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

Moderator: **Kassa Ayalew, MD, MPH**
Division Director | DCCE | OSI | OC | CDER | FDA

Jenn Sellers, MD, PhD
Branch Chief | GCPAB | DCCE | OSI | OC | CDER | FDA

Jennifer Adams, MPH
Lieutenant Commander (LCDR) | USPHS
Foreign Cadre Director | OBIMO | OMPTO | ORA | FDA

Rachel Mead, BSc
Senior GCP Inspector | MHRA

Remote Regulatory Assessment (RRA) for Marketing Application Review

Jenn Sellers, M.D., Ph.D., FAAP

Branch Chief
GCP Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations
Office of Compliance/CDER/FDA

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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.

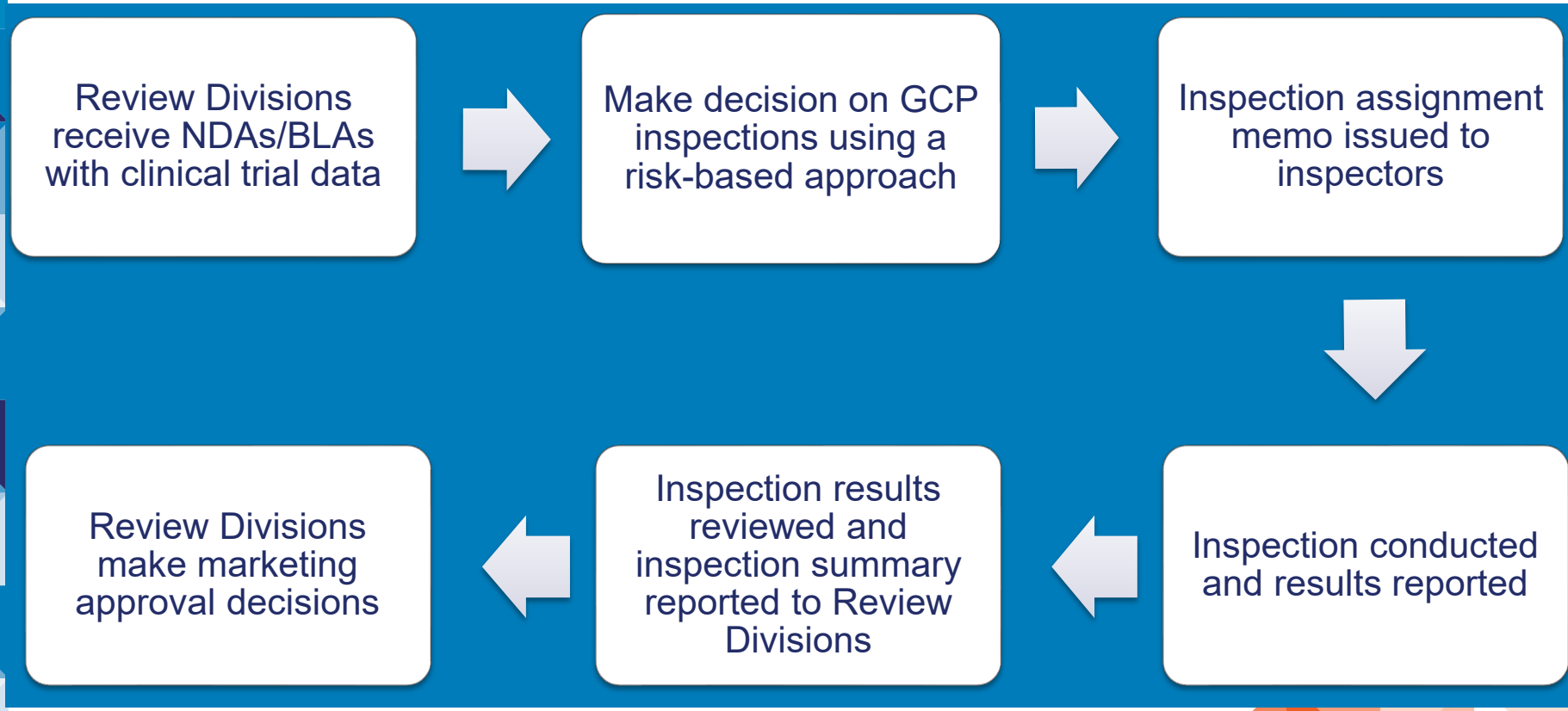
Overview

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

GCP Inspections for NDAs/BLAs

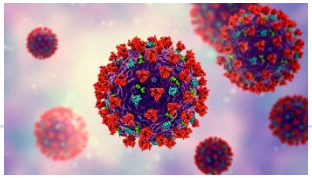
- Clinical Investigator (CI)
- Sponsor-investigator
- Sponsor
- Contract Research Organization (CRO)

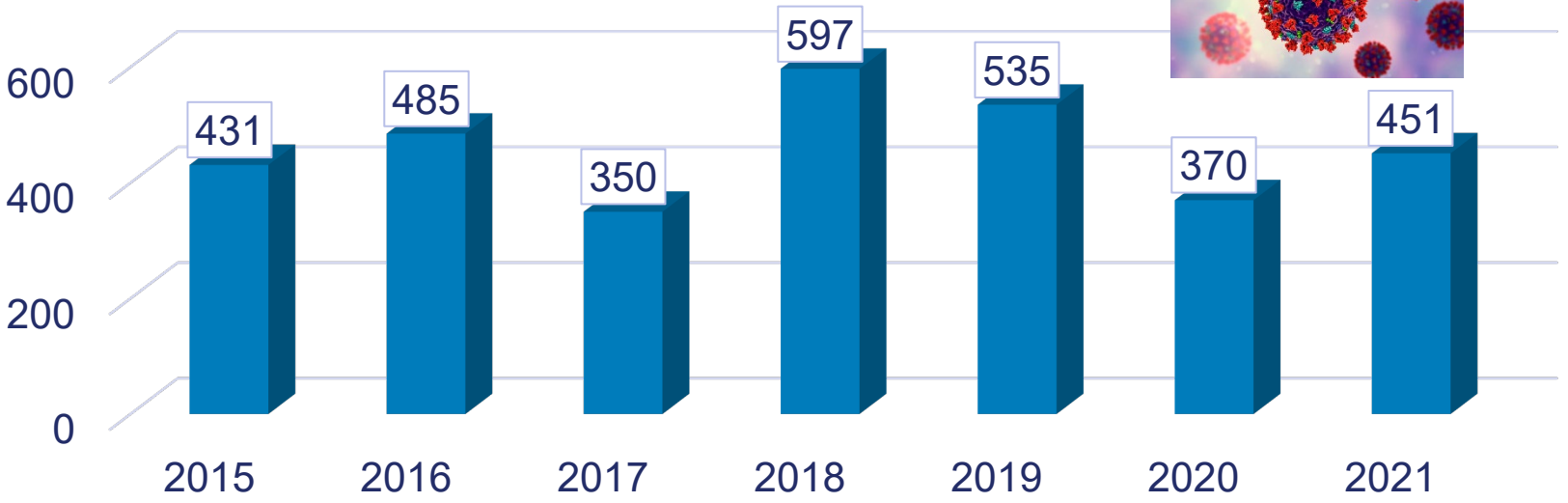
Compliance Review Process for NDAs/BLAs



Pandemic Impact on GCP Inspection

Number of Inspections by Fiscal Year





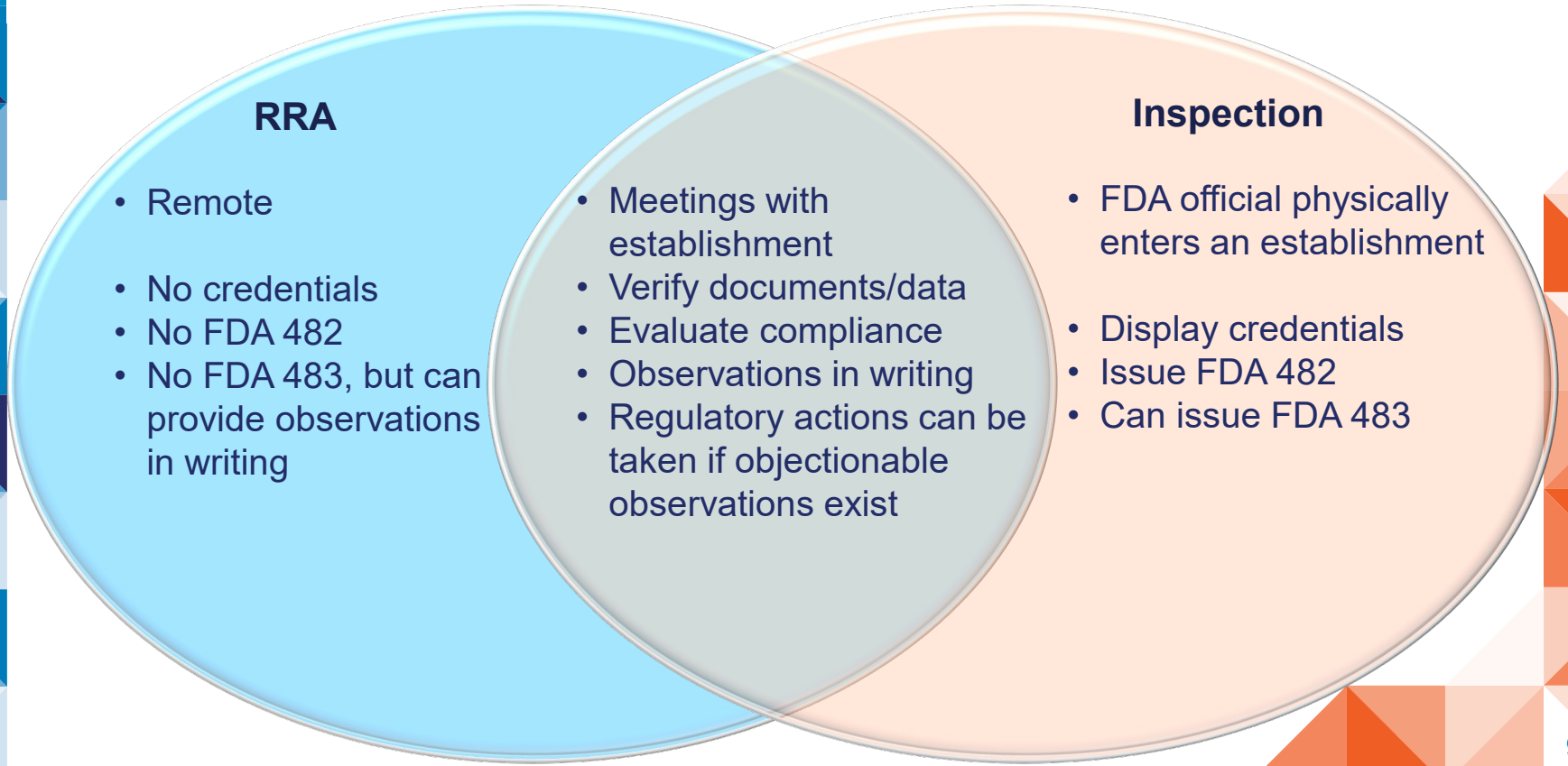
The yearly average in FY2015-19: 481

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

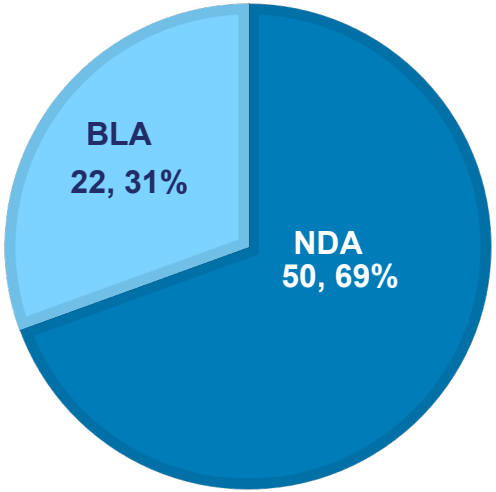
FY21

- 33 RRAs
- Oncology and rare diseases

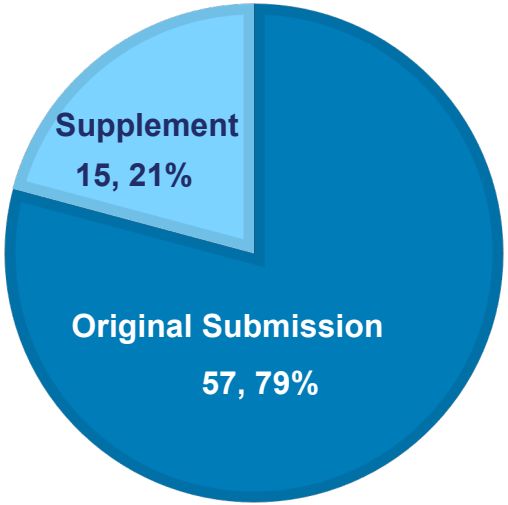
Total Number = 72

RRAs in FY20-21

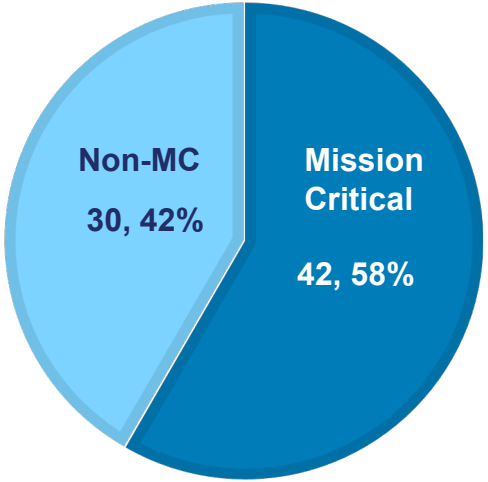
Application



Submission



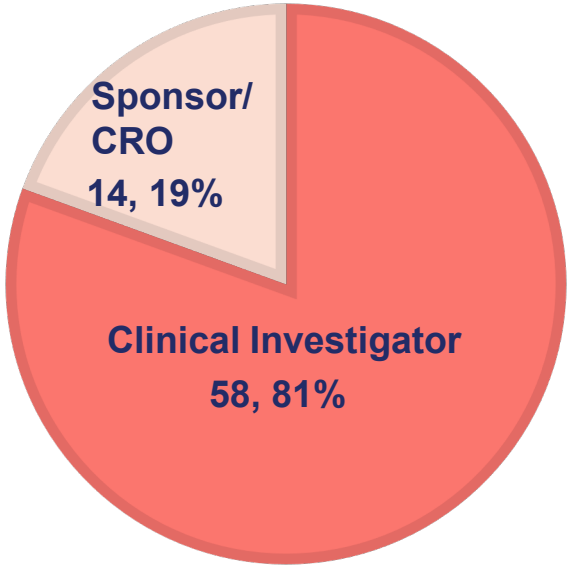
Mission Critical (MC)



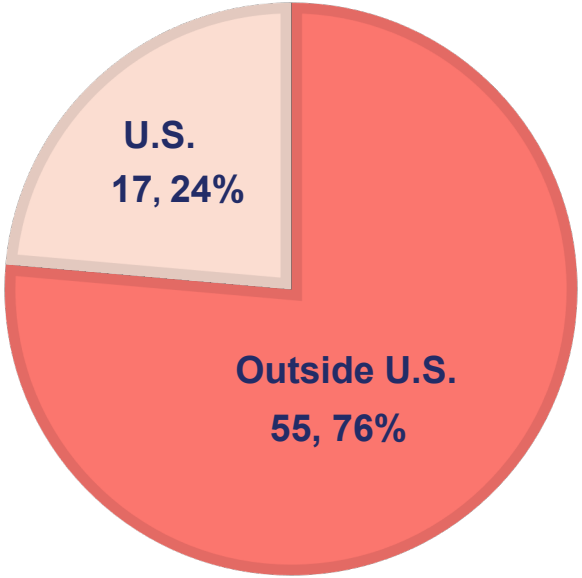
Total Number = 72

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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- Yolanda Patague
- 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

Jennifer Adams
Lieutenant Commander, US Public Health Service
Foreign Cadre Director
Office of Bioresearch Monitoring | U.S. Food and Drug Administration

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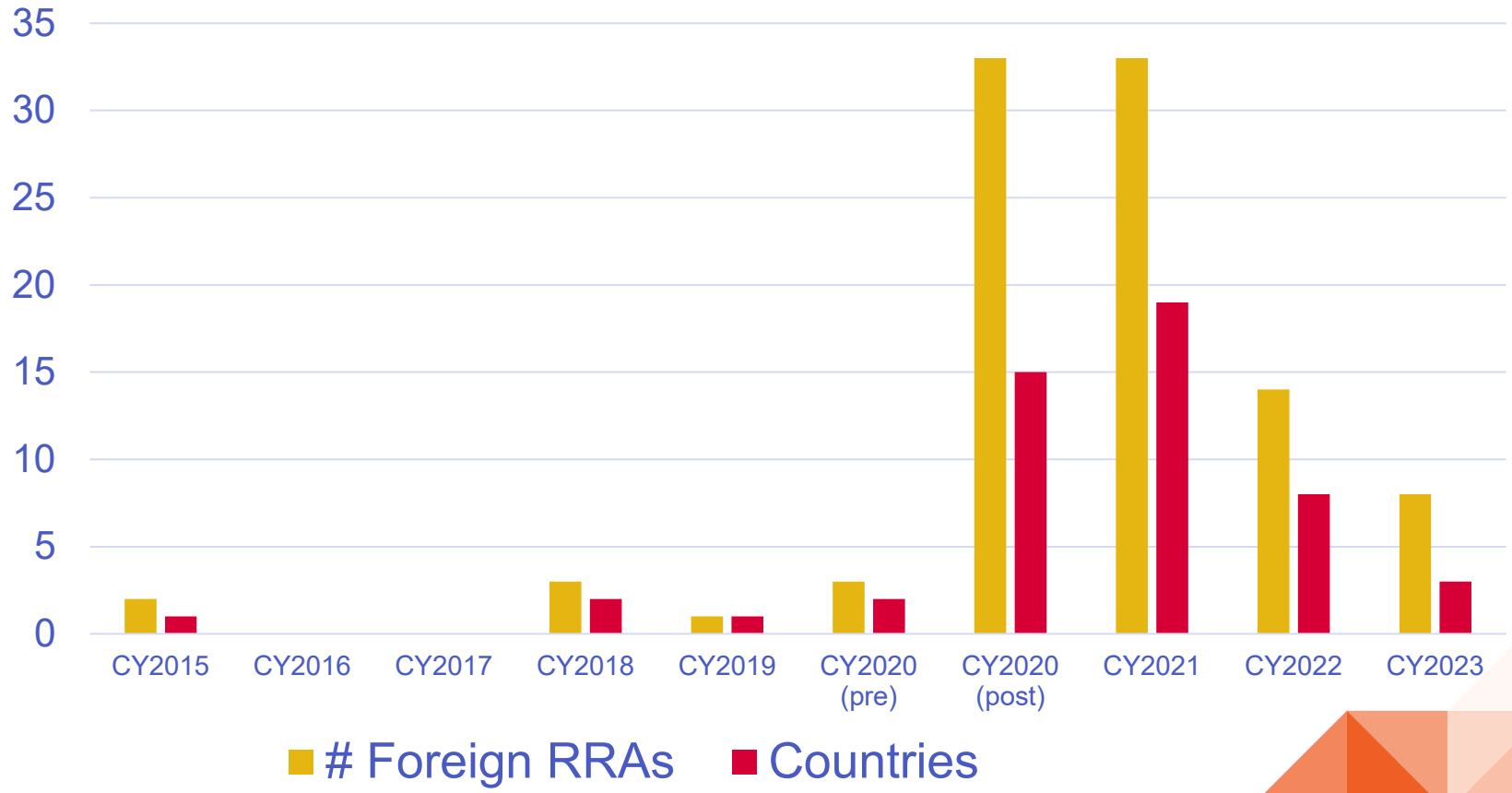
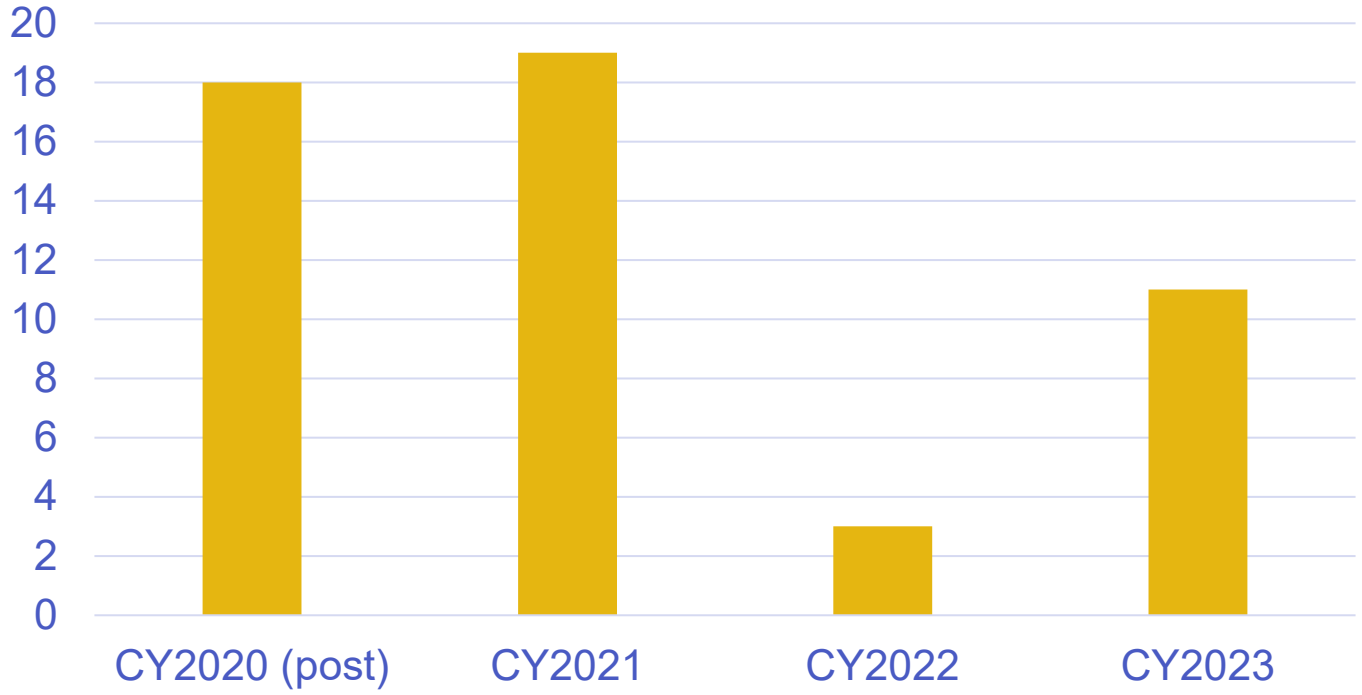
Topics

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

Evolution of the RRA - Foreign



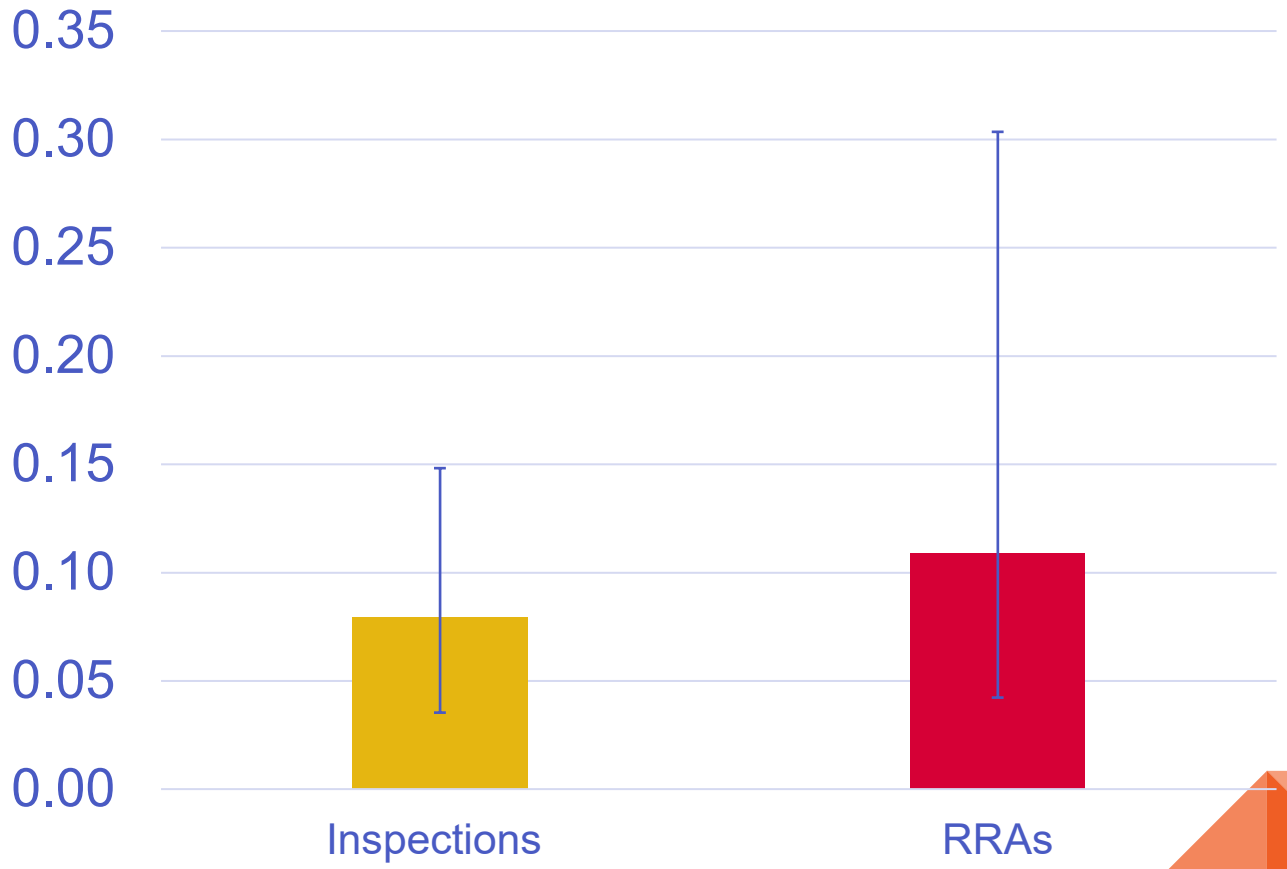
Evolution of the RRA – Domestic



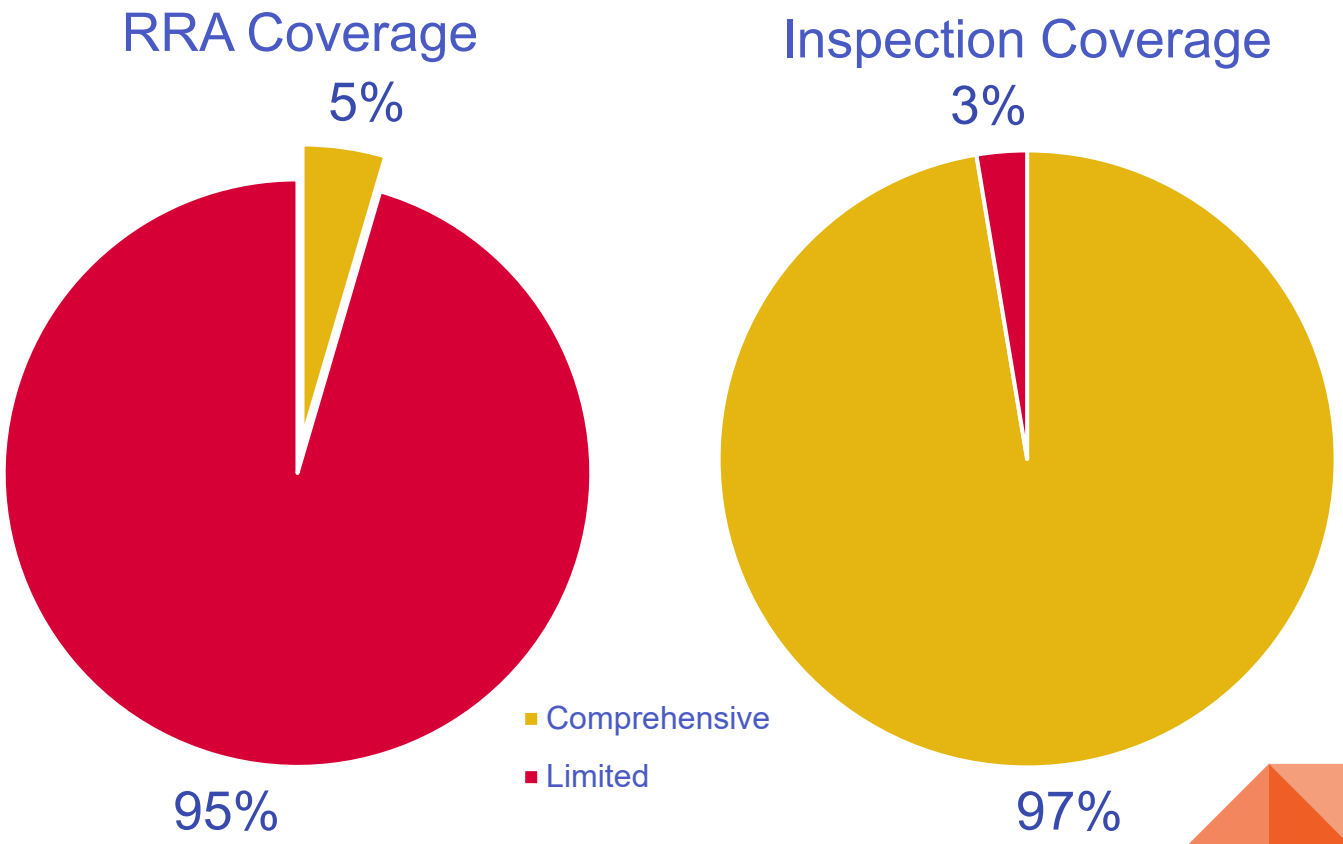
Pandemic RRAs - Analysis

- Resource Burn
- Coverage

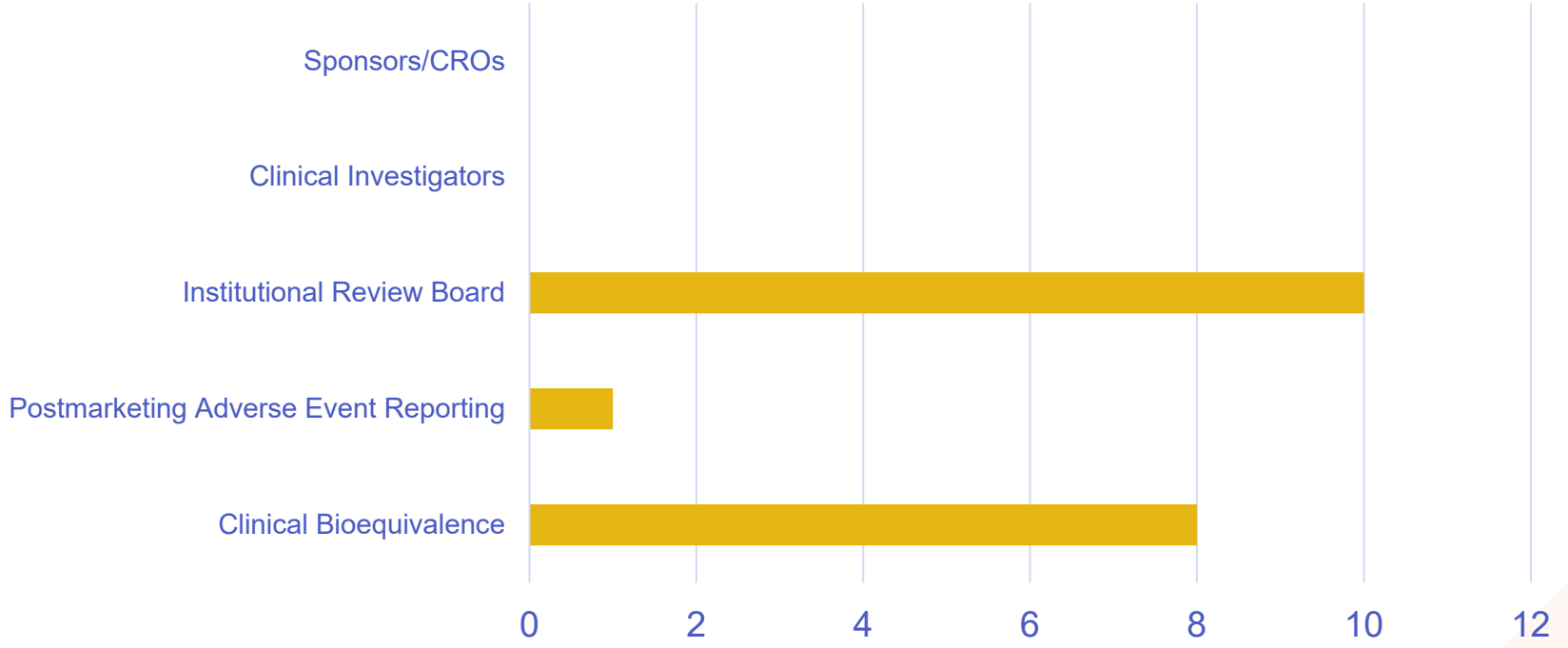
Resource Burn



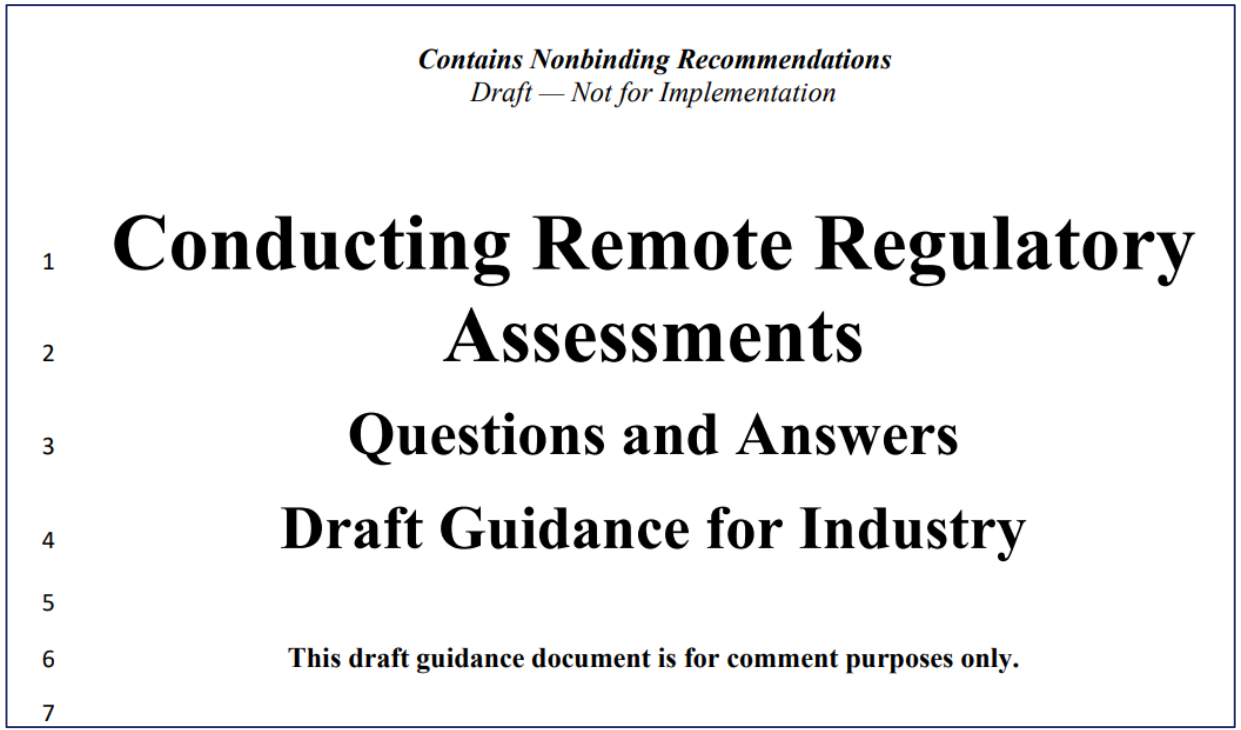
Coverage


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

Rachel Mead
Senior GCP Inspector
Compliance Team 1
Medicines and Healthcare products Regulatory Agency

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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

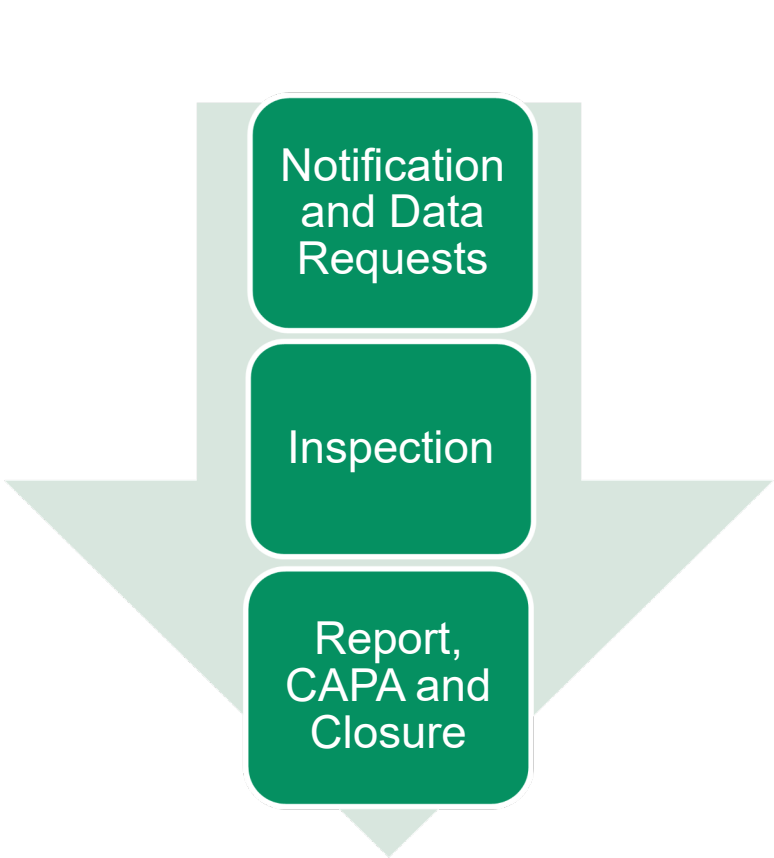
Types of MHRA GCP inspections

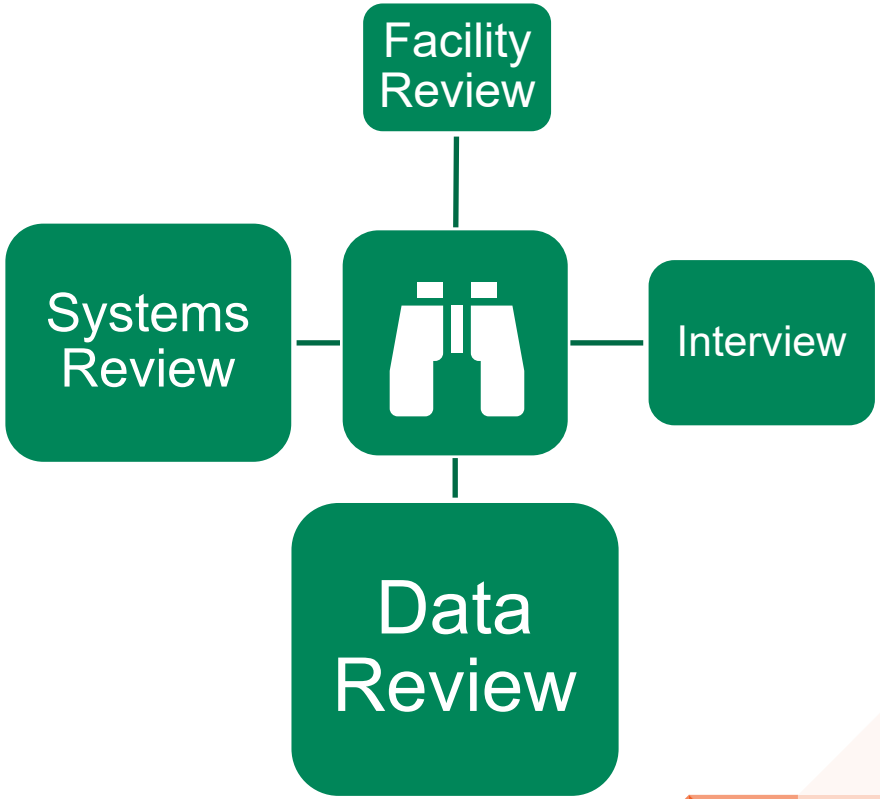
- National Programme
  - Risk-based: systems or study-specific
  - Triggered: systems or study-specific
  - Voluntary Phase 1 Accreditation Scheme
- Requested Inspections, MAA - related
  - Requested by MHRA Assessors
- Joint inspections with other agencies

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?

Rachel Mead
Senior GCP Inspector
Compliance Team 1
Medicines and Healthcare products Regulatory Agency

clintrialhelpline@mhra.gov.uk

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.