

Protocol non-compliance monitoring: a retrospective review of submitted protocol deviations and EC decisions

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Introduction

- ❑ Post-approval review include assessment of protocol non-compliance/deviations (NCs/PDs).
- ❑ ICH-GCP and WHO clearly defined the roles and responsibilities of the investigator/institution, sponsor & ethics committees in the reporting, management, and recommending actions on NCs/PDs.
- ❑ Very few published studies looked at protocol non-compliance monitoring, while none for EC assessment

Compliance

adherence to the trial-related requirements, GCP requirements

(ICH GCP E6(R3))

Protocol non-compliance/ deviation

any change, divergence, or departure from the study design or procedures defined in the protocol

(US DHHS, FDA, Guidance for industry E3 Q&A(R1))

Important protocol deviations

those that impact rights, safety, and well-being of trial participants, and reliability of results

(ICH GCP E6(R3))

Protocol non-compliance monitoring:
A retrospective review of submitted protocol deviations and EC decisions

OBJECTIVES

- Review the protocol non-compliance/deviations

- Categorize deviations
- Identify patterns
- Identify gaps in reporting
- Identify gaps in assessment

METHODOLOGY

RESULTS

CONCLUSION

Protocol non-compliance monitoring: A retrospective review of submitted protocol deviations and EC decisions

OBJECTIVES

METHODOLOGY

RESULTS

CONCLUSION

- Retrospective review of NC/PD database

The screenshot shows a Google Forms interface for a document titled "UPMREB FORM 3(D)2012: STUDY NON-COMPLIANCE (DEVIATION OR VIOLATION) REPORT (version 30052023)". The form is currently in a preview mode, showing the title, instructions to the principal investigator, and the start of Section 2 of 11, "STUDY PROTOCOL INFORMATION".

Section 1 of 11

UPMREB FORM 3(D)2012: STUDY NON-COMPLIANCE (DEVIATION OR VIOLATION) REPORT (version 30052023)

INSTRUCTIONS TO THE PRINCIPAL INVESTIGATOR: *This form refers to the requirements in ICH-GCP Sections 4.5: COMPLIANCE WITH PROTOCOL and 5.20: NONCOMPLIANCE. Consolidating several deviation reports in one form is not acceptable. Fill out separate forms for different deviation reports. Strictly one form per deviation. This form will be temporarily used pending completion of iREB modules on protocol deviations and violations.*

This form is automatically collecting emails from all respondents. [Change settings](#)

After section 1 Go to section 2 (STUDY PROTOCOL INFORMATION)

Section 2 of 11

STUDY PROTOCOL INFORMATION

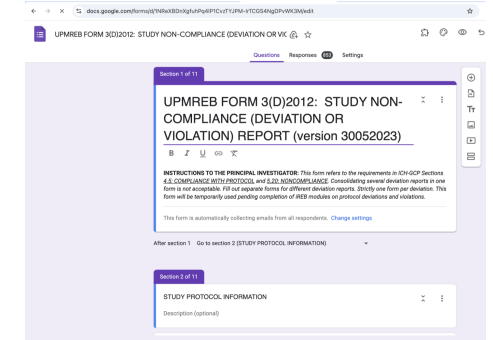
Description (optional)

Protocol non-compliance monitoring: A retrospective review of submitted protocol deviations and EC decisions

OBJECTIVES

UPMREB Form 3D Sections:

- Protocol Info
- Investigator, Sponsor details
- Deviation attribution (Subject, PI, Sponsor)
- Description of the NC/PD
- PI/sponsor assessment (minor/major; impact on safety/data)
- CAPA
- Submission details
- REB Assessment (impact on data quality or patient safety)



The screenshot shows a web browser displaying the UPMREB Form 3D(2012) interface. The title bar reads 'UPMREB FORM 3(D)2012: STUDY NON-COMPLIANCE (DEVIATION OR VIOLATION) REPORT (version 30052023)'. The main content area is divided into sections. The first section, 'Section 1 of 11', contains the title and instructions for the Principal Investigator. The instructions state: 'INSTRUCTIONS TO THE PRINCIPAL INVESTIGATOR: This form refers to the requirements in CDISC Section 4.6 COMPLIANCE WITH PROTOCOLS and 4.20.30052023. Consider only deviation reports in one form if not applicable. Fill out separate forms for different deviation reports. Study one form per deviation. This form will be temporarily used pending completion of REB modules on protocol deviations and violations.' Below the instructions, there is a note: 'This form is automatically collecting emails from all respondents. Change settings'. A navigation bar indicates 'After section 1 Go to section 2 (STUDY PROTOCOL INFORMATION)'. The second section, 'Section 2 of 11', is titled 'STUDY PROTOCOL INFORMATION' and has a sub-section for 'Description (optional)'. The interface includes a top navigation bar with 'Questions', 'Responses', and 'Settings' tabs, and a right-hand sidebar with various icons.

METHODOLOGY

RESULTS

CONCLUSION

Protocol non-compliance monitoring: A retrospective review of submitted protocol deviations and EC decisions

OBJECTIVES

METHODOLOGY

RESULTS

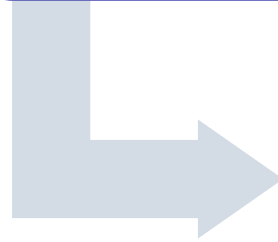
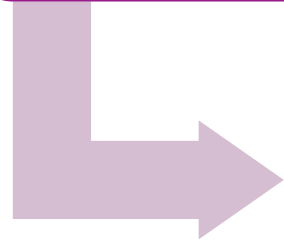
CONCLUSION

Extract
report

Clean the
data

Check REB
decisions

Analysis



Protocol non-compliance monitoring: A retrospective review of submitted protocol deviations and EC decisions

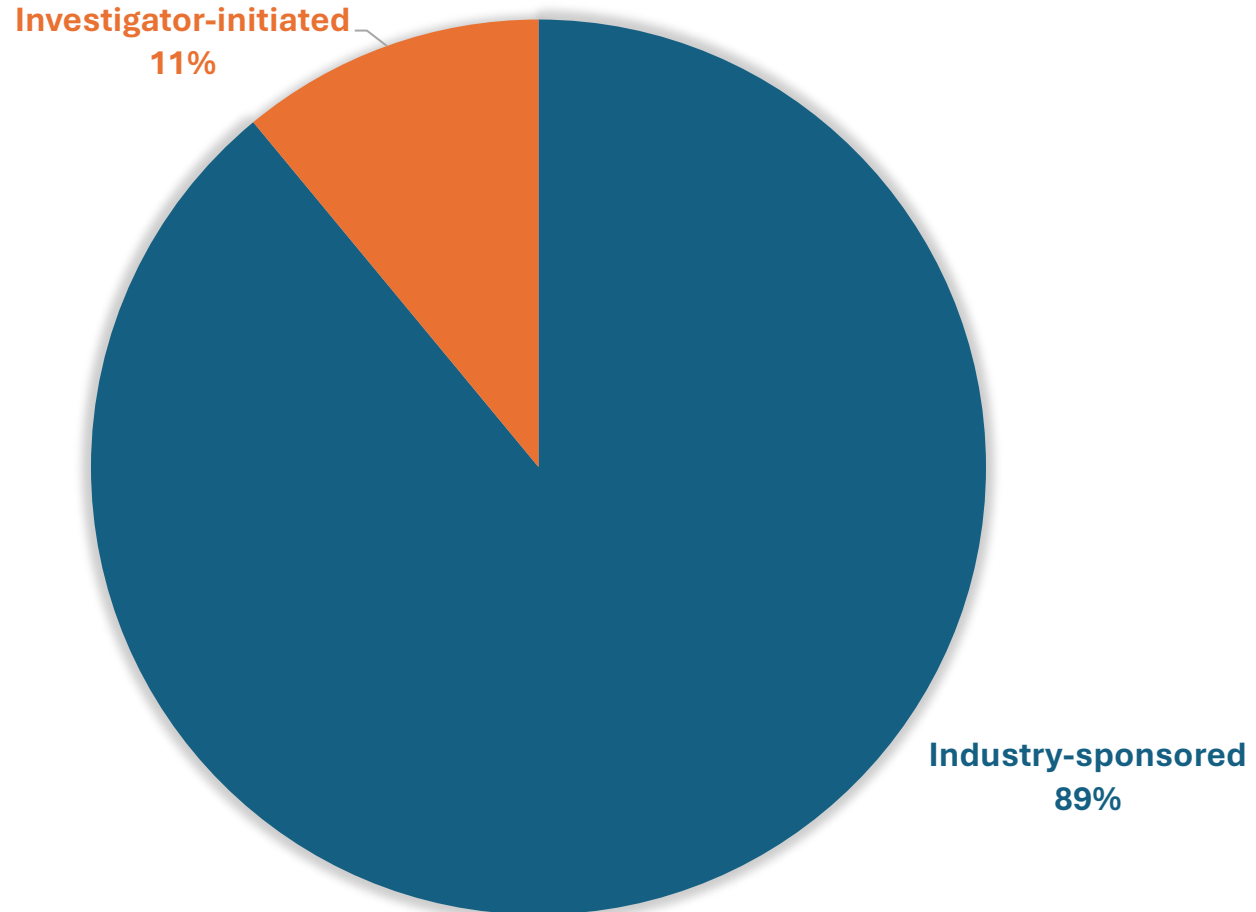
OBJECTIVES

METHODOLOGY

RESULTS

CONCLUSION

TYPE OF STUDIES



Protocol non-compliance monitoring: A retrospective review of submitted protocol deviations and EC decisions

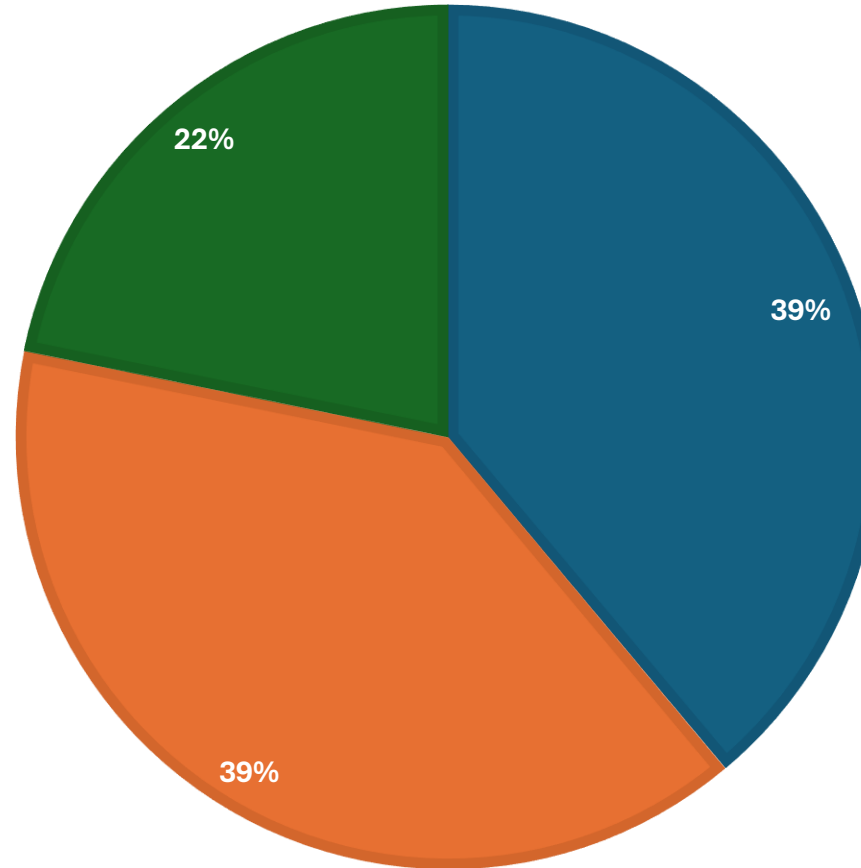
NC/PD ATTRIBUTED TO:

OBJECTIVES

METHODOLOGY

RESULTS

CONCLUSION



■ Investigator ■ Subject ■ Other research staff

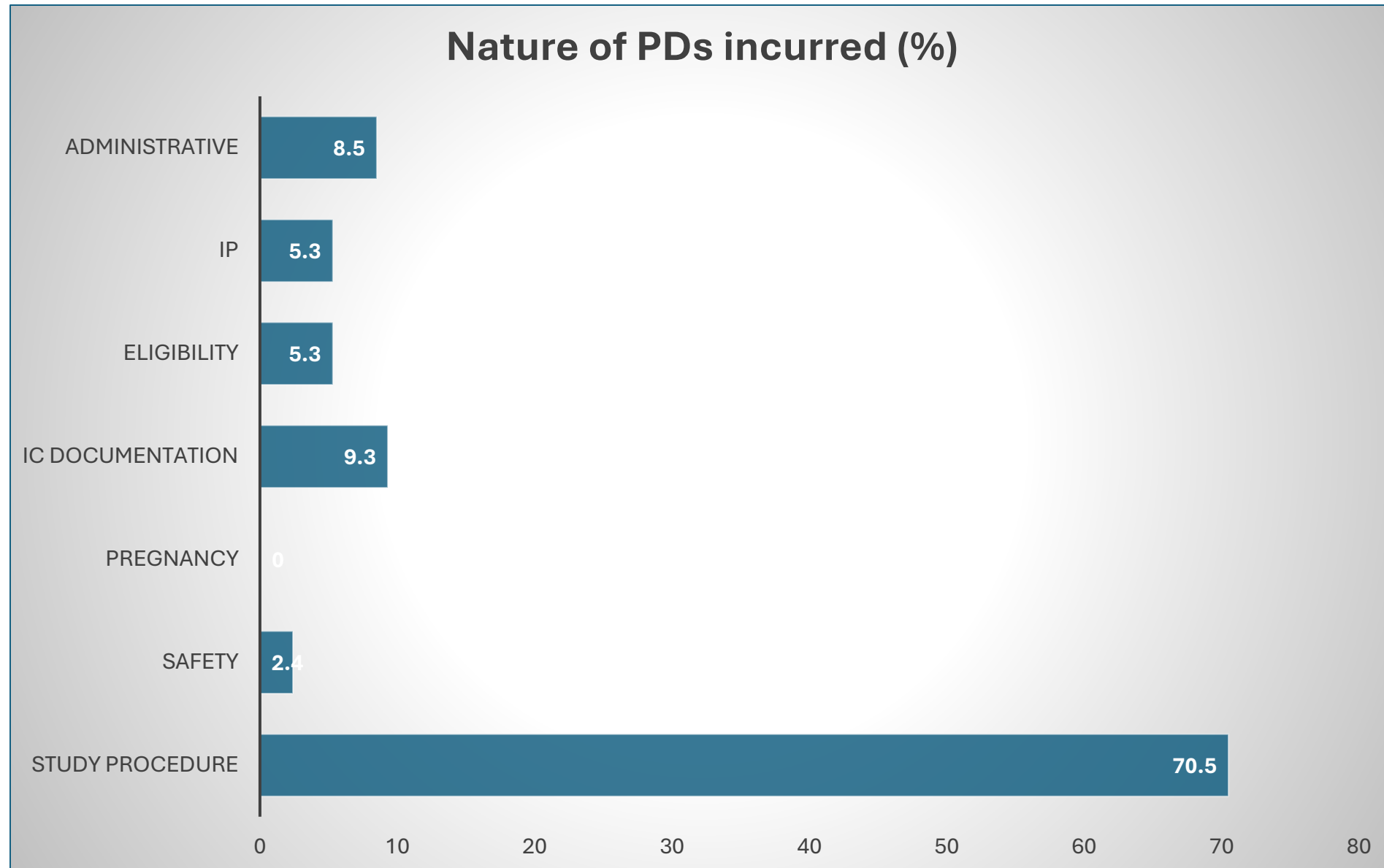
Protocol non-compliance monitoring: A retrospective review of submitted protocol deviations and EC decisions

OBJECTIVES

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Protocol non-compliance monitoring: A retrospective review of submitted protocol deviations and EC decisions

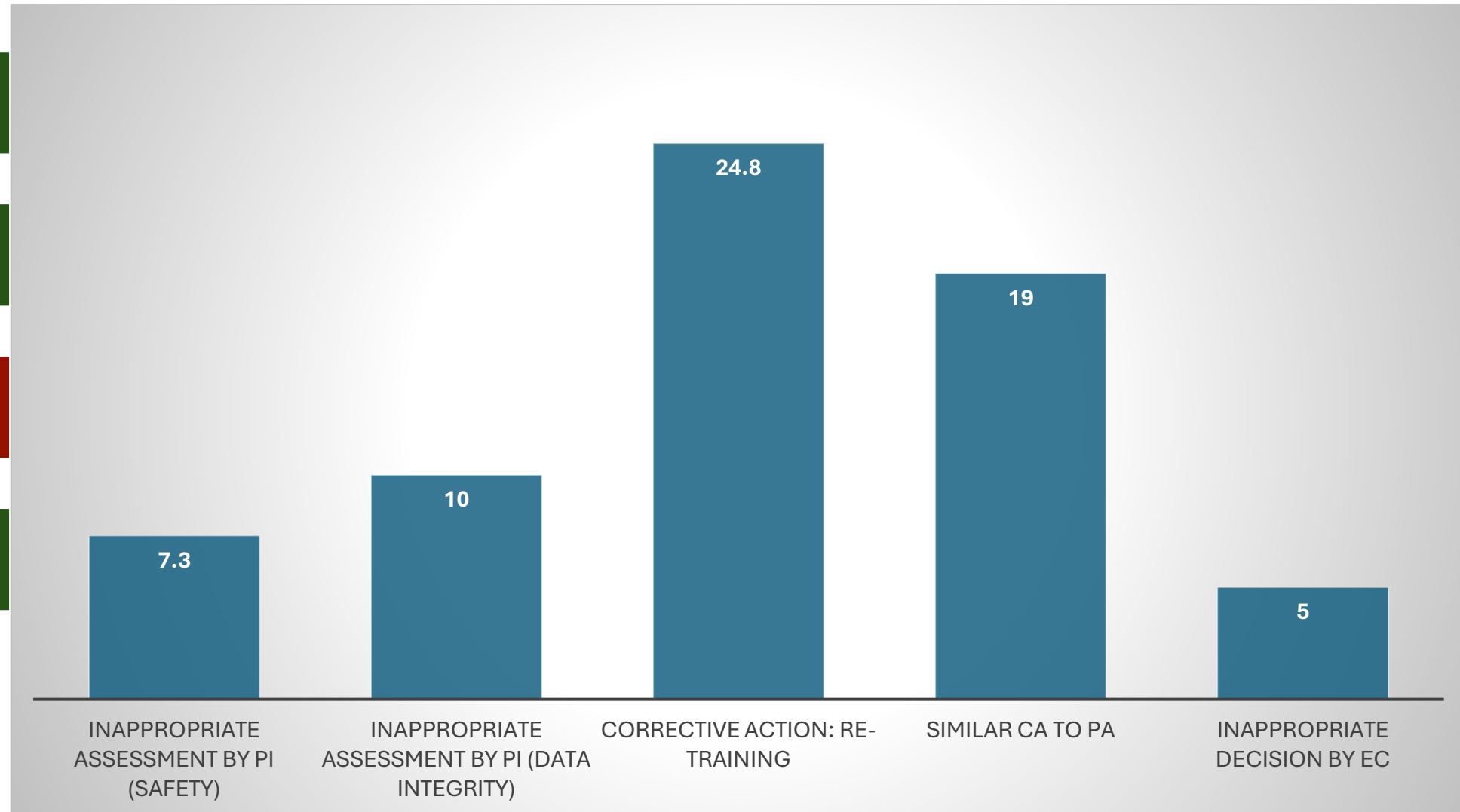
OBJECTIVES

METHODOLOGY

RESULTS

CONCLUSION

Assessment of PDs submitted by PI & EC Decision



Protocol non-compliance monitoring:
A retrospective review of submitted protocol deviations and EC decisions

OBJECTIVES

Deviation:

Plasma sample for ctDNA/MRD and blood-borne biomarkers was not collected at Week 1 Day 1

METHODOLOGY

PI Assessment: No impact on credibility of data

RESULTS

REB Decision: No further action

CONCLUSION

Protocol non-compliance monitoring:
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OBJECTIVES

Deviation:

Vital signs was obtained before the ICF was signed.

METHODOLOGY

Corrective Action: All site staff to synchronize their time

RESULTS

CONCLUSION

Preventive Action: The site staff confirmed in the source document that the vital signs measurement was done after the ICF was signed.

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OBJECTIVES

Deviation:

*Subject 3*****'s Covid 19 vaccine history included mRNA vaccine. However, the subject still proceeded with the enrolment last 23 Dec 2022 and received 2nd dose of vaccine last 24 Jan 2023.*

METHODOLOGY

RESULTS

PI Assessment: No impact on credibility of data

CONCLUSION

CA/PA: Reminded all sub-investigators to review and checked the inclusion-exclusion criteria in adherence to the latest approved protocol prior to enrollment of the subject

Protocol non-compliance monitoring:
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OBJECTIVES

Deviation:

ECG was performed on Day 1 instead of performing ECG during the screening

METHODOLOGY

Corrective Action: retraining of study personnel

RESULTS

Preventive Action: retraining of study personnel

CONCLUSION

Protocol non-compliance monitoring:
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OBJECTIVES

Deviation:

- a. ECG was performed on Day 1 instead of performing ECG during the screening*
- b. ECG was ordered but was not performed*

METHODOLOGY

RESULTS

Corrective Action: retraining of study personnel

CONCLUSION

Preventive Action: retraining of study personnel

Protocol non-compliance monitoring: A retrospective review of submitted protocol deviations and EC decisions

OBJECTIVES

METHODOLOGY

RESULTS

CONCLUSION

- Protocol non-compliance/deviations are often committed by the site (PI, other research staff).
- Most of the deviations are related to the study procedures.
- There is room for improvement in terms of reporting and analyzing the PDs submitted by the PI as well as the assessment by the Ethics Committee.
- As part of quality assurance in reviews, regular analysis of assessment and decisions on PDs by the EC should be done.
- Regular training of both the researcher and EC members on PD management is needed.

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