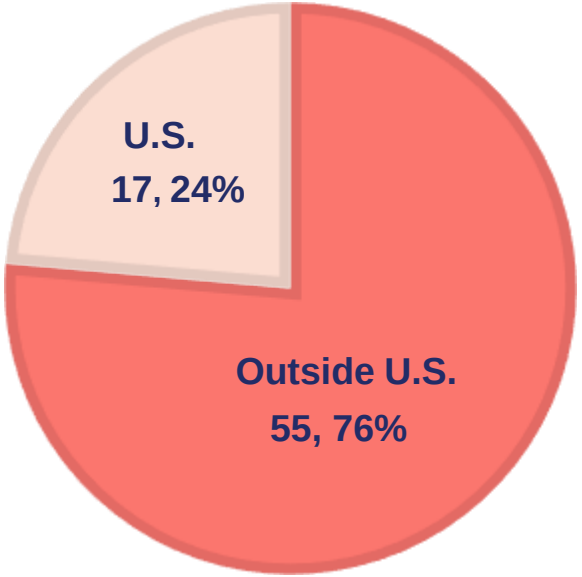
Total Number = 72

RRAs in FY20-21 - Continued

Establishment Type



Location



Total Number = 72

Lesson Learned

- RRAs were useful in the assessment of data reliability, subject safety, and clinical trial conduct

- RRAs supported FDA's mission and informed the agency the regulatory decisions for the marketing applications during the pandemic

Benefits of an RRA

- Valuable tool to verify data submitted
- Allow FDA to assess GCP and regulatory compliance remotely to support regulatory decisions
- Expand the breadth of FDA's GCP oversight
- Potential to save resources (travel time, money)

When May FDA Request an RRA?

- When FDA determines that an RRA will assist in the oversight of establishments or support regulatory decisions

- When FDA cannot conduct an inspection due to travel limitations

Take-home Message

RRA is a valuable tool for regulatory authorities to assess GCP compliance

Acknowledgement

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- Amir Tahami, M.B.A.
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- Staff in the Office of Regulatory Affairs

Resources

- Conducting Remote Regulatory Assessments Questions and Answers. Draft Guidance for Industry. JANUARY 2024

- ORIGINAL RESEARCH

  The United States Food Drug Administration's Innovative Alternative Tools to Evaluate Good Clinical Practice During the COVID-19 Public Health Emergency

  Kassa Ayalew, Jenn W. Sellers, Phillip D. Kronstein, Laurie Muldowney, Emily Gebbia, Jean Mulinde and David Burrow

The Future of GCP Inspections

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Lieutenant Commander, US Public Health Service
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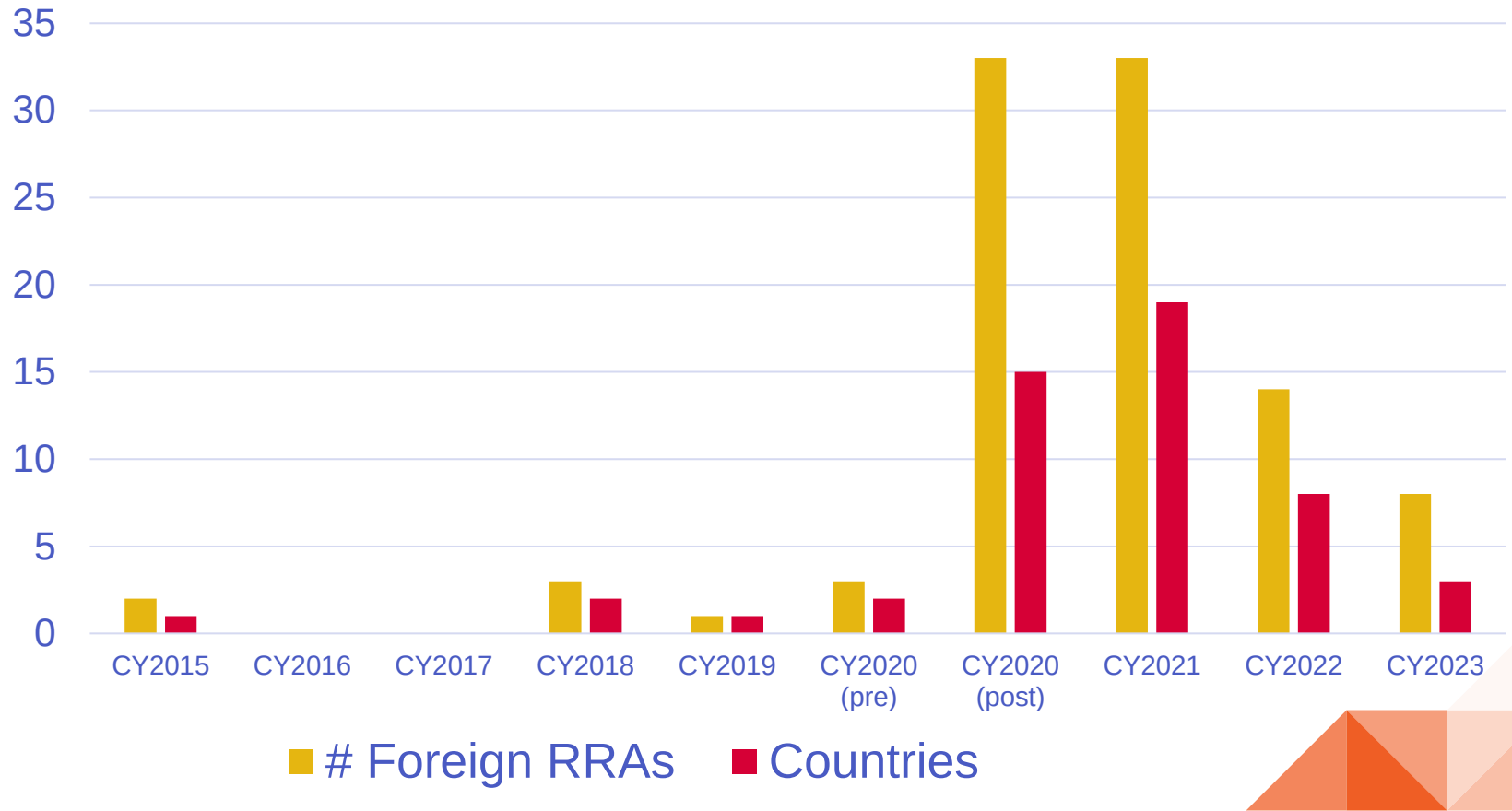
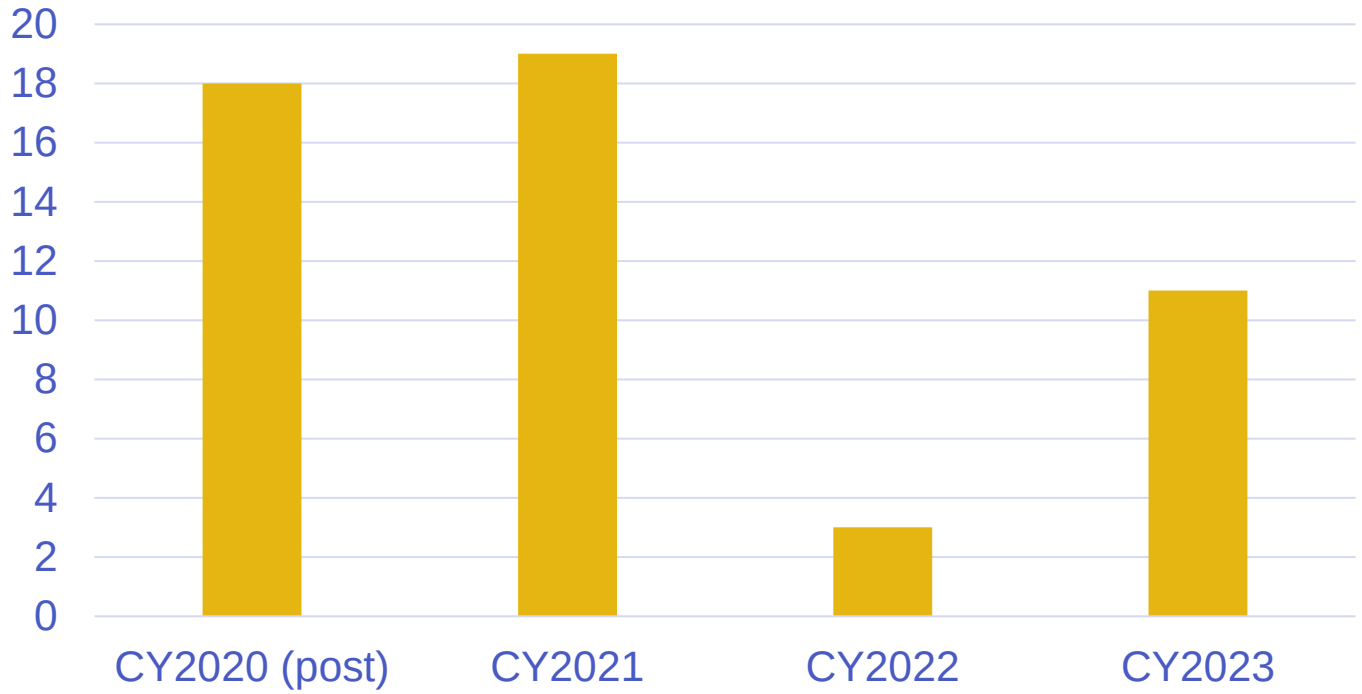
Topics

- Evolution of the Remote Regulatory Assessment (RRA)
- RRAs in the transition and steady state
- Looking towards our future

Evolution of the RRA - Foreign



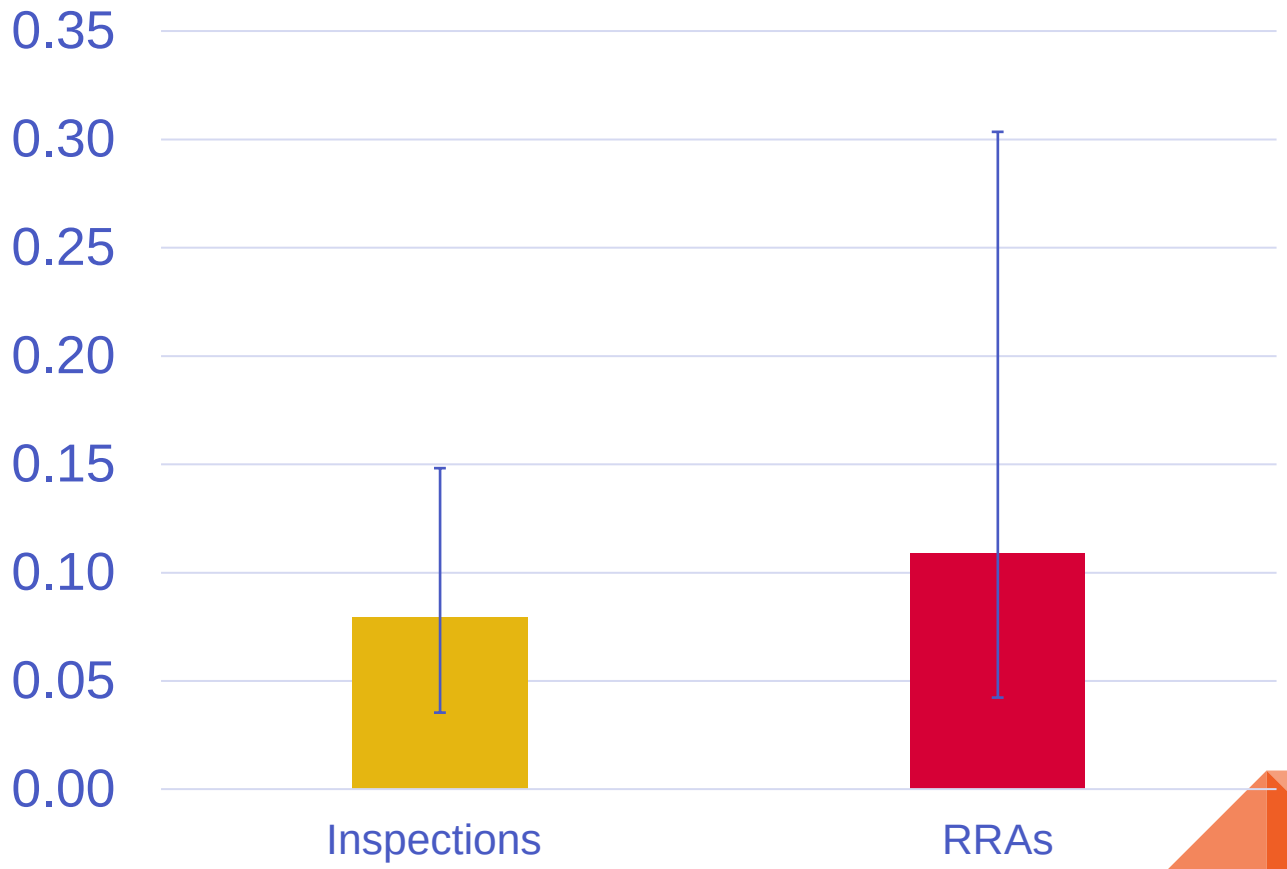
Evolution of the RRA – Domestic



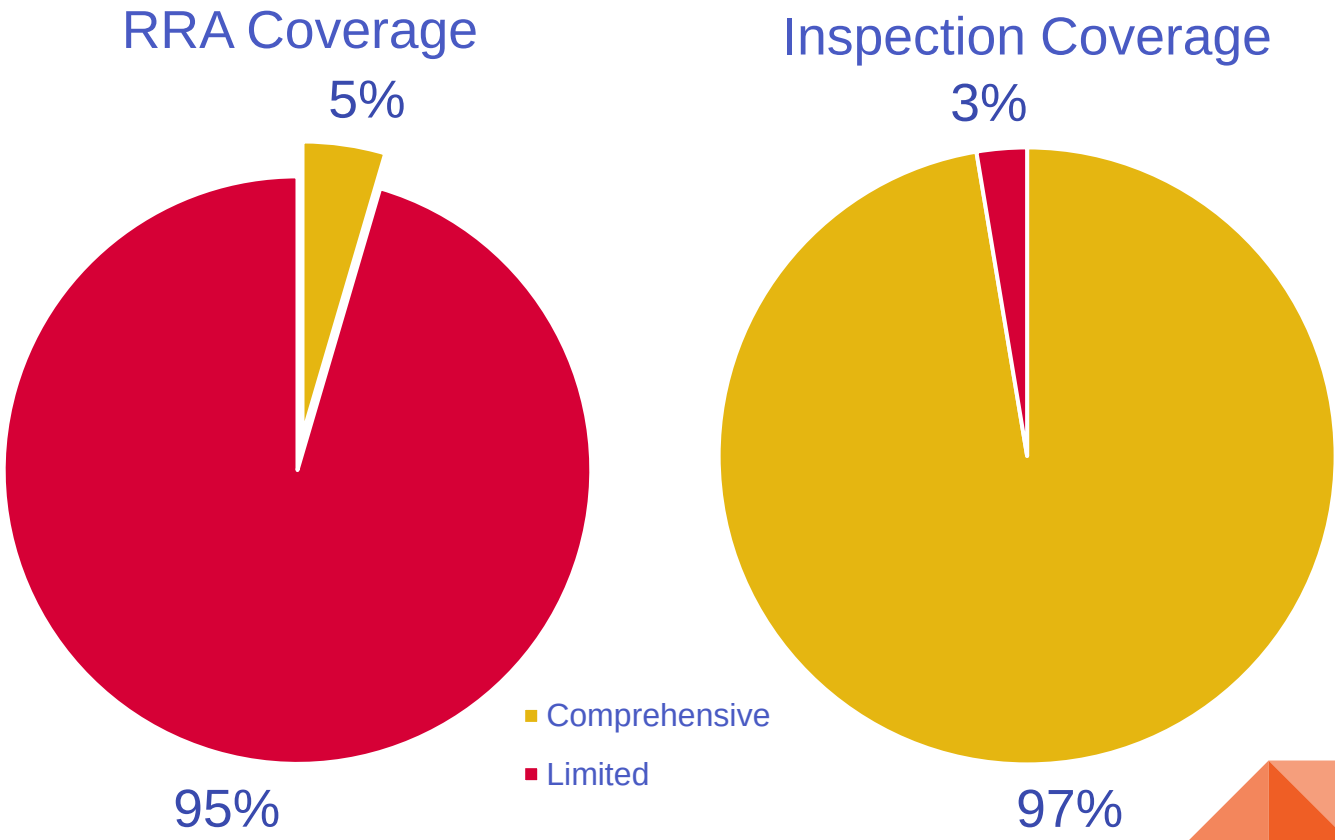
Pandemic RRAs - Analysis

- Resource Burn
- Coverage

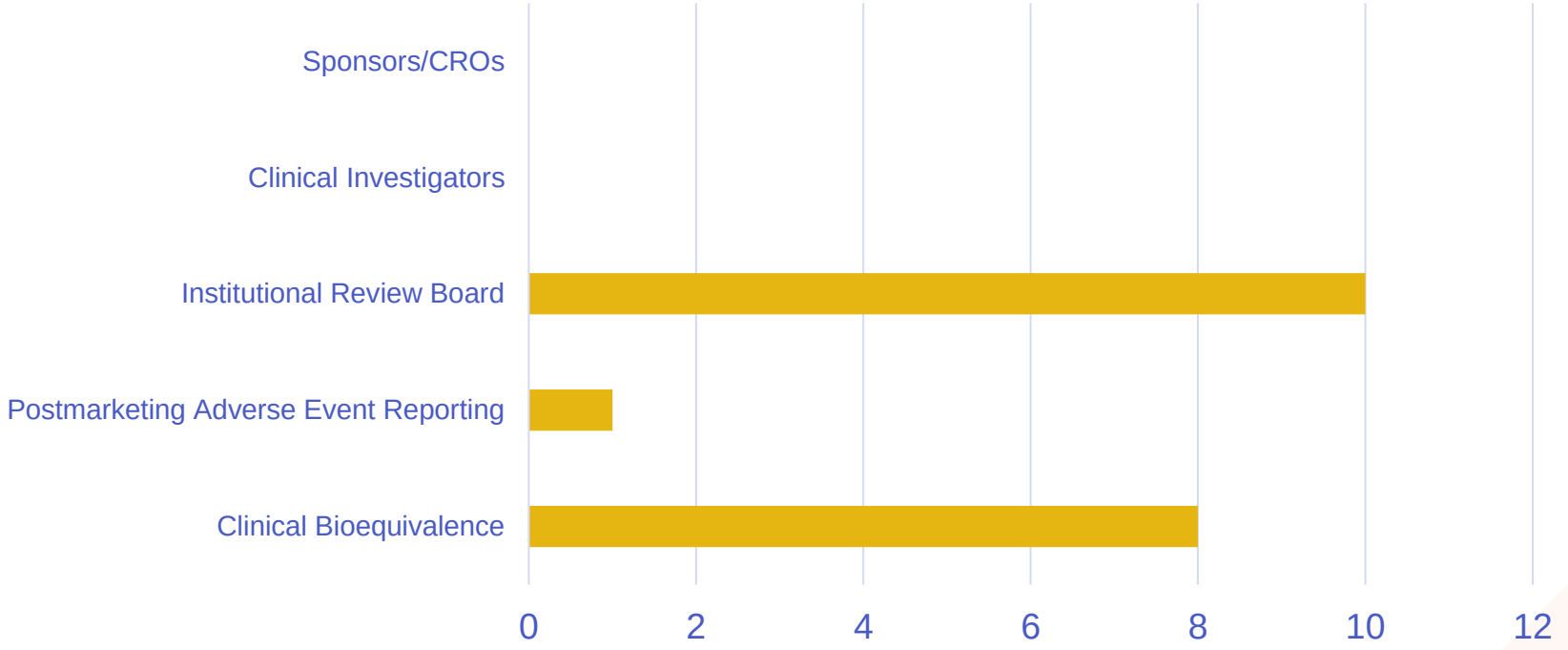
Resource Burn



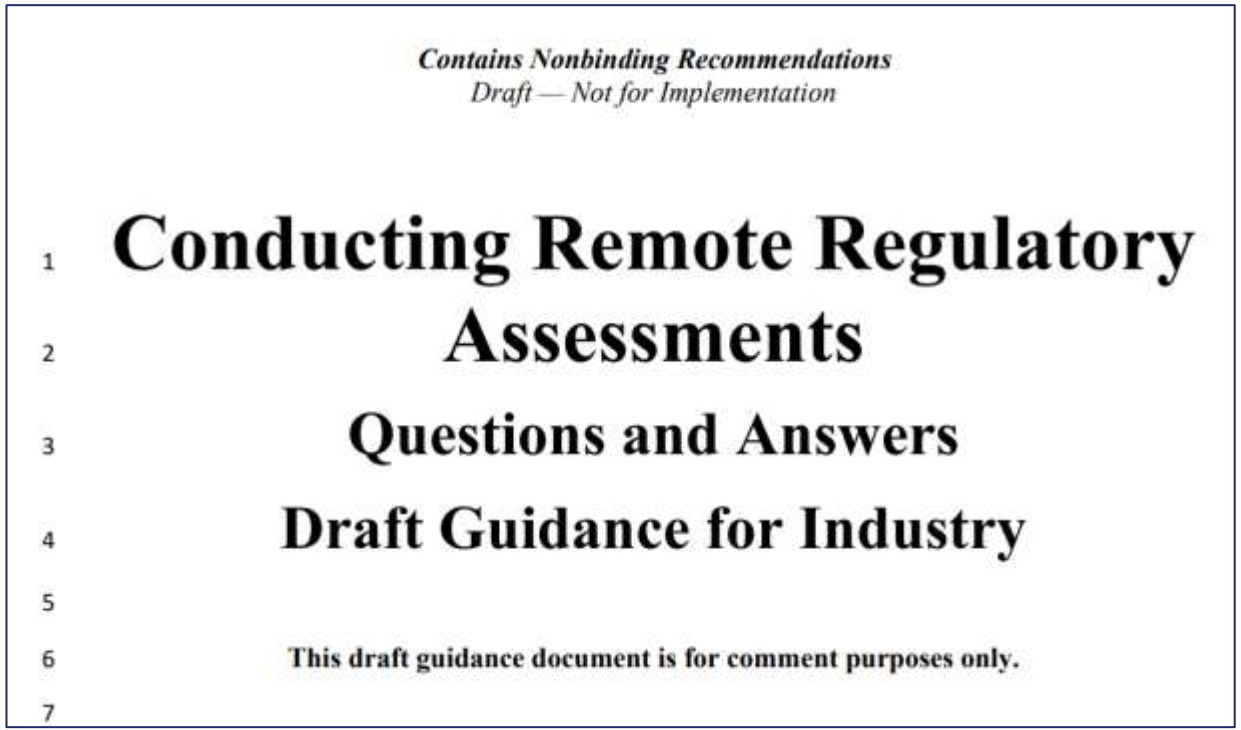
Coverage


RRA Coverage
5%
95%
Inspection Coverage
3%
97%
Comprehensive
Limited

RRAs in the steady state - 2023



Looking towards our future



Contains Nonbinding Recommendations
Draft — Not for Implementation

1 **Conducting Remote Regulatory**
2 **Assessments**
3 **Questions and Answers**
4 **Draft Guidance for Industry**
5
6 **This draft guidance document is for comment purposes only.**
7

The Future of GCP Inspections

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UK inspections

- SI 2004/1031 and SI 2006/1928
  - Right to inspect any site involved in clinical trial activities in the UK
  - Fees to be charged for inspections associated with clinical trials
- HMR 2012/1916 Regulations 325, 327 and 328
  - Covers rights of entry, powers of inspection and sampling and seizure

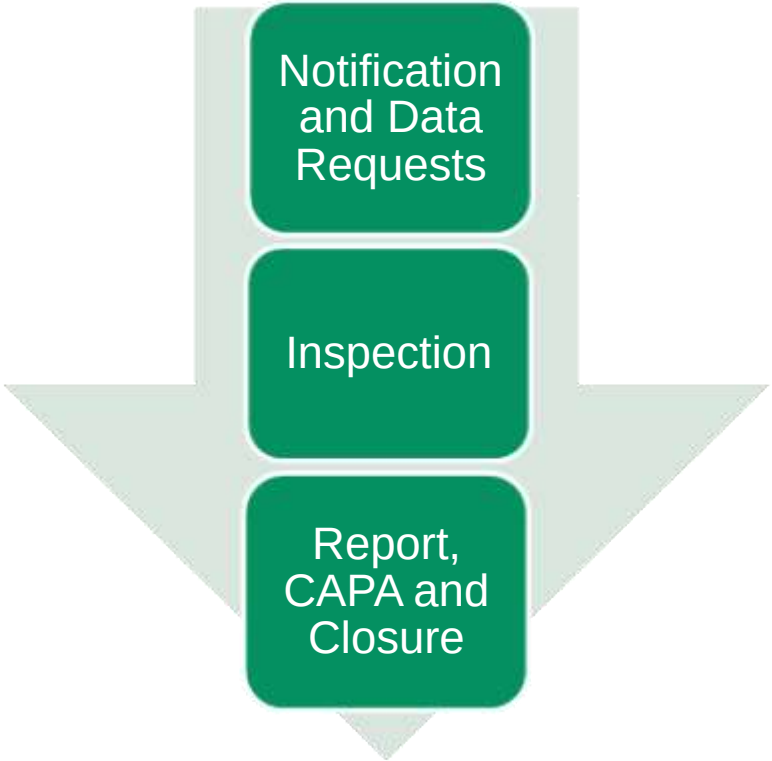
Types of MHRA GCP inspections

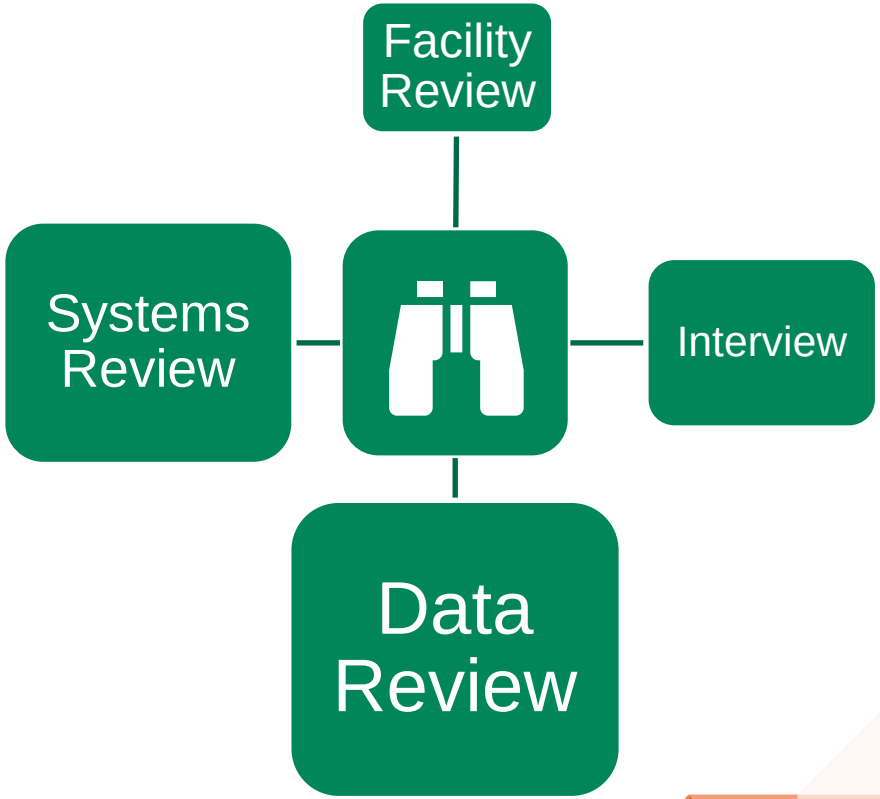
- National Programme
  - Risk-based: systems or study-specific
  - Triggered: systems or study-specific
  - Voluntary Phase 1 Accreditation Scheme
- Requested Inspections, MAA - related
  - Requested by MHRA Assessors
- Joint inspections with other agencies

Types of organisations inspected

- Commercial and non-commercial sponsors
- Investigator sites
- Contract Research Organisations (CROs)
- Specialist providers (e.g. eSystem Vendors)
- Laboratories
- Non-commercial Clinical Trial Units
- Phase 1 units
- Bioequivalence/Biosimilar facilities

Typical inspection format





What did the pandemic change?

- Move to a remote only programme
  - Review TMF remotely
  - Focus on trial oversight and effective change control procedures
  - eSystem focus on data integrity and controls

GCP challenges for trials

- Recruitment pauses and temporary halts
- Missing data
- Scientific advice on usability of data
- Protocol deviations
- Re-monitoring required?
- Participants receiving vaccines, vaccine trials unblinding

GCP remote inspection outcomes

- Consent of trial participants
- Reliability of the trial endpoints
- QC activities in relation to data management
- Monitoring for data integrity

The future of remote inspections?

- A hybrid approach to GCP inspections will continue to be used
- A positive response from industry
- Also a benefit to the public

The future of GCP inspections?

- Work has commenced on drafting proposed changes to UK legislation based on public consultation (2138 responses received)
- New International Recognition Procedure
- Upcoming programme of MAA inspections

Copyright information

Questions?

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Summary

- GCP RRAs are a valuable tool for regulatory authorities to assess compliance, but will not replace GCP inspections due to their limitations.
- Preparation for onsite and remote inspections is similar. Document review, interviews and document requests don’t change just because an inspector is in their home office rather than a conference room in your head office.