8 November 2024
EMA/INS/GCP/164938/2024
Inspections Office
Quality and Safety of Medicines Department

Annual Report of the Good Clinical Practice (GCP) Inspectors' Working Group (IWG) 2023

Adopted by the GCP IWG on 26 November 2024

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List of Abbreviations

AE	Adverse Event
BE	Bioequivalence
CHMP	Committee for Medicinal Products for Human Use
CMDh	Coordination Group for Mutual Recognition and Decentralised Procedures - Human
CRF	Case Report Form
CRO	Clinical/Contract Research Organisation
CSR	Clinical Study Report
CTCG	Clinical Trials Coordination Group
CTIS	Clinical Trials Information System
CVMP	Committee for Medicinal Products for Veterinary Use
DCP	Decentralised Procedure
eCRF	electronic Case Report Form
EEA	European Economic Area
EMA	European Medicines Agency
EU	European Union
EWG	Expert Working Group
FDA	(United States) Food and Drug Administration
GCP	Good Clinical Practice
GMDP	Good Manufacturing Practice/Good Distribution Practice
HMA	Heads of Medicines Agencies
IC	Informed Consent
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ICMRA	International Coalition of Medicines Regulatory Authorities
IEC	Independent Ethics Committee
IIR	Integrated Inspection Report
IMP	Investigational Medicinal Product
IRB	Institutional Review Board
IWG	Inspectors Working Group
MS	Member State
MRP	Mutual Recognition Procedure
PDCO	Paediatric Committee
PhV	Pharmacovigilance
PMDA	Pharmaceuticals and Medical Devices Agency (Japanese competent authority)
Q&A	Question & Answer
ROW	Rest of the World
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
SDV	Source Data Verification
SUSAR	Suspected Unexpected Serious Adverse Reaction
TMF	Trial Master File
UK	United Kingdom
US(A)	United States (of America)
WHO	World Health Organisation

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1. Introduction

This document is the sixteenth Annual Report of the GCP IWG. This group was established in 1997 under the scope of Article 51(e) of Council Regulation (EEC) No. 2309/93, subsequently amended as Article 57(1)(i) of Regulation (EC5 No. 726/2004.

The GCP IWG focuses on the harmonisation and coordination of GCP related activities at European Union (EU)/European Economic Area (EEA) level. The group's role and activities are described in more detail in its mandate, which was revised in 2013, its current Work Plan and also in Volume 10, chapter IV of the publication "The rules governing medicinal products in the European Union".

The group supports the coordination of the provision of GCP advice and maintains a dialogue with other groups, such as the Committee for Medicinal Products for Human Use (CHMP), the Committee for Medicinal Products for Veterinary Use (CVMP), the Coordination Group for Mutual Recognition and Decentralised Procedures - Human (CMDh), the Pharmacovigilance (PhV) IWG, the Good Manufacturing Practice/Good Distribution Practice (GMDP) IWG, and other groups, as needed, in areas of common interest.

This Annual Report has been drawn up in line with the format and objectives of the 2021-2023 Work Plan.

2. Meetings

Four regular GCP IWG meetings took place in 2023:

- 21-22 March 2023 (Hybrid).
- 20-21 June 2023 (Virtual).
- 19-20 September 2023 (Virtual).
- 28-29 November 2023 (Hybrid).

During 2023 the following GCP inspectors' subgroups/working parties were involved in the discussion of specific topics and drafting documents:

- GCP IWG/CMDh working party (refer to section 5.5).
- GCP IWG subgroup on drafting guidance on electronic systems used in clinical trials (refer to section 4.1).
- GCP IWG subgroup on serious breaches submitted and assessed according to the new Clinical Trials Regulation (CTR).
- GCP IWG-assessors subgroup on embedding the outcome of GCP inspections into the benefit-risk assessment and modernisation of the GCP inspection process.
- GCP IWG subgroup on drafting a Q&A about the considerations when direct remote access of identifiable personal and health data is required in a clinical trial (former Subgroup on remote source data verification).
- GCP IWG subgroup on selection of procedures and site exploiting the individual patient data listings (raw data pilot).
- GCP IWG subgroup on the redaction of inspection reports for publication in the Clinical Trials Information System (CTIS).

- GCP-GMDP IWG subgroup on the Recommendation paper on travel advice.

3. Inspections conducted in support of the centralised procedure

3.1. CHMP requested inspections

3.1.1. General overview

a) Foreword

The data in this report relates to inspections carried out in 2023.

In total, 67 GCP site inspections including 58 routine and 9 triggered were requested by CHMP and carried out by the inspectorates of the EU/EEA Member States (MSs) in 2023. It should be noted that several inspections requested in 2022 were conducted in 2023, which are therefore included in this report. In addition, several inspections requested in 2023 were carried out in 2024, which are therefore not included in this report.

The figures cited above reflect the number of inspections performed at a given site. If a site was inspected for several clinical trials, it was counted once for the purpose of this report. It should be noted that different methods for counting inspections coordinated by the European Medicines Agency (EMA) can be used in other reports, for instance when the indicator is the number of fees invoiced for distinct inspections, as defined in the Rules for the implementation of Council Regulation (EC) No 297/95 on fees payable to the European Medicines Agency and other measures.

b) Geographical distribution

Similarly to the 2022 annual report, this report distinguishes the following regions:

- EU/EEA.
- North America:
  - United States of America (USA).
  - Canada.
- Rest of the World (ROW):
  - Africa.
  - Asia.
  - Eastern Europe, non-EU (Belarus, Bosnia, the Republic of North Macedonia, Moldova, Russia, Serbia, Ukraine).
  - Western Europe, non-EU (Switzerland, United Kingdom [UK]).
  - Latin America and the Caribbean.
  - Oceania.

c) Inspection figures

In Figure 1 and Table 1, the number of inspections conducted in 2023 is shown by region and type of inspection. Most inspections were carried out in the EU/EEA (34.3%) followed by Asia (28.4%) and North America (17.9%).

Table 1: Number of inspections conducted per region and type of inspection

Region	Routine	Non-Routine	Total	%
EU/EEA	23	0	**23**	**34.3%**
North America	12	0	**12**	**17.9%**
Africa	2	2	**4**	**6.0%**
Asia	12	7	**19**	**28.4%**
Eastern Europe, non-EU	2	0	**2**	**3.0%**
Western Europe, non-EU	5	0	**5**	**7.5%**
Latin America and the Caribbean	0	0	**0**	**0.0%**
Oceania	2	0	**2**	**3.0%**
Grand Total	**58**	**9**	**67**	**100.0%**

Figure 1: Inspections conducted per region and type of inspection.

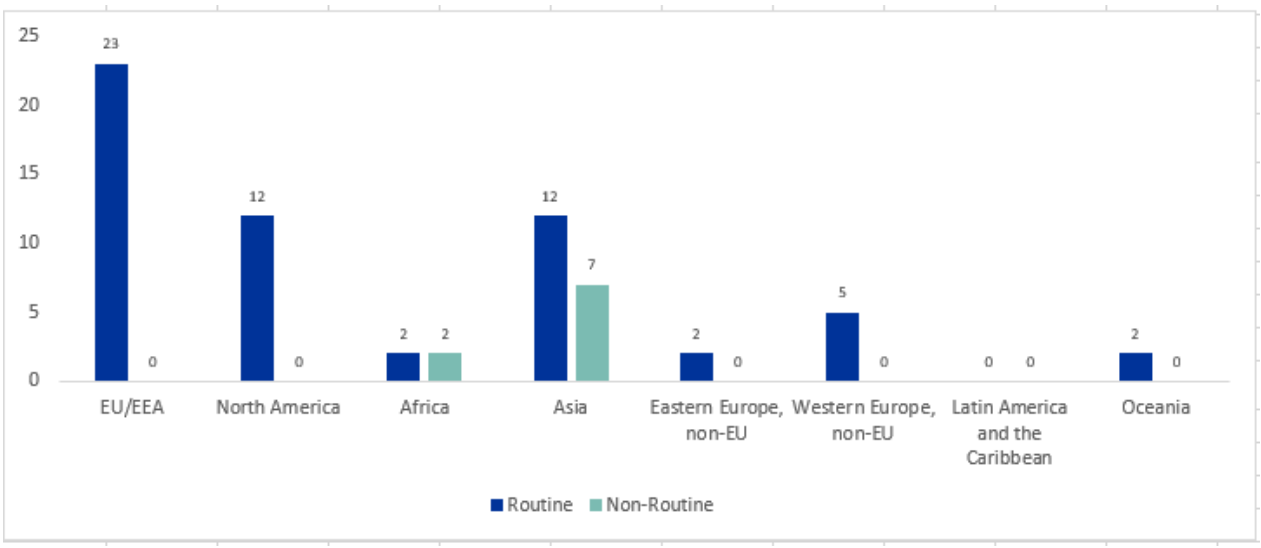
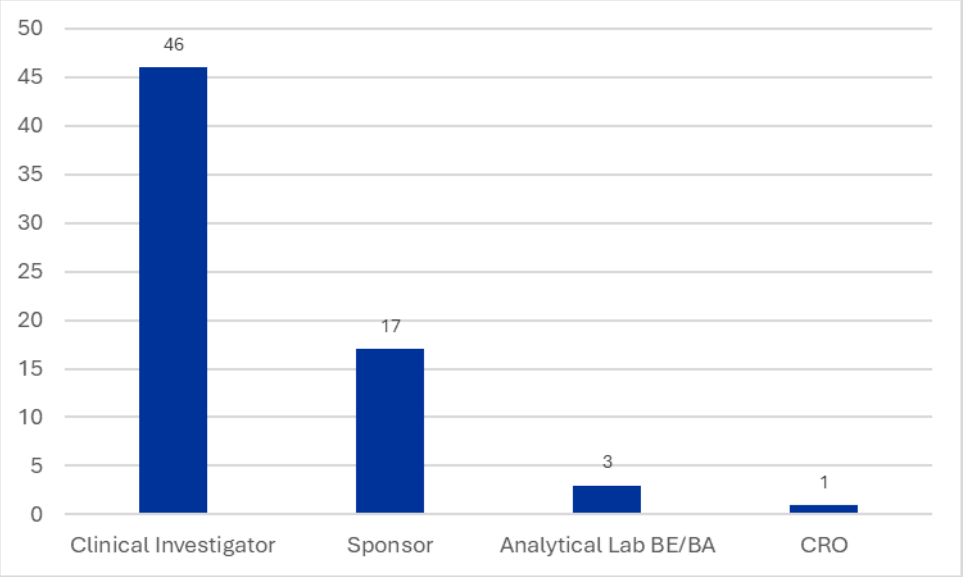


Table 2 and Figure 2 represent the number of inspections conducted in 2023 per type of site. Most of the inspections were conducted at clinical investigator sites, followed by sponsors and analytical laboratories (BE/BA).

Table 2: Inspections conducted per type of site.

Inspection Site Type	# Inspected Sites	% Inspected Sites
Clinical Investigator	**46**	**68.7%**
Sponsor	**17**	**25.4%**
Analytical Lab BE/BA	**3**	**4.5%**
CRO	**1**	**1.5%**
Grand Total	**67**	**100.0%**

Figure 2: Inspections conducted per type of site.



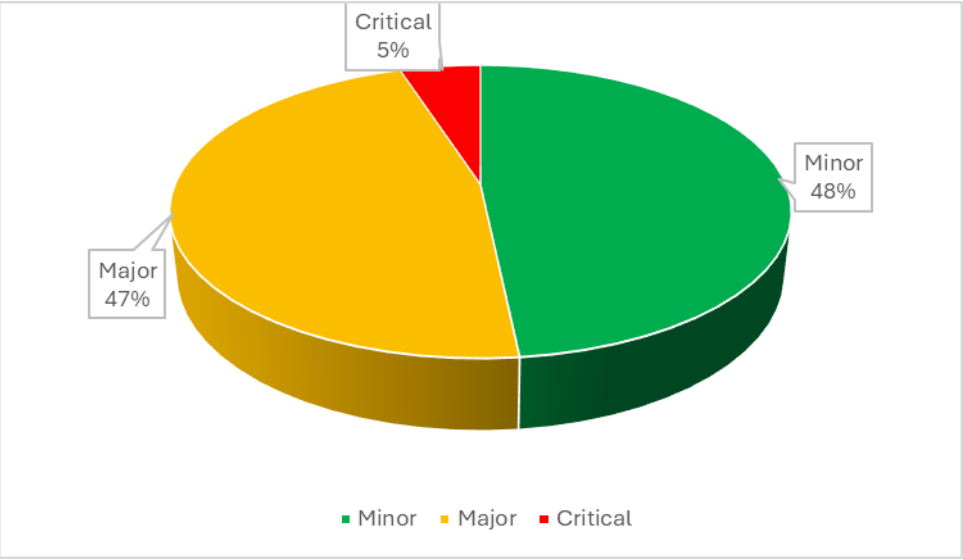
3.1.2. Categorisation of findings

a) General overview

A total of 720 deficiencies, comprising 36 critical (5.0%), 336 major (46.7%) and 348 minor (48.3%) findings were recorded for the 67 CHMP requested inspections conducted in 2023. This represents an average of 11 findings per site inspected.

The main findings observed in the 2023 inspections are detailed below in accordance with the GCP categorisation of findings agreed by the GCP IWG.

Figure 3: Number of findings by grading category: critical, major, and minor.

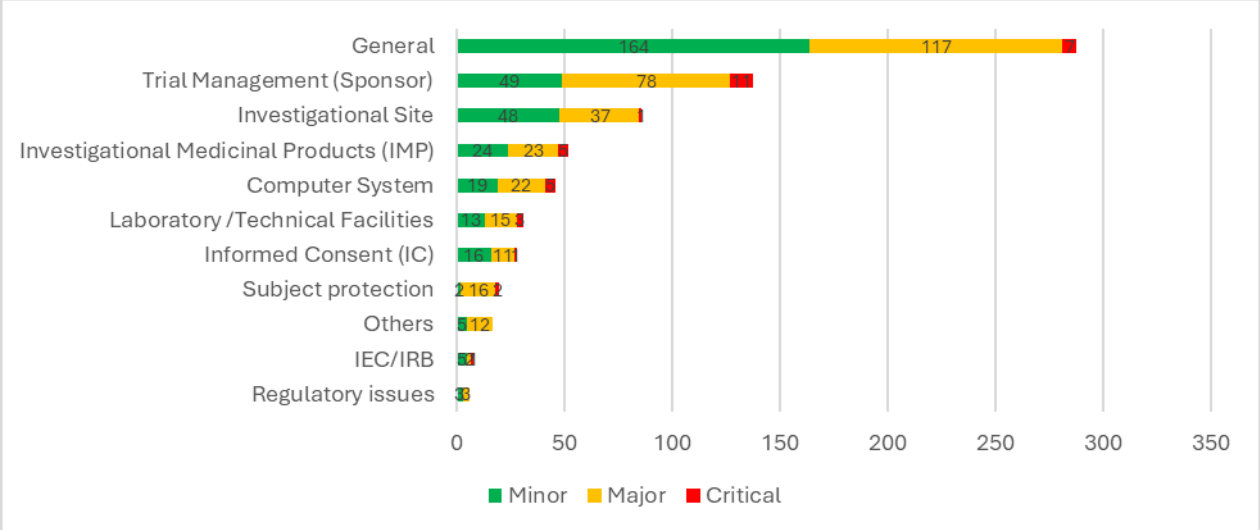


b) Distribution by categories and sub-categories

Table 3: Number of findings by main category and grading categories: critical, major, and minor.

Main category	Minor	Major	Critical	Total
General	164	117	7	**288**
Trial Management	49	78	11	**138**
Investigational Site	48	37	1	**86**
Investigational Medicinal Products (IMPs)	24	23	5	**52**
Computer System	19	22	5	**46**
Laboratory/ Technical Facilities	13	15	3	**31**
Informed Consent	16	11	1	**28**
Participant protection	2	16	2	**20**
Other	5	12	0	**17**
Independent Ethics Committee (IEC)/Institutional Review Board (IRB	5	2	1	**8**
Regulatory Issues	3	3	0	**6**
Total	**348**	**336**	**36**	**720**

Figure 4: Number of findings by main category and grading category: critical, major, and minor.



Findings are detailed below for the top three categories: General, Trial Management, and Investigational Site.

Table 4: Number of findings per sub-category of the top 3 main categories (General, Trial Management and Investigational Site) graded as critical, major, and minor.

		# Inspected deficiencies			Total
Deficiency category name	**Deficiency sub-category name**	**Minor**	**Major**	**Critical**	
General	Contracts/Agreements	15	8	0	**23**
	Direct Access to Data	5	2	3	**10**
	Essential Documents	42	32	0	**74**
	Facilities and Equipment	10	18	0	**28**
	Organisation and Personnel	16	6	1	**23**
	Qualification/Training	29	15	1	**45**
	Randomisation/Blinding/Codes IMP	3	4	0	**7**
	SOPs	14	14	1	**29**
	Source Documentation	30	18	1	**49**
General Total		**164**	**117**	**7**	**288**
Trial Management	Audit	2	1	0	**3**
	Clinical Study Report (CSR)	4	8	1	**13**
	Data Management	16	27	5	**48**
	Document Control	4	6	0	**10**
	Monitoring	15	21	4	**40**
	Protocol/ Case Report Form (CRF)/ Diary/ Questionnaires design	4	12	1	**17**
	Statistical Analysis	4	3	0	**7**
Trial Management Total		**49**	**78**	**11**	**138**
Investigational Site	Protocol Compliance (Others)	11	9	1	**21**
	Protocol Compliance (Assessment of Efficacy)	1	0	0	**1**
	Protocol Compliance (Safety Reporting)	11	9	0	**20**
	Protocol Compliance (Selection Criteria)	3	**12**	0	**15**
	Reporting in CRF/Diary	22	7	0	**29**
Investigational Site Total		**48**	**37**	**1**	**86**

Examples of common areas of critical and major findings in the subcategories of the three main categories "General", "Trial Management", and "Investigational Site" are listed below.

General

Contracts/Agreements:

- Lack of /unclear documentation of duties/tasks delegated to service providers by the sponsor.
- Lack of contracts/agreements between the investigator and facilities involved in the trial.

Essential Documents & Direct Access to Data:

- Lack of inspection readiness: limitations in eTMF access.
- Limited access or lack of access to medical records of trial participants for monitors.
- Insufficient assessment of the suitability of storage locations of essential documents.
- Deficiencies in maintaining essential documents: missing documents, location of documents (including source data) not defined.
- Lack of access at the trial site to trial relevant electronic systems containing essential documents/data.

Facilities and Equipment:

- Facilities not suitable for trial procedures.
- Lack of or insufficient assessment of the suitability of facilities for trial procedures.
- Lack of calibration documentation for the equipment used in the trial.
- Long term archiving facility not suitable to prevent premature destruction of clinical trial documentation.

Organisation and Personnel:

- Deficiencies in delegation of trial related tasks:
  - Persons not delegated to perform trial related tasks involved in the trial.
  - Access to trial related systems given to persons not authorised to be involved in the trial.
  - Lack of documented delegation of trial related tasks.
  - Delegation of tasks documented retrospectively.
  - Incomplete list of personnel involved in the trial.

Qualification/Training:

- Lack of documentation (e.g. training records, training certificates, etc.) evidencing site personnel training in GCP and trial relevant documents.
- Incomplete documentation of qualification, delegation, and training of trial staff.

Randomisation/Blinding/Codes IMP:

- Potential bias due to unblinding:
  - Unblinded pharmacy activities and blinded clinical activities monitored by the same monitor.

- Investigators' involvement in the assessment of SUSARs for regulatory reporting purposes, requiring unblinding.
- Deficiencies in the management of blinding in the context of interim analysis and outcome assessment.

Standard Operating Procedures (SOPs):

- Lack of SOPs for the development of essential trial documents.
- Deficient process to select, review, and approve SOPs for critical trial related processes.

Trial management

Audit:

- Lack of independent quality assurance personnel available for the study. Deficiencies in the performance of routine quality assurance activities:
  - No audits conducted of partners/vendors engaged in activities on behalf of the sponsor.
  - No audits conducted of any sponsor processes/activities.
  - No audits conducted of investigator sites.

CSR:

- The CSR lacked information on protocol deviations or serious breaches.
- Lack of information on investigators and study administrative structure.
- Personal data of investigator site staff was reported in the CSR without consent.

Data Management:

- Insufficient communication lines between trial sites and service providers to ensure good communication and quick solving of issues with regard to data handling processes.
- Handling of protocol deviations was deficient, leading to incorrect per-protocol analysis set.
- Deficiencies in the data query process leading to incorrect information in the CSR.

Monitoring:

- Monitoring procedures failed to detect protocol deviations, reconcile IMP accountability, manage issues detected in SDV and IC processes.
- Assessment of AEs, eligibility, and physical examination not done by the physician was not detected by the trial monitor.

Protocol/ CRF/ Diary/ Questionnaires design:

- The protocol was lacking important information about the methods for the recording, reporting, and assessing trial data.
- Discrepancies between protocol and eCRF design. Protocol amendments not implemented in the eCRF.

Statistical Analysis:

- Inconsistencies and lack of traceability in the finalisation of the statistical analysis plan and unblinding for the purposes of data analysis.
- Lack of a statistical analysis plan.
- Statistical analysis plan not available/finalised prior to the unblinding of the trial.
- Lack of traceability of the final data analysis.
- It could not be verified whether operating procedures for data analysis had been followed.
- Deficiencies in the documentation of data extraction from the eCRF for reporting in the final CSR.
- Final data analysis did not include an analysis of the primary endpoint.
- No QC performed on the final data analysis.

Investigational Site

Protocol Compliance (Others)

- Compliance with the study protocol was not sufficient:
  - Large number of protocol deviations related to IMP administration.
  - Late detection of protocol deviations.
- Protocol deviations relevant to participant safety:
  - Eligibility assessment was not completed before IMP administration.
  - Compliance with trial treatment could not be verified from the documentation.
  - Dose of the IMP was higher than specified in the protocol.

Protocol Compliance (Safety Reporting)

- Deficiencies in the safety reporting process at the site leading to underreporting of AEs and SAEs.

Protocol Compliance (Selection Criteria)

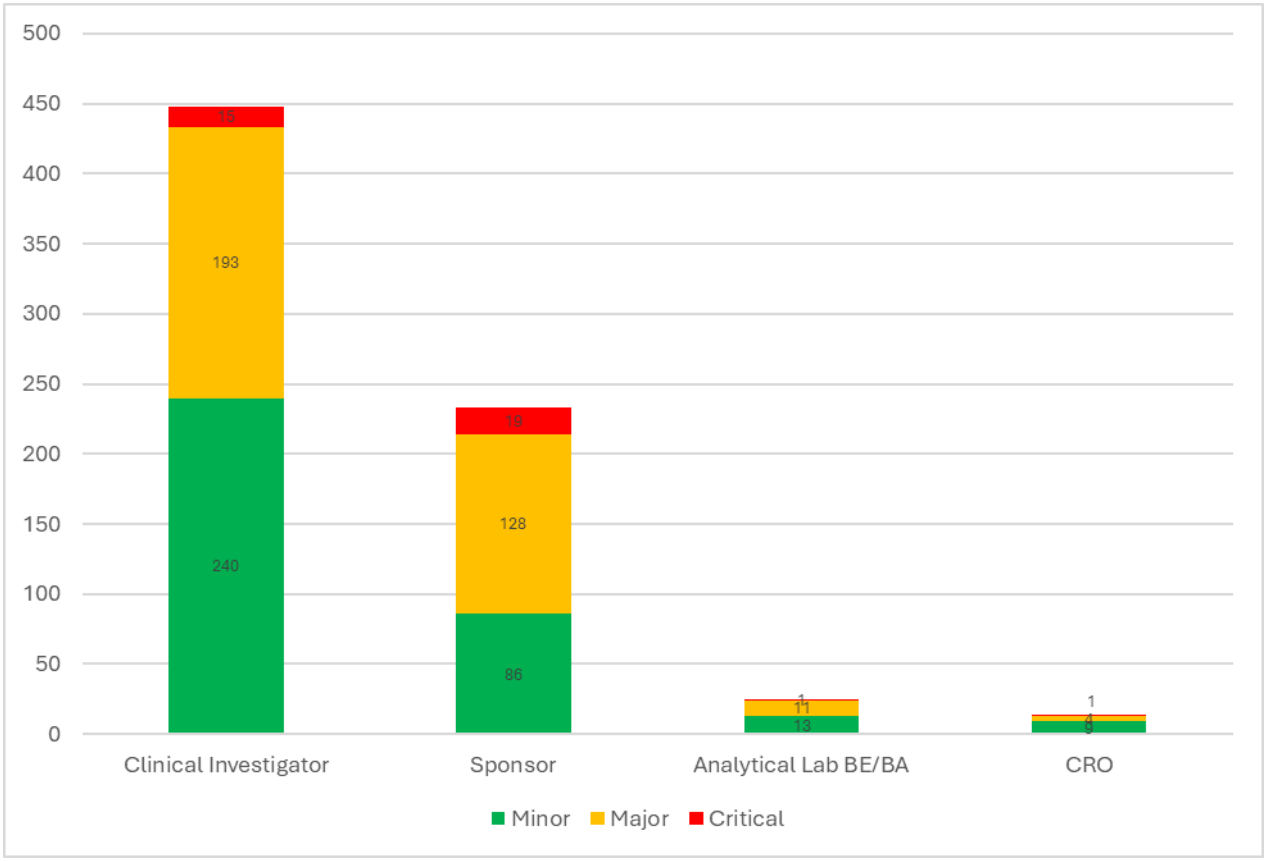
- Protocol deviations approved prospectively, and eligibility waivers granted by the sponsor.

c) Distribution by type of site inspected

Table 5. Findings graded as critical, major, and minor per site type.

Inspection Site Type	Minor	Minor %	Major	Major %	Critical	Critical %	Findings	Findings(%)
Clinical Investigator	240	33.3%	193	26.8%	15	2.1%	**448**	**62.2%**
Sponsor	86	11.9%	128	17.8%	19	2.6%	**233**	**32.4%**
Analytical Lab BE/BA	13	1.8%	11	1.5%	1	0.1%	**25**	**3.5%**
CRO	9	1.3%	4	0.6%	1	0.1%	**14**	**1.9%**
Grand Total	**348**	**48.3%**	**336**	**46.7%**	**36**	**5.0%**	**720**	**100.0%**

Figure 5: Findings graded as critical, major, and minor per site type.



The figures below present the categories of findings at the four types of sites: clinical investigators, sponsors, analytical laboratory BE/BA sites, and CROs.

Table 6. Number and categorisation of findings at clinical investigator sites.

Main category	Minor	Major	Critical	Total
General	123	71	4	198
Investigational Site	47	34	1	82
Investigational Medicinal Products (IMP)	21	17	4	42
Informed Consent (IC)	15	11	0	26
Trial Management (Sponsor)	12	26	1	39
Computer System	6	7	2	15
Laboratory /Technical Facilities	6	12	1	19
IEC/IRB	5	1	0	6
Others	3	2	0	5
Subject protection	1	12	2	15
Regulatory issues	1	0	0	1
Total	**240**	**193**	**15**	**448**

Figure 6: Number and categorisation of findings at clinical investigator sites.

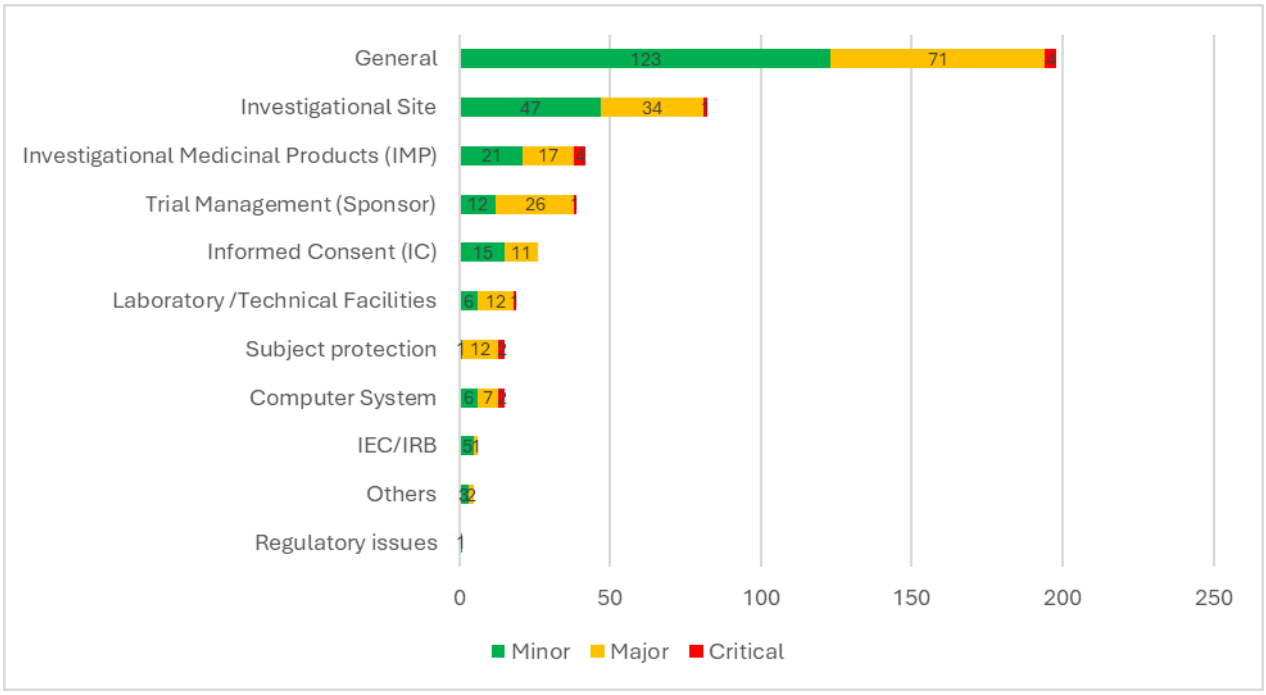


Table 7. Number and categorisation of findings at sponsor sites.

Main category	Minor	Major	Critical	Total
Trial Management (Sponsor)	31	50	9	**90**
General	35	37	3	**75**
Computer System	10	12	3	**25**
Others	2	10	0	**12**
Investigational Medicinal Products (IMPs)	3	6	1	**10**
Regulatory Issues	2	3	0	**5**
Subject protection	1	4	0	**5**
Laboratory /Technical Facilities	0	3	1	**4**
Investigational Site	1	2	0	**3**
IEC/IRB	0	1	1	**2**
Informed Consent (IC)	1	0	1	**2**
Total	**86**	**128**	**19**	**233**

Figure 7: Number and categorisation of findings at sponsor sites.

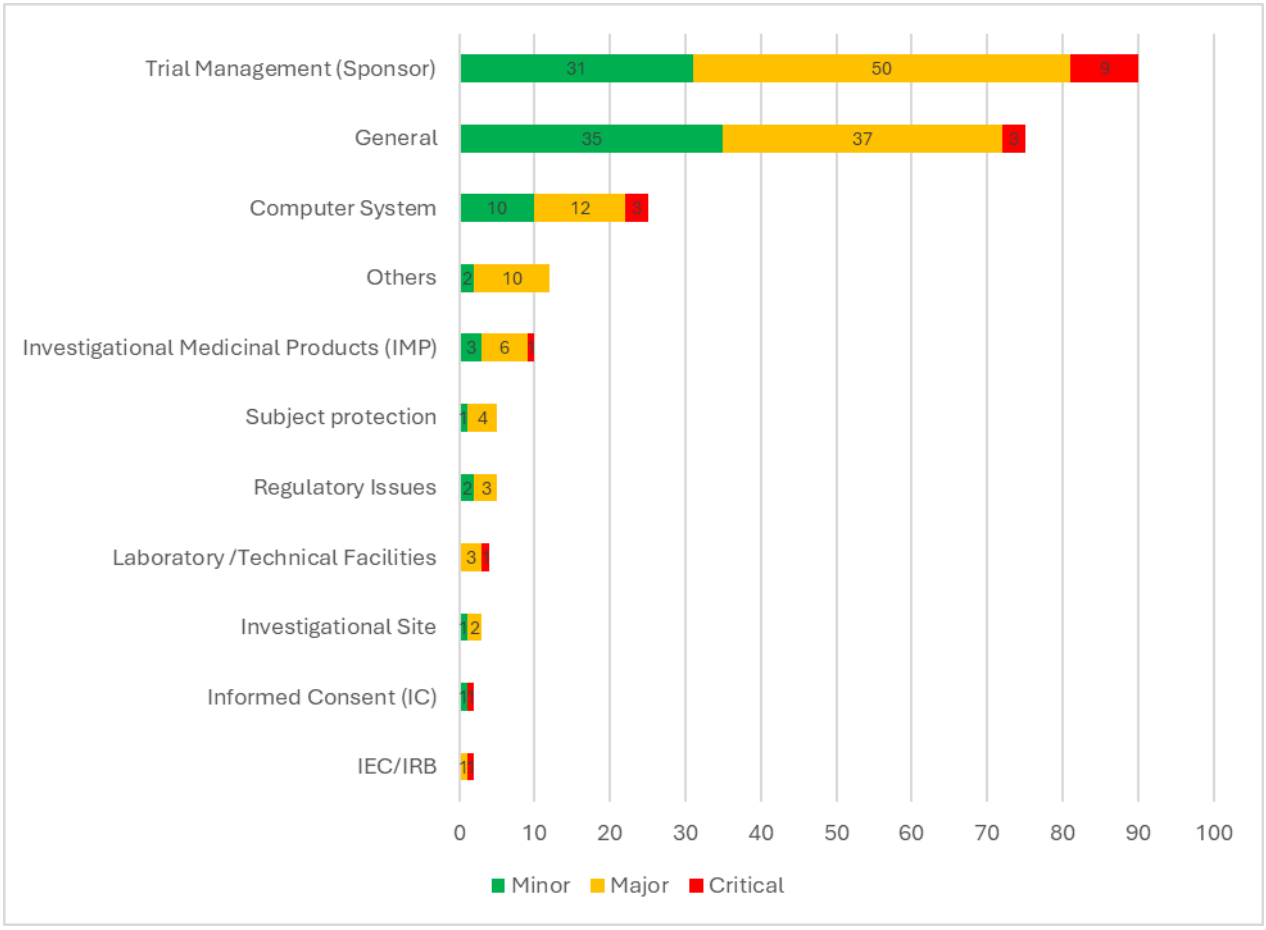


Table 8. Number and categorisation of findings at CRO sites.

Main category	Minor	Major	Critical	Total
General	4	1	0	5
Trial Management (Sponsor)	4	2	1	7
Computer System	1	0	0	1
Investigational Site	0	1	0	1
Total	**9**	**4**	**1**	**14**

Figure 8: Number and categorisation of findings at CRO sites.

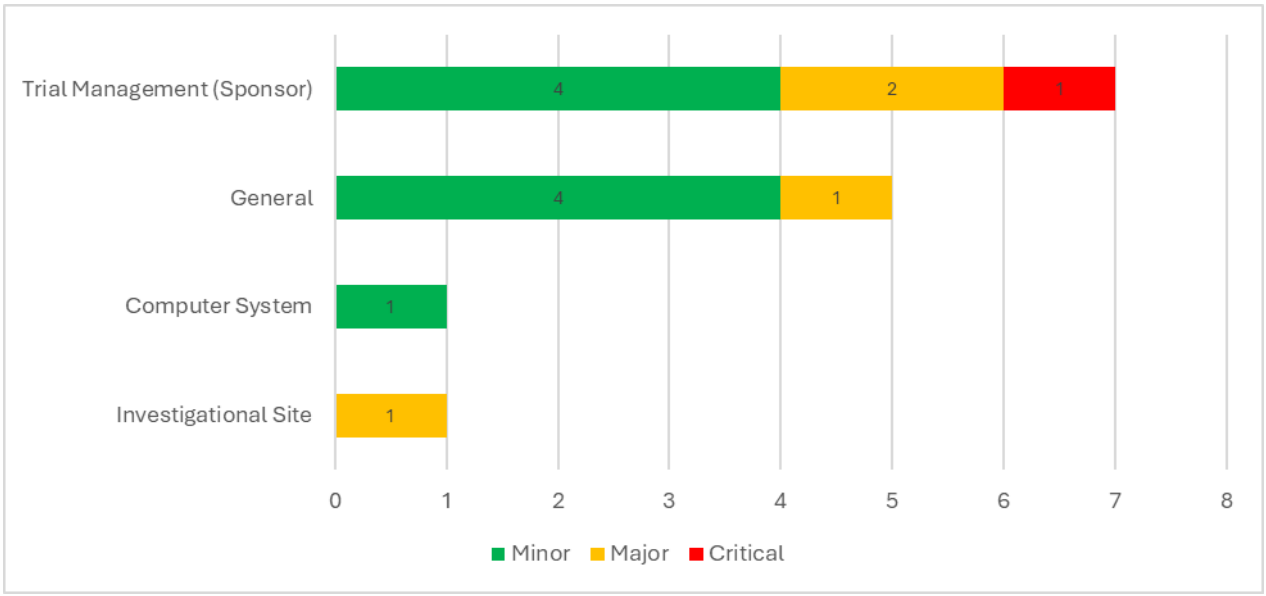
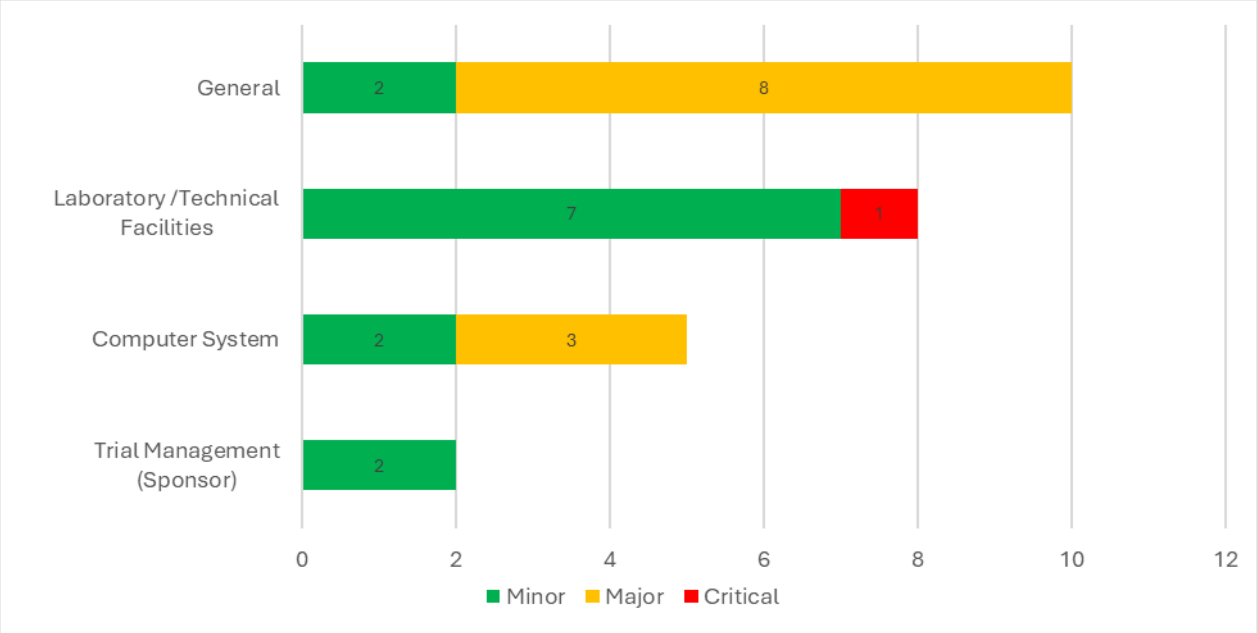


Table 9. Number and categorisation of findings at analytical laboratory BE/BA sites.

Main category	Minor	Major	Critical	Total
Trial Management (Sponsor)	2	0	0	**2**
Computer System	2	3	0	**5**
Laboratory /Technical Facilities	7	0	1	**8**
General	2	8	0	**10**
Total	**13**	**11**	**1**	**25**

Figure 9: Number and categorisation of findings at Analytical laboratory BE/BA sites.



d) Distribution by responsible party

Finally, Table 10 shows the distribution of responsibilities for each grading of finding.

Table 10. Responsibility of findings from each type of site.

Responsibility	# Minor findings	% Minor findings	# Major findings	% Major findings	# Critical findings	% Critical findings	# Total findings	% Total findings
Sponsor	109	31.3%	158	47.0%	23	63.9%	**290**	**40.3%**
Multiple Responsibility	75	21.6%	89	26.5%	10	27.8%	**226**	**24.2%**
Investigator	147	42.2%	76	22.6%	3	8.3%	**174**	**31.4%**
IEC/IRB	0	0.0%	0	0.0%	0	0.0%	**30**	**0.0%**
CRO	17	4.9%	13	3.9%	0	0.0%	**0**	**4.2%**
Grand Total	**348**	**100.0%**	**336**	**100.0%**	**36**	**100.0%**	**720**	**100.0%**

Of note, the CHMP requested GCP inspections described in this section are just a small part of the total number of inspections performed by EU/EEA inspectors as there are many others performed as part of their national programmes in the following contexts:

- Oversight of the conduct of clinical trials in Europe.
- Marketing authorisation applications (MRP, DCP or national procedures).

4. Harmonisation topics

4.1. Procedures and guidance documents

The GCP inspectors contributed to and/or adopted the following documents in 2023:

- The GCP IWG adopted on 7 March 2023 the Guideline on computerised systems and electronic data in clinical trials (europa.eu).
- EMA GCP IWG points to consider regarding the management of ongoing clinical trials impacted by political conflicts, natural disasters or other major disruptions: https://www.ema.europa.eu/en/documents/other/ema-gcp-iwg-points-consider-regarding-management-ongoing-clinical-trials-impacted-political_en.pdf
- Guidance on remote GCP inspections during public health threats emergencies and crisis situations (europa.eu) which replaces the 'Guidance on remote inspections during COVID-19 pandemic ' and intends to provide guidance on the steps to be followed during remote good clinical practice (GCP) inspections which may be conducted during public health threats, political conflicts, natural disasters, or other major disruptions.
- Guidance document on how to approach the protection of personal data and commercially confidential information while using the Clinical Trials Information System (CTIS). This document was worked on in 2021-2022 and published in 2023 (Version 1.1)[1].
- 2024-2026 Work Plan of the Good Clinical Practice Inspectors Working Group (GCP IWG).

Two new GCP Q&As were published on the EMA website (https://www.ema.europa.eu/en/human-regulatory/research-development/compliance/good-clinical-practice/qa-good-clinical-practice-gcp):

- B.18: What are the expectations for productivity applications used in clinical trials?
- D.3: What are the considerations when direct remote access of identifiable personal and health data is required in a clinical trial?

In addition, the following Q&A published on the EMA website was revised in 2023:

- B.11: According to the applicable EU laws and ICH E6, is it allowed that the sponsor could contract service providers to conduct trial-related tasks, procedures, duties and functions that are under the responsibility of the investigator?

The contribution of the GCP IWG to the third revision of the ICH GCP guideline (E6 R3) is described in section 4.5.

4.2. Inspection cooperation

- Cooperation between the EU/EEA MSs:

All the inspections conducted in 2023 were joint inspections involving inspectors from at least two MSs.

- Cooperation with third countries:

Observers from countries outside the EU/EEA are systematically invited to observe the EU/EEA GCP inspections performed in those countries in the context of the centralised procedure. In 2023,

[1] This document was updated on 18 June 2024 Annex I to the Guidance document on protection of PD and CCI (europa.eu) for alignment with the Revised CTIS transparency rules (europa.eu)

inspectors from Australia, Botswana, China, Israel, Switzerland, and USA observed GCP inspections requested by the CHMP. In addition, one inspection was conducted jointly with the FDA.

4.3. GCP training and development

- 2023 European Union Good Clinical Practice Inspectors Working Group Workshop

The on-site 2023 EU GC IWG Workshop took place on 17-19 October 2023 at the EMA premises. Participants included 118 inspectors from the EU/EEA/EFTA and third countries.

The 2023 workshop lasted for two and a half days and covered the following topics in the form of presentations and breakout sessions:

- EMA GCP inspections the roles of EMA and the National Competent Authority inspectors
- Draft ICH E6(R3): Overview of main changes
- EMA GCP inspections at the sponsor site:
    - Preparation and conduct
    - Data management and Statistical Analysis
    - Interviews and interactions with inspected entities
- Inspection of computerised systems
- Inspection reporting and interactions with assessors
- International Collaborations in the area of GCP inspections
- Guest presentations from non-EU countries

Training in the Bioequivalence area

- The 2023 hybrid Forum on Bioequivalence (BE) Inspections BE Forum took place in a hybrid setting on 16 October 2023 at the EMA premises. GCP inspectors from the EU/EEA and non-EU (FDA, WHO, MHRA, Health Canada, Swissmedic) were present.

  The BE Forum lasted one day, and topics covered in the form of presentations and case studies included:

  - BE inspections preparation and conduct
  - Demonstration on analyst data set and audit trail
  - Tools to identify data anomalies
  - Discussion on case/document from past inspections
- A further one-day training event was organised on data analytics to identify compliance issues of BE studies.

4.4. GCP IWG meetings and topics of interest

4.4.1. GCP IWG meetings

- During the plenary meetings of the GCP IWG held on 21-22 March 2023, 20-21 June 2023, 19-20 September 2023 and 28-29 November 2023, the following topics were discussed:
  - Regulation (EU) No 536/2014 (Clinical Trials Regulation) implementation, CTIS and Union controls.
  - European Commission revision of the pharmaceutical legislation.
  - Accelerating Clinical Trials in the EU (ACT EU) initiative and relevant priority actions.
    - Decentralised clinical trials initiative
  - Guidelines, Q&As and procedures under development.
  - Renovation of ICH E6, and new ICH M11.
  - Update on ongoing inspections of interest.
  - Update from subgroups on their activities.
  - Updated inspection templates.
  - GCP compliance interpretation matters and ethical issues; response to queries received from third parties.
  - Coordination and observation of EMA inspections, and GCP inspection programme.
  - National inspections.
  - Training activities.

4.4.2. GCP IWG meeting with interested parties

- During the "GCP IWG virtual meeting with interested parties: Rethinking clinical trials" held virtually on 18 September 2023 the following topics were covered, including:
  - Database decommissioning and data formats.

- Audit Trail and Audit Trail Review.
- Distributed Trial Master File: Overview and Access.
- Direct remote access of identifiable personal and health data required in clinical trials.

4.4.3. GCP IWG joint workshop with clinical assessors

- During the GCP IWG-clinical assessors' joint workshop held virtually on 26 June 2023, a combination of presentations and breakout sessions were used to cover the following topics:
  - GCP Inspections and the Marketing Authorisation Application Assessment Timelines.
  - EMA GCP inspections- purpose, focus and outcome, inspectors' and assessors' perspectives.
  - Selection of trials and sites for EMA GCP inspections.
  - Guidance document on communication steps between inspectors and assessors.
  - Grading and impact of EMA GCP inspection findings.
  - Ethical issues and their impact on the benefit/risk evaluation.
  - Final conclusions in the Integrated Inspection Report (IIR).

4.5. Clinical trial legislation and related guidance documents

- The GCP IWG, EMA Inspections Office, the European Commission and HMA collaborated on the preparation of the Guidance document on how to approach the protection of personal data and commercially confidential information while using the Clinical Trials Information System (CTIS), which was first published in May 2023. The first update of this document, in July 2023 included specific recommendations on the redaction of GCP inspection reports. In line with the revised CTIS transparency rules, inspection reports are no longer being published in CTIS as of 18 June 2024. (see section 4.1).
- The European Commission appointed two experts to the ICH E6(R3) Expert working group (EWG) ICH Official web site : ICH and the head of the Inspections Office at EMA as the Regulatory Chair of this EWG. These experts and the EMA Inspections Office have worked closely on the draft ICH E6 (R3) document and the organisation and planning of an ACT EU PA04 - Multi-stakeholder Workshop on ICH E6 R3 - Public Consultation | European Medicines Agency (EMA) (europa.eu) dedicated to the revision and associated public consultation of the ICH E6 guideline.
- In March 2023, the GCP IWG published the points to consider document on the management of ongoing clinical trials impacted by political conflicts, natural disasters or other major disruptions and in November 2023, the Guidance on remote GCP inspections during public health threats, political conflicts, natural disasters, or other major disruptions (see section 4.1).
- A number of Q&As on GCP aspects were revised or newly drafted by GCP IWG members under the coordination of the EMA Inspections Office and published on the EMA website in 2023 (see section 4.1):
  - Revised Q&As: B11(related to the delegation by the sponsor to service providers of trial related activities).

- New Q&As: B18 (on the expectations for productivity applications used in clinical trials); B19 (on the expectations for distribution of updated IBs and ICFs to clinical sites/investigators); D3 (on considerations when direct remote access of identifiable personal and health data is required in a clinical trial).

4.6. Clinical Trials Information System (CTIS)

The Clinical Trials Regulation became applicable on 31 January 2022, and the CTIS went live on the same day. GCP IWG members were kept up to date, during GCP IWG plenary meetings in 2023 on CTIS related topics, e.g. on the serious breaches and inspections modules. The topics of harmonisation between MSs on the assessment of serious breaches submitted through CTIS and of the redaction of inspection reports for clinical trials submitted under the CTR were also extensively discussed in the meetings of the GCP IWG and the related sub-groups.

4.7. EU enlargement

In 2023, none of the EU enlargement countries, Albania, Bosnia and Herzegovina, Kosovo, Montenegro, North Macedonia, Serbia, Türkiye, Georgia, Moldova, and Ukraine attended the meetings of the GCP IWG as observers.

5. Liaison with other EU groups

5.1. GMDP IWG

The GCP IWG maintains a dialogue with the GMDP IWG on areas of common interest. In 2023, the two IWGs collaborated in particular on the Recommendation paper on travel advice. This paper aims to assist GxP inspectors who are travelling to certain third countries outside EU/EEA where the context would add risk to inspectors' safety and where special attention to specific practicalities is emphasised.

5.2. PhV IWG

The GCP IWG maintains a dialogue with the PhV IWG on areas of common interest and in particular concerning PhV issues observed in relation to GCP inspections.

5.3. HMA/ CTCG

The GCP IWG maintains a collaboration with the Heads of Medicines Agencies (HMA) and the Clinical Trials Coordination Group (CTCG) on areas of mutual concern in the supervision of clinical trials conducted in the EU/EEA. In 2023, the GCP IWG and the CTCG collaborated on the revision of the CTIS transparency rules.

5.4. CHMP

The GCP IWG maintains a dialogue with the CHMP on areas of common interest and in particular on matters related to GCP inspections. The GCP IWG-assessors subgroup on embedding the outcome of GCP inspections into the benefit-risk assessment and modernisation of the GCP inspection process continued its work in 2023 and organised a joint, virtual workshop (see section 4.4.3).

5.5. CMDh

The GCP IWG and the CMDh, mainly through the GCP/CMDh Working Party, which met 5 times in 2023, have contributed to the following topics:

- CROs of interest and CRO inspection programme.
- CRO inspection planned, conducted, outcomes and subsequent actions.
- Referral procedures.
- BE inspection resources and training needs.
- BE inspector's curriculum.
- Bioequivalence Forum.
- International collaboration, working group, and clusters in the BE area.

5.6. Paediatric Committee (PDCO)

Communication on inspection issues with the PDCO continued in 2023 with the exchange of information on inspections of clinical trials with a paediatric population and the decentralised clinical trials initiative.

6. Liaison with international partners

6.1. Regulatory agencies from outside the EEA

- The EMA and the FDA have had a collaboration initiative in place since 2009 in the area of GCP[2]. This collaboration was extended in 2013 to BE, together with some of the EU/EEA MSs[3].
  - During 2023 there were 5 regular teleconferences of the EMA-FDA GCP collaboration and 4 teleconferences as part of the EMA-FDA-WHO-MSs BE collaboration. There was also one ad-hoc meeting focused on the EMA raw data pilot.
  - In addition, the EMA Inspections Office attended the EMA - FDA – MHRA – Health Canada – Swissmedic – Israeli MoH generics cluster, where data integrity issues were discussed.
  - As part of the EMA-FDA GCP initiative the FDA observed two EMA inspections, and there were two joint EMA/FDA inspection. In addition, in 2023, the French inspectorates observed two FDA inspections on their territory, the Dutch, Italian and Danish inspectorates each observed one FDA inspection in their territories.
  - Several FDA representatives also attended the BE Forum.
- Pharmaceuticals and Medical Devices Agency (PMDA, Japan):
  - PMDA joined the FDA-EMA initiative as an observer in June 2017 for an 18-month pilot phase. Based on the outcomes of this pilot initiative, EMA and FDA agreed to add PMDA as an official member of the GCP initiative and to continue the activity.
  - Regular exchanges of information have occurred during EMA and PMDA meetings.
  - PMDA participated in all regular teleconferences with EMA and FDA as part of the GCP collaboration.

[2] Announcement of the EMA-FDA GCP Initiative
[3] Announcement of the generic medicines application inspections initiative

- WHO:
  - Since 2018, WHO has been an observer of the GCP IWG under the EMA, European Commission and WHO confidentiality arrangement.
  - WHO participated in all regular teleconferences with EMA and FDA as part of the BE collaboration.
  - EMA, WHO and the EU/EEA MSs that perform the highest number of BE inspections had 4 teleconferences to pursue the existing collaboration and exchange BE inspection information.
- Swissmedic:
  - The Swiss Agency for Therapeutic Products (Swissmedic) is an observer of the GCP IWG under the European Commission, EMA, Swiss Federal Department of Home Affairs and Swissmedic confidentiality arrangement, in place since 2015.
  - In 2023, Swissmedic observed four inspections requested by the CHMP.
- Other regulatory agencies:
  - As noted in section 4.3, Argentina, China, Turkey, and UK also observed GCP inspections requested by the CHMP.
  - Collaboration is being strengthened with additional regulatory agencies. Regular exchange of information occurs with the regulatory authorities with which EMA has confidentiality arrangements in place.

6.2. International initiatives

- Inspection information was exchanged with the regulatory authorities in Argentina, Australia, Botswana, Taiwan and Singapore.

For details on the activities of the GCP IWG for the period 2024-2026 please see the Work Plan for 2024-2026.