FY 2021 CI 483 OBSERVATION TRENDS

Acronyms

AE (Adverse Event)

CI (Clinical Investigator)

FDA (Food and Drug Administration)

ICF (Informed Consent Form)

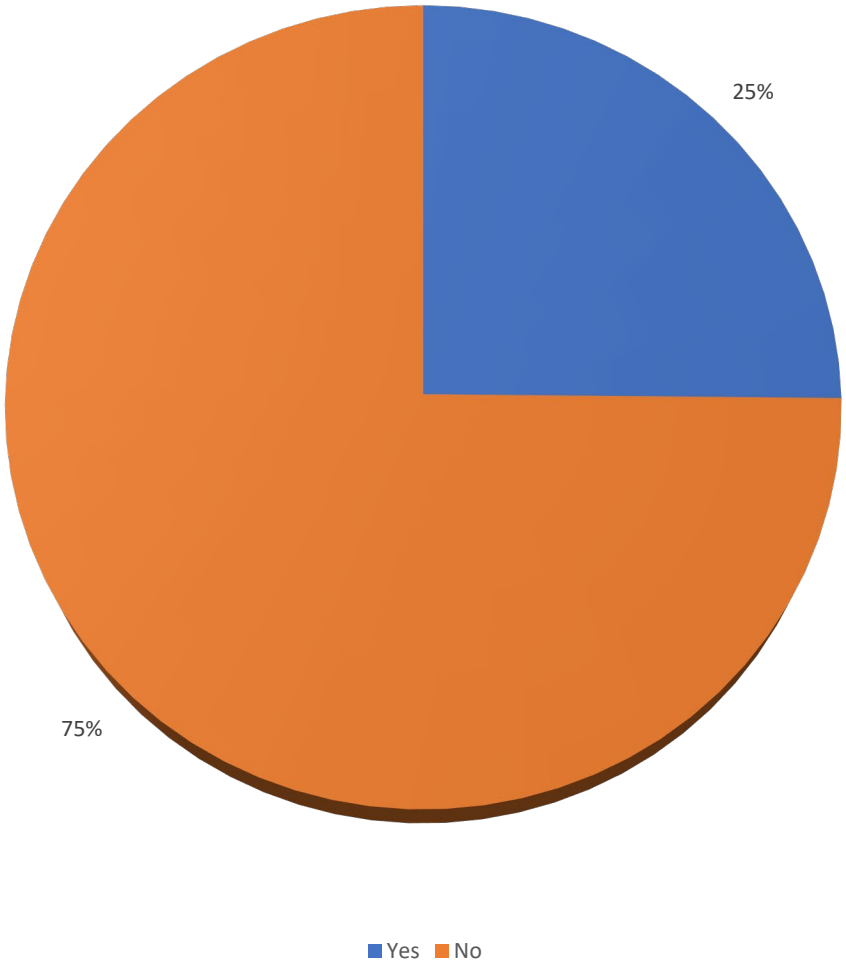
IP (Investigational Product)

IRB (Institutional Review Board)

OOW (Out of Window)

SAE (Serious Adverse Event)

FY2021 Clinical Investigators Issued a 483



FY 21 data from ORA's Online Reporting Analysis Decision Support System Query, Last updated 8/24/2022

Purpose

Broadly written regulations do not always convey the specific details of the observed violation(s).

FDA 483 citations issued during this fiscal year were reviewed and sub-categorized into more granular themes in order to identify trends.

These data slides are the result of the sub-categorization efforts.

Themes Identified in FY 2021

Protocol Compliance (312.60 / 812.100 *& 812.110 (b))

Accurate/Adequate Case Histories (312.62(b)/812.140(a)(3))

IP Accountability Records (312.62(a) / 812.140(a)(2))

ICF (50.27.a)

Failure to Report Adverse Events to Sponsor Promptly (312.64(b))

Institutional Review Board (312.66) (812.150(a)(3))

* Indicates new Cite Reference number(s)

Protocol Compliance Themes
(312.60/812.100 *& 812.110 (b))

ICF Not Per Investigational Plan

- ICF Not Per Investigational Plan
- Revised Consent Not Obtained/Timely
- ICF Not Obtained Prior to Screening/Reconsent/IP Administration
- ICF Not Obtained at Rescreening
- ICF Not obtained
- ICF Not obtained for Sub-Study
- *ICF Copy Not Provided
- *ICF changes not approved by IRB

Eligibility

- Inclusion Criteria Not Met
- Exclusion Criteria Met
- Randomized prior to meeting eligibility

Drugs

- Prohibited Medication
- Missed Concomitant Medication
- Dose Modification

Adverse Events

- Missed AE/SAE
- Late Report AE/SAE

Protocol visits/ assessments

- Missed Visit
- Missed Assessment
- Missed Lab
- OOW Visit/Assessment/Lab

* Indicates new Cite Reference number(s) and new reason

Protocol Compliance Themes, contd.
(312.60/812.100 *& 812.110 (b))

Investigational Product

- Randomization Error
- Unblinding
- Treatment Compliance
- IP Kit Selection Error
- IP Preparation Documentation
- Missing IP
- Inadequate IP Storage/ Preparation

Other Protocol Requirements

- Documentation PK Sample Process/ Storage
- Missing Protocol Required Documentation
- Study Procedures Performed Incorrectly
- Not Personally Supervised/ Unidentified Sub- investigator/ Unqualified Personnel

Records and Documentation Themes

Accurate/Adequate Case Histories (312.62(b)/812.140(a)(3))

- Record Not Maintained - Missing or Inadequate Record
- Missing Data or Inadequate Data
- Data Discrepancy or Inaccurate Records/Data (not contemporaneous)
- ICF Not Maintained/Signed/Dated

IP Accountability Records (312.62(a) / 812.140(a)(2))

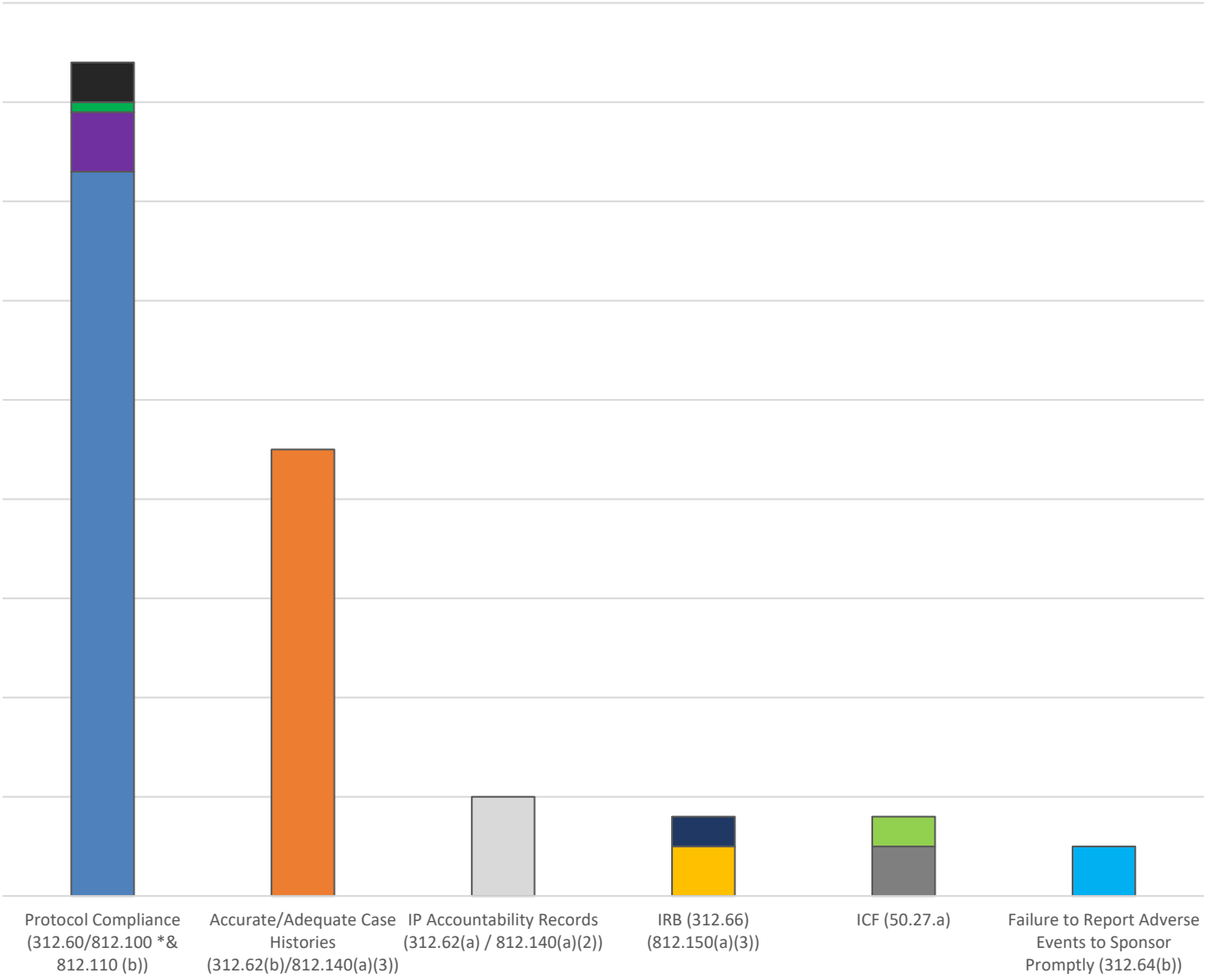
- Missing IP Records
- Missing IP Use/Exposure by Subject
- Missing IP Date
- Inadequate/Inaccurate/Missing IP Quantity
- Missing IP Batch/Code

Informed Consent and Financial Disclosure Themes

ICF (50.20)	Failure to Report Financial Disclosure to Sponsor (312.64(d))/*812.110(d))
• ICF Not Obtained • ICF Not in Understandable Language • ICF Short Form Not Witnessed • ICF Circumstances - Not Sufficient Opportunity/Not Enough Time • ICF Coercion	• Unreported Financial Disclosure

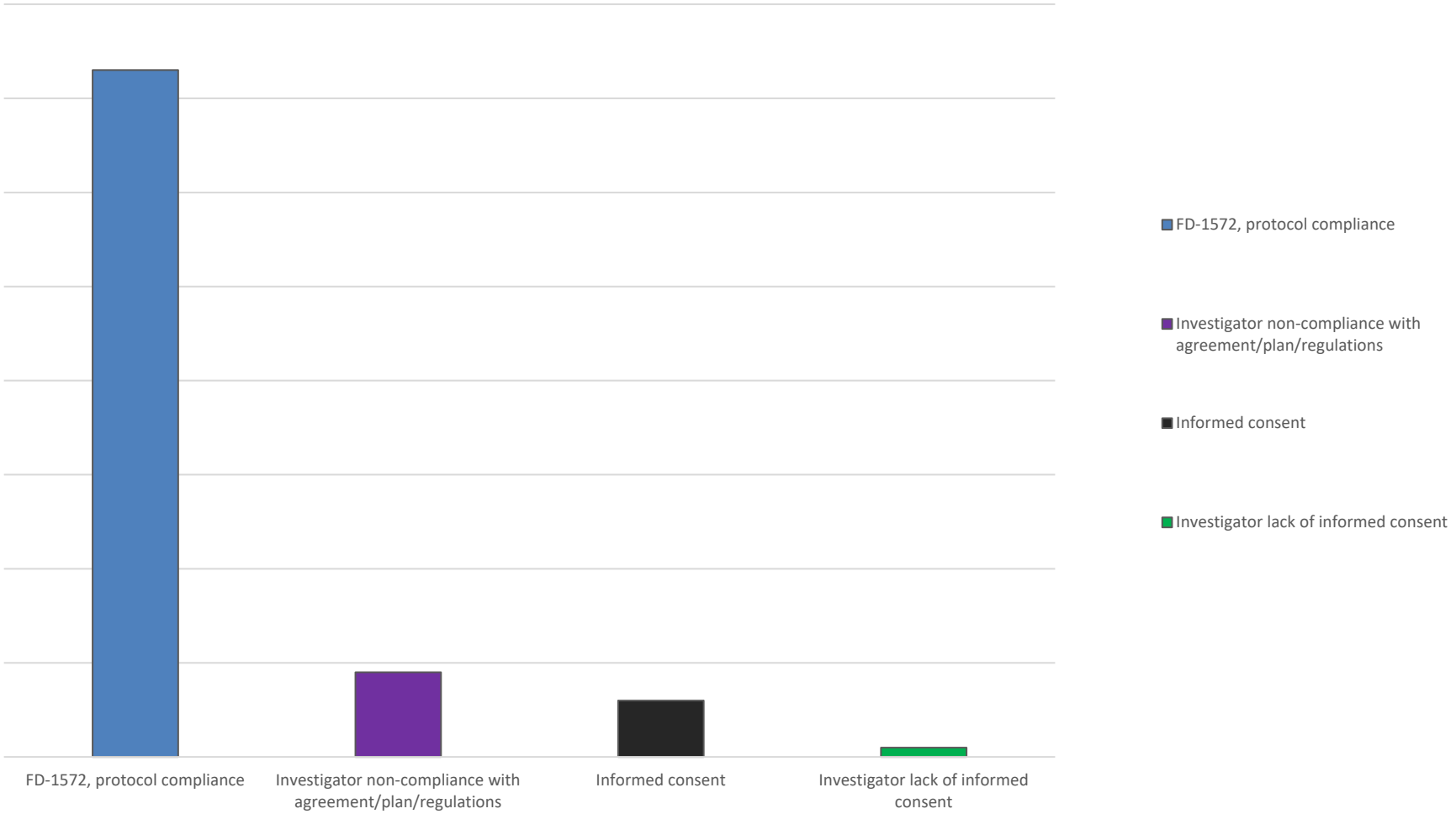
* Indicates new Cite Reference number(s)

FY 2021 Most Common Clinical Investigators 483 Short Cites

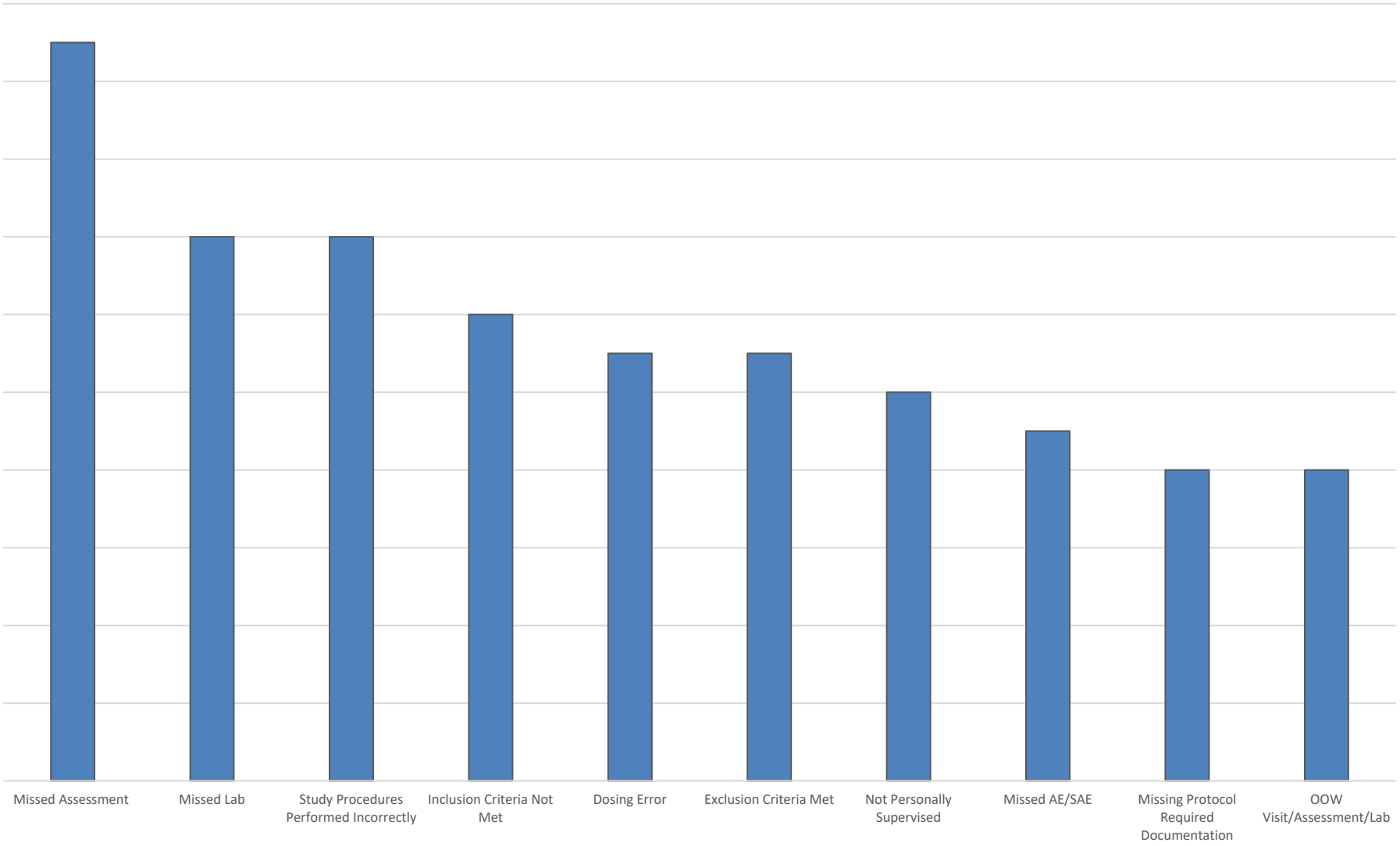


* Indicates new Cite Reference number(s)

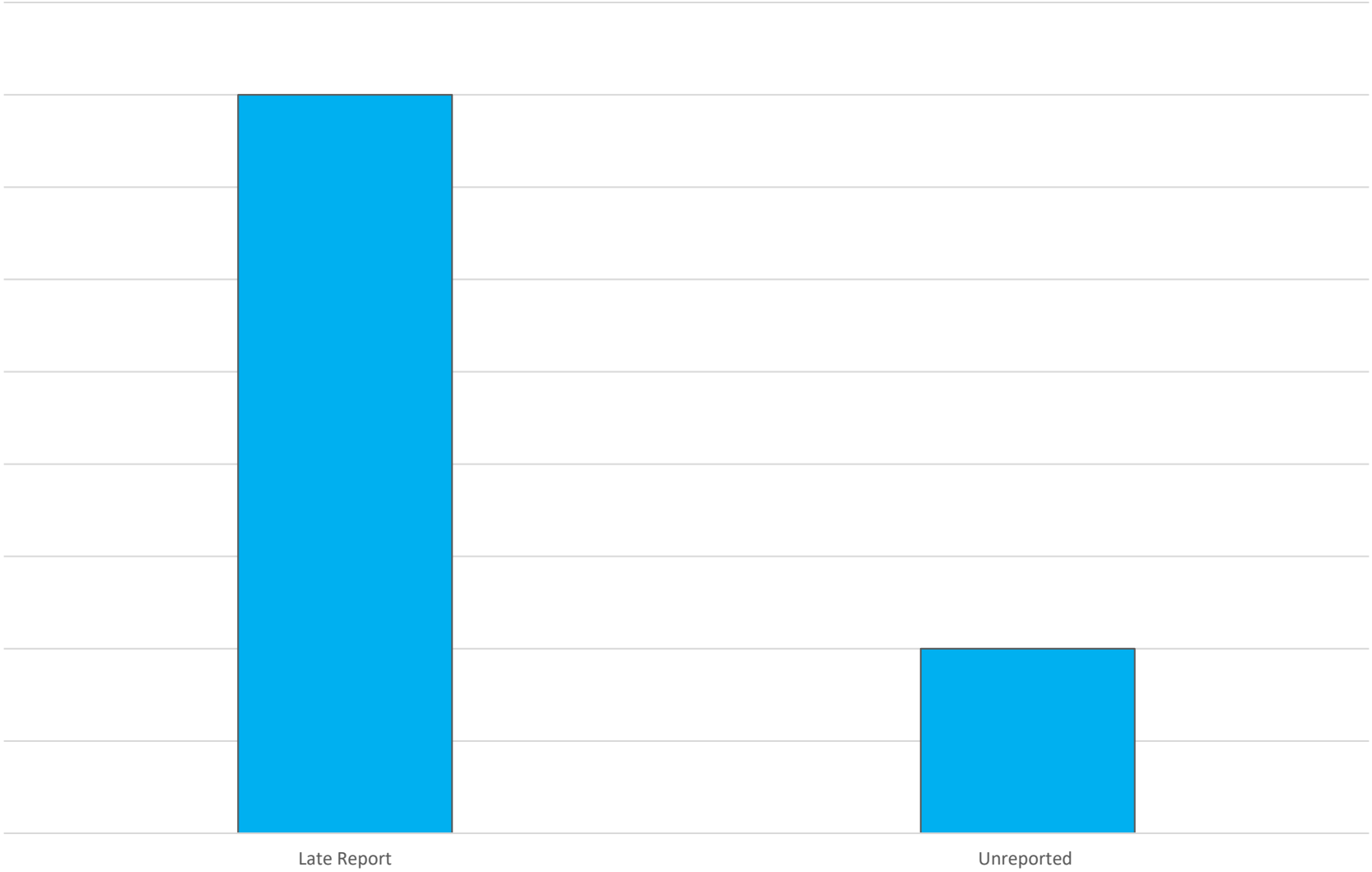
Protocol Compliance (312.60/812.100 *& 812.110 (b)) by Short Cite



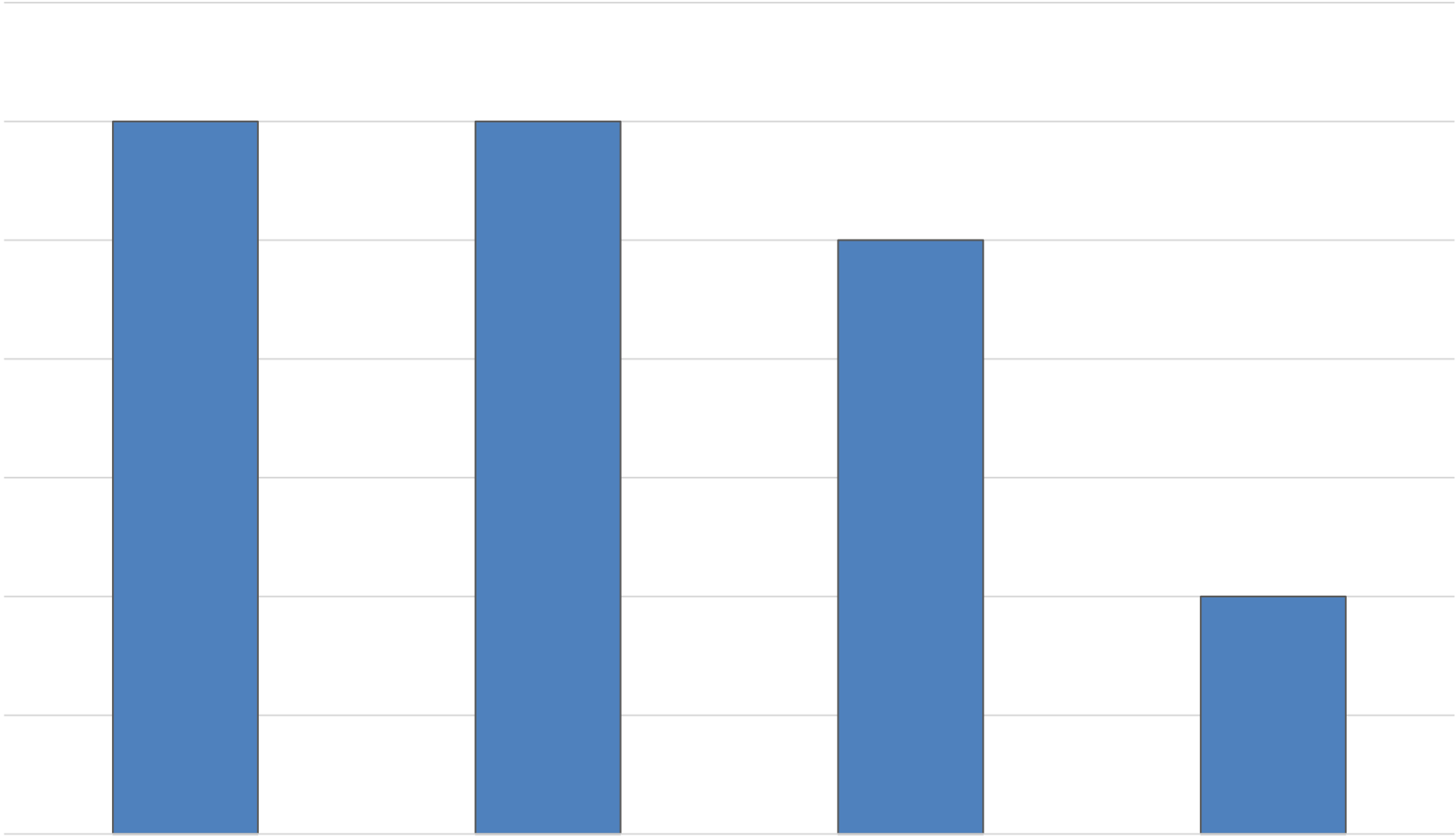
1572-Protocol Compliance Theme Details



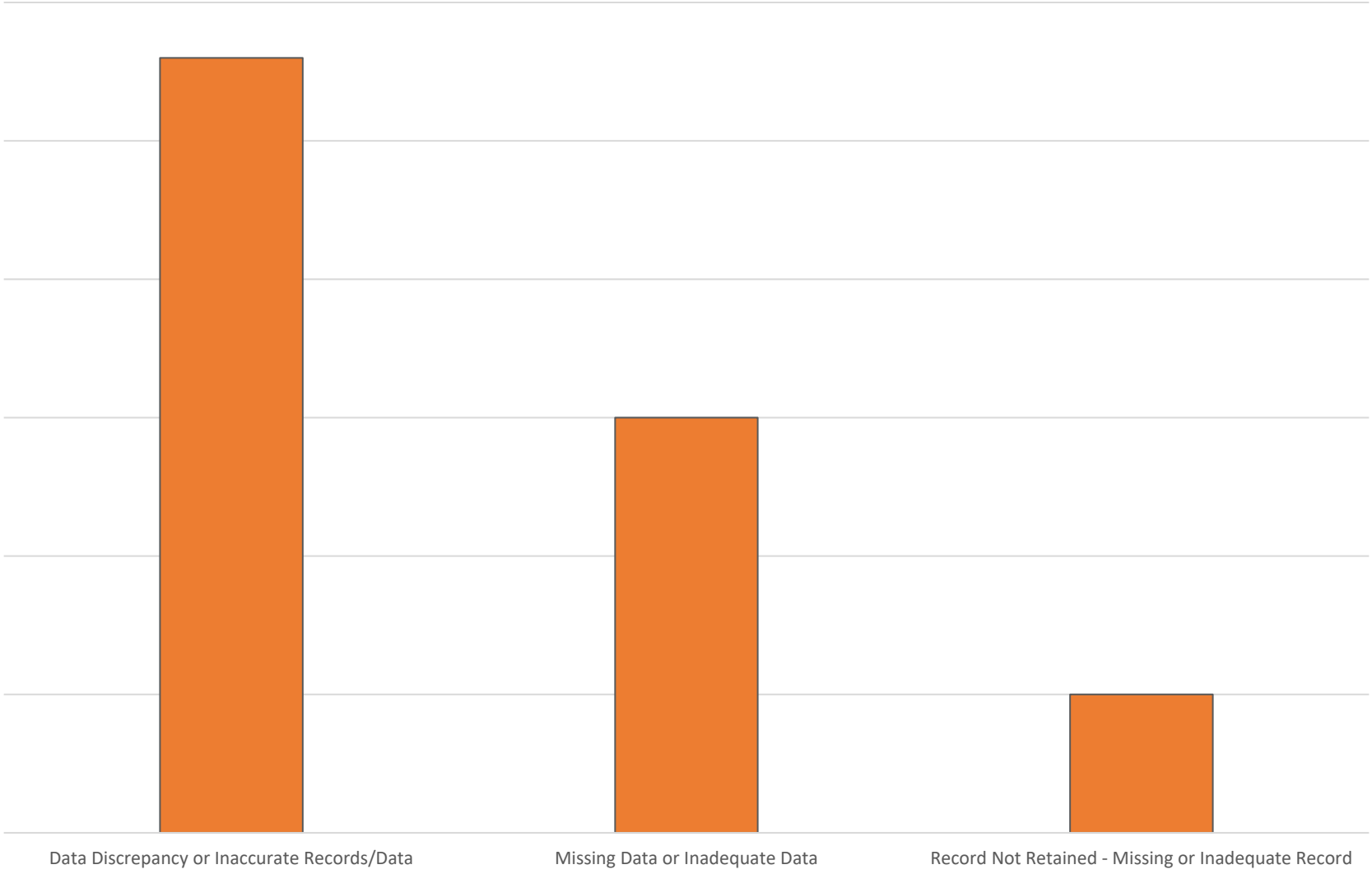
Failure to Report Adverse Events to Sponsor Promptly (312.64(b)) Details



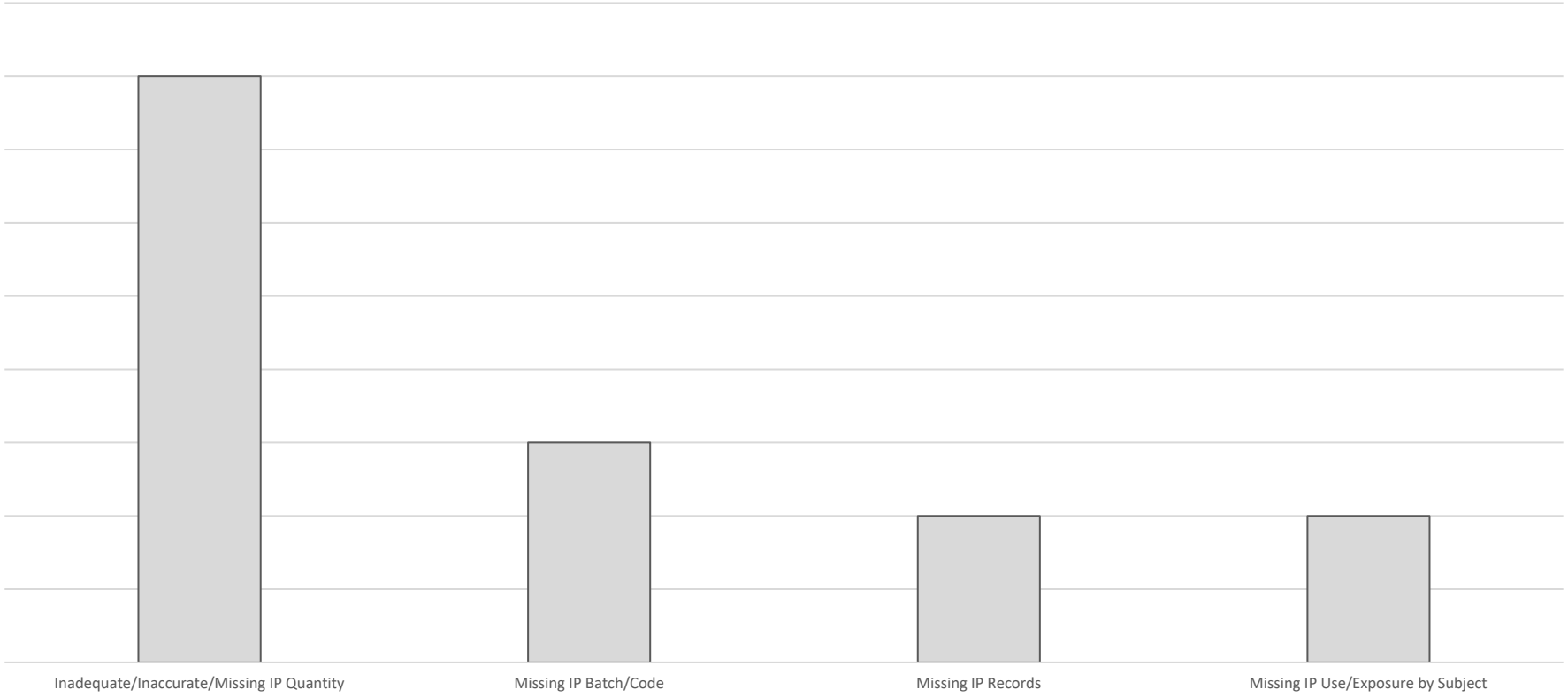
Dosing Error Type Theme Details



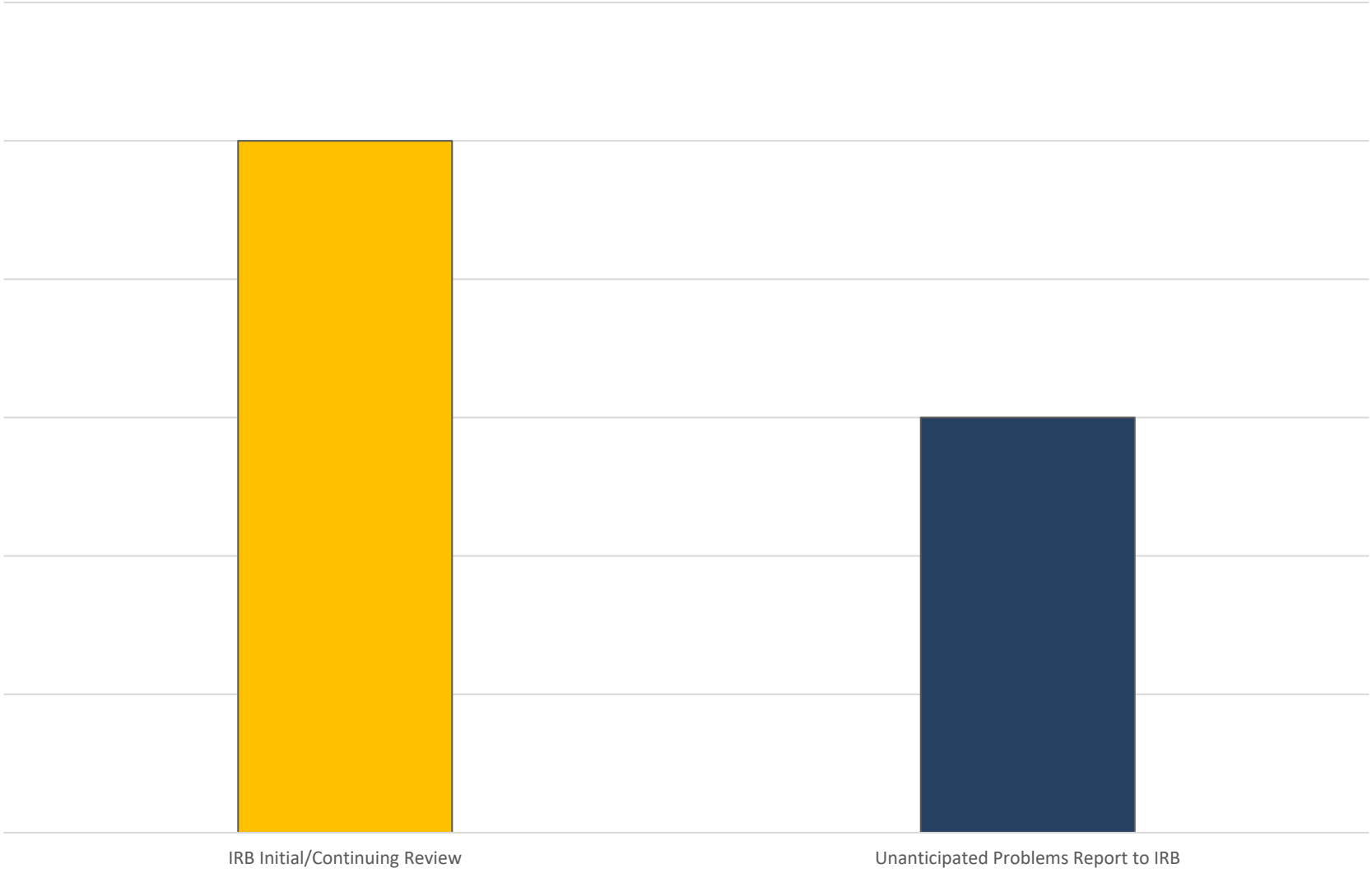
Accurate/Adequate Case Histories (312.62(b)/812.140(a)(3)) Theme Details



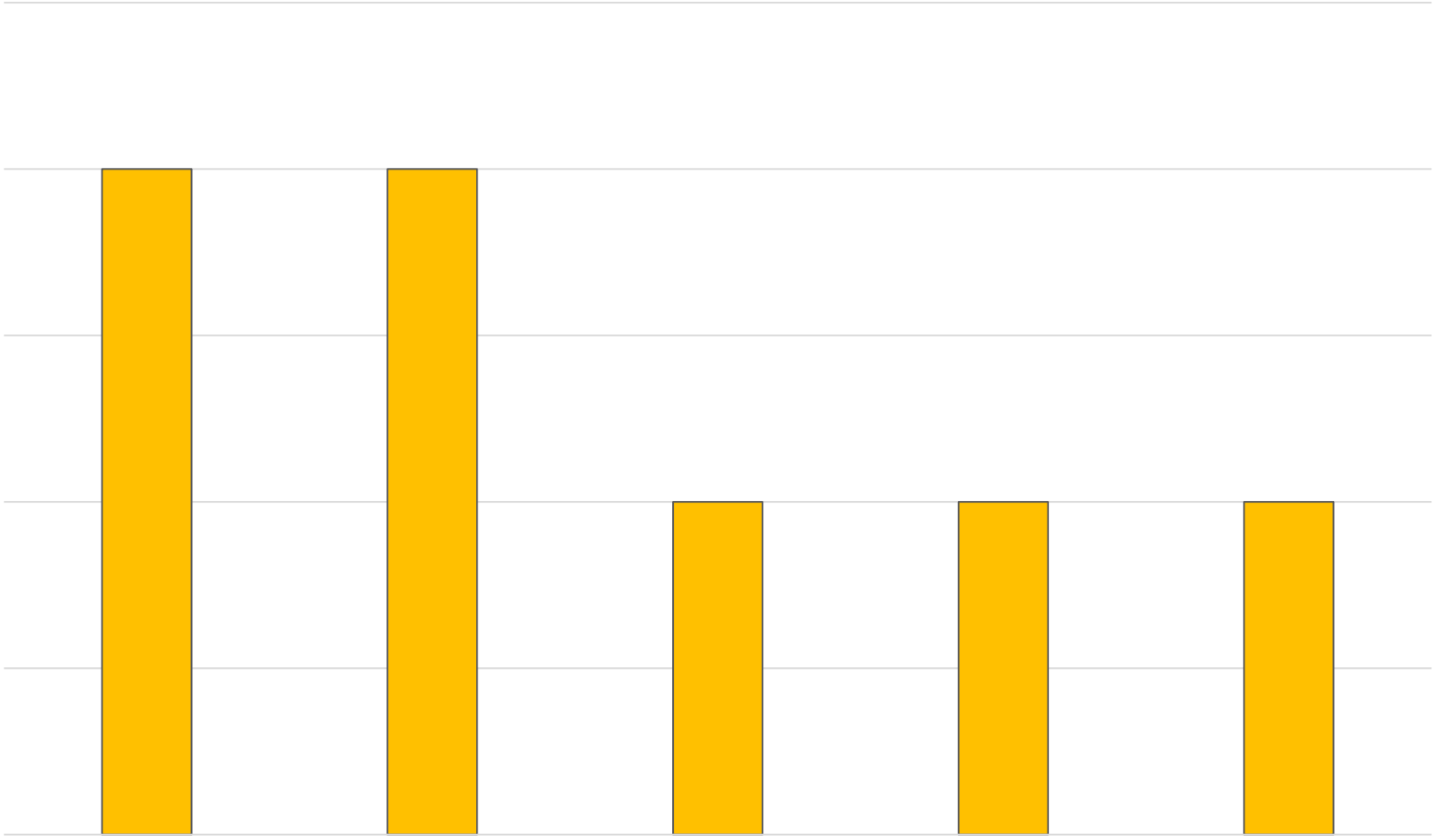
IP Accountability Records (312.62(a) / 812.140(a)(2)) Theme Details



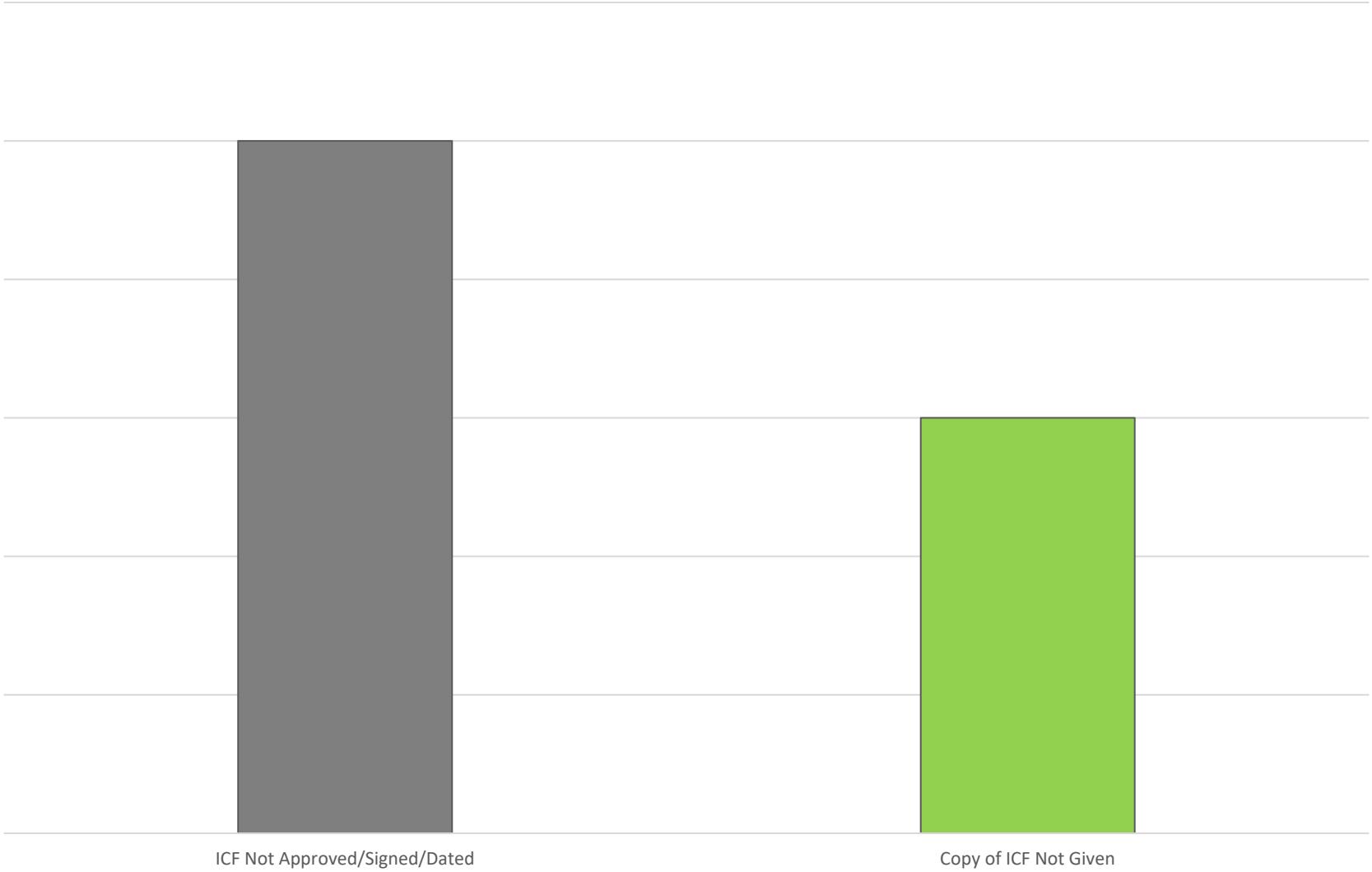
IRB (312.66) (812.150(a)(3)) Theme Details



Assurance of IRB Theme Details (312.66)



ICF 50.27(a) Theme Details

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