FY 2022 CI 483 OBSERVATION TRENDS

Acronyms

AE (Adverse Event)

CI (Clinical Investigator)

FDA (Food and Drug Administration)

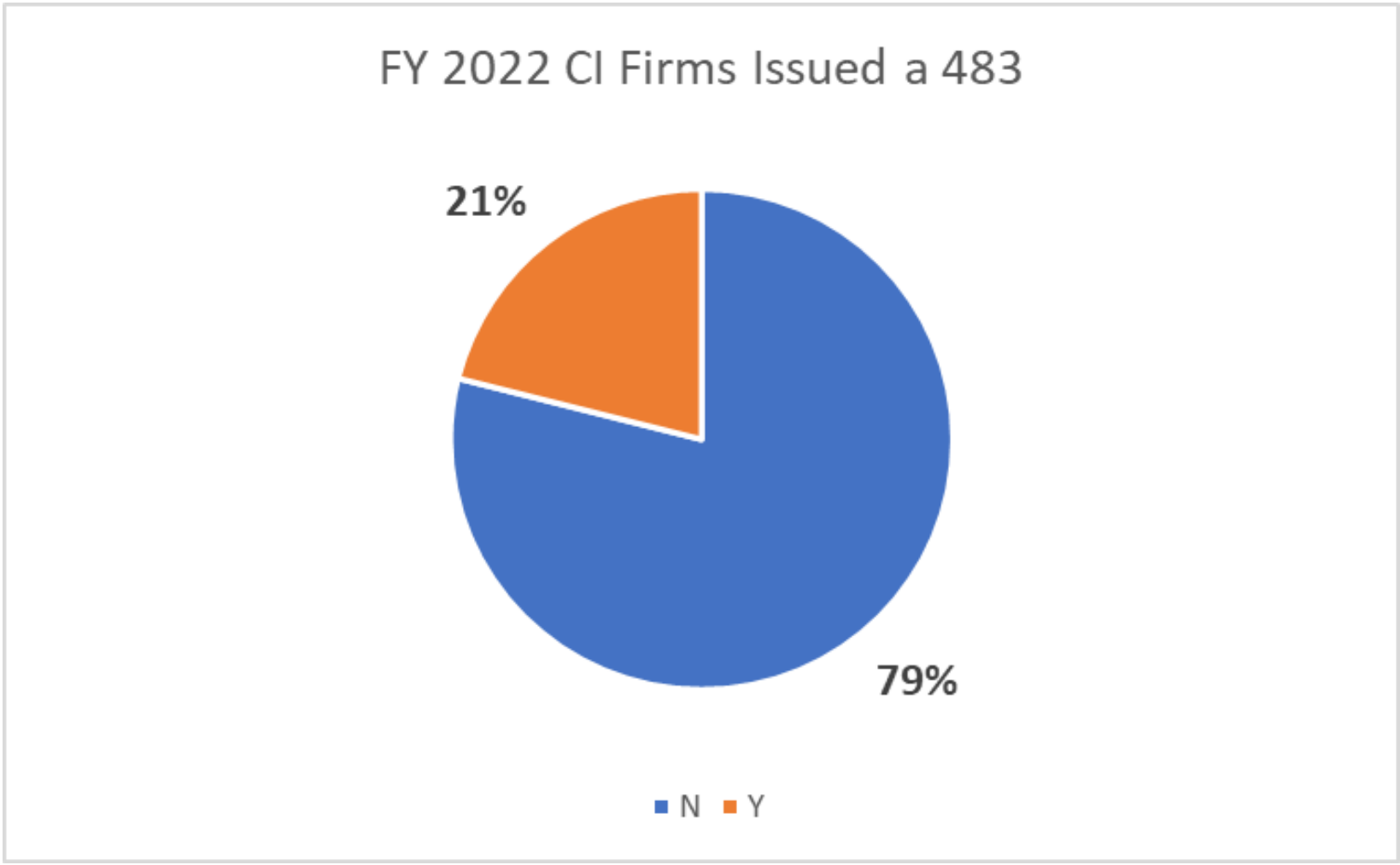
ICF (Informed Consent Form)

IP (Investigational Product)

IRB (Institutional Review Board)

OOW (Out of Window)

SAE (Serious Adverse Event)


FY 2022 CI Firms Issued a 483
21%
79%
N
Y

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 2022

- Protocol Compliance (312.60 / 812.100 & 812.110 (b))
- Accurate/Adequate Case Histories (312.62(b)/812.140(a)(3))
- IMP Accountability Records (312.62(a) / 812.140(a)(2))
- Institutional Review Board (312.66) (812.150(a)(3))
- Failure to Report Adverse Events to Sponsor Promptly (312.64(d))
- ICF Required Elements (50.25)
- ICF (50.27 (a))
- ICF (50.20)

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 error

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
- IMP Kit Selection Error
- IMP Preparation Documentation
- Missing IMP
- Inadequate IMP 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
- Failure to Discontinue from Study

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
- Missing IP return/ repair/ disposition

IRB and Adverse Events Reporting

Assurance of IRB review (312.66 & 812.150(a)(3))

- Not All Changes Approved by IRB Prior to Implementation
- Unanticipated Problems Report to IRB
- IRB Initial/ Continuing Review
- Progress Reports Not Submitted to IRB/ IRB Lapse

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

- Unreported Financial Disclosures

* Indicates new Cite Reference number(s)

Informed Consent Themes

ICF Required Elements (50.25 (a-e))

- Basic elements of Informed Consent
- Additional Elements of Informed Consent
- Information About ClinicalTrials.gov
- Information about lack of pre-emption from local, state or federal laws
- Authority of physicians to provide emergency medical care

Documentation of ICF (50.27(a))

- Copy of ICF Not Given
- ICF Not Approved/ Signed/ Dated

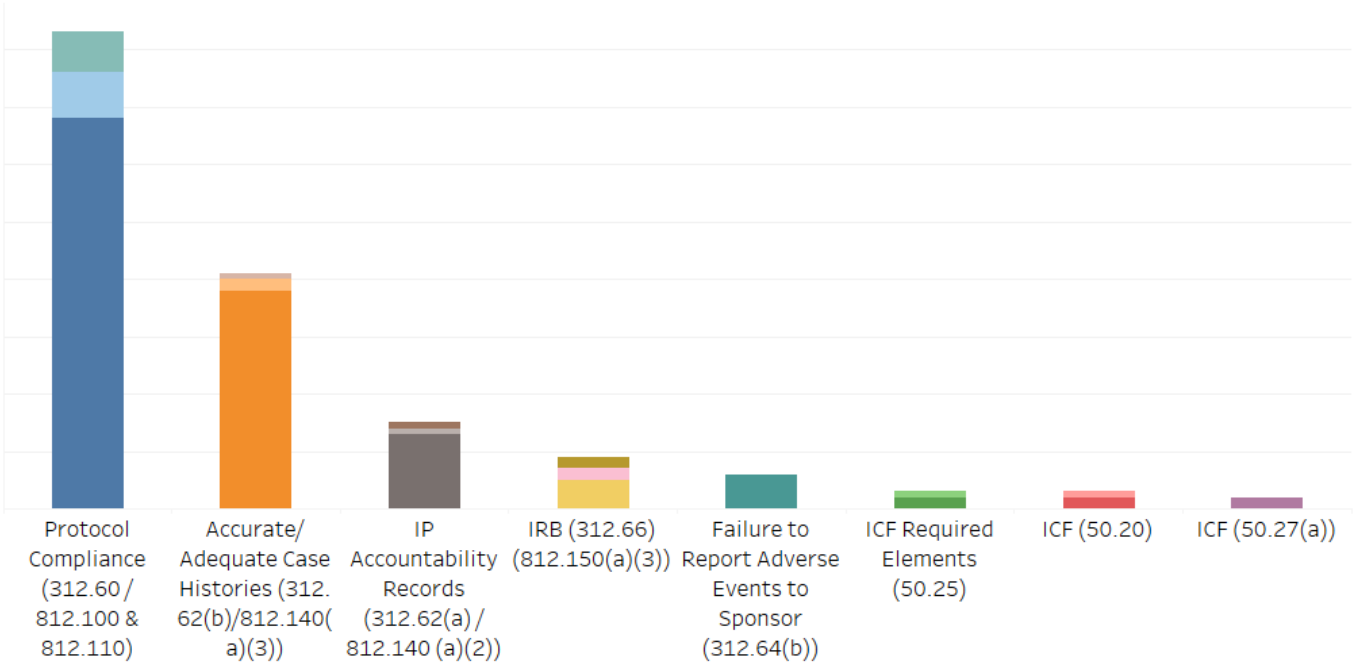
ICF (50.20)

- ICF Not Obtained
- ICF Not in Understandable Language
- ICF Short Form Not Witnessed
- ICF Circumstances - Not Sufficient Opportunity/Not Enough Time
- ICF Coercion

* Indicates new Cite Reference number(s)

FDA U.S. FOOD & DRUG ADMINISTRATION

FY 2022 Most Common Clinical Investigators 483 Short Cites by Theme

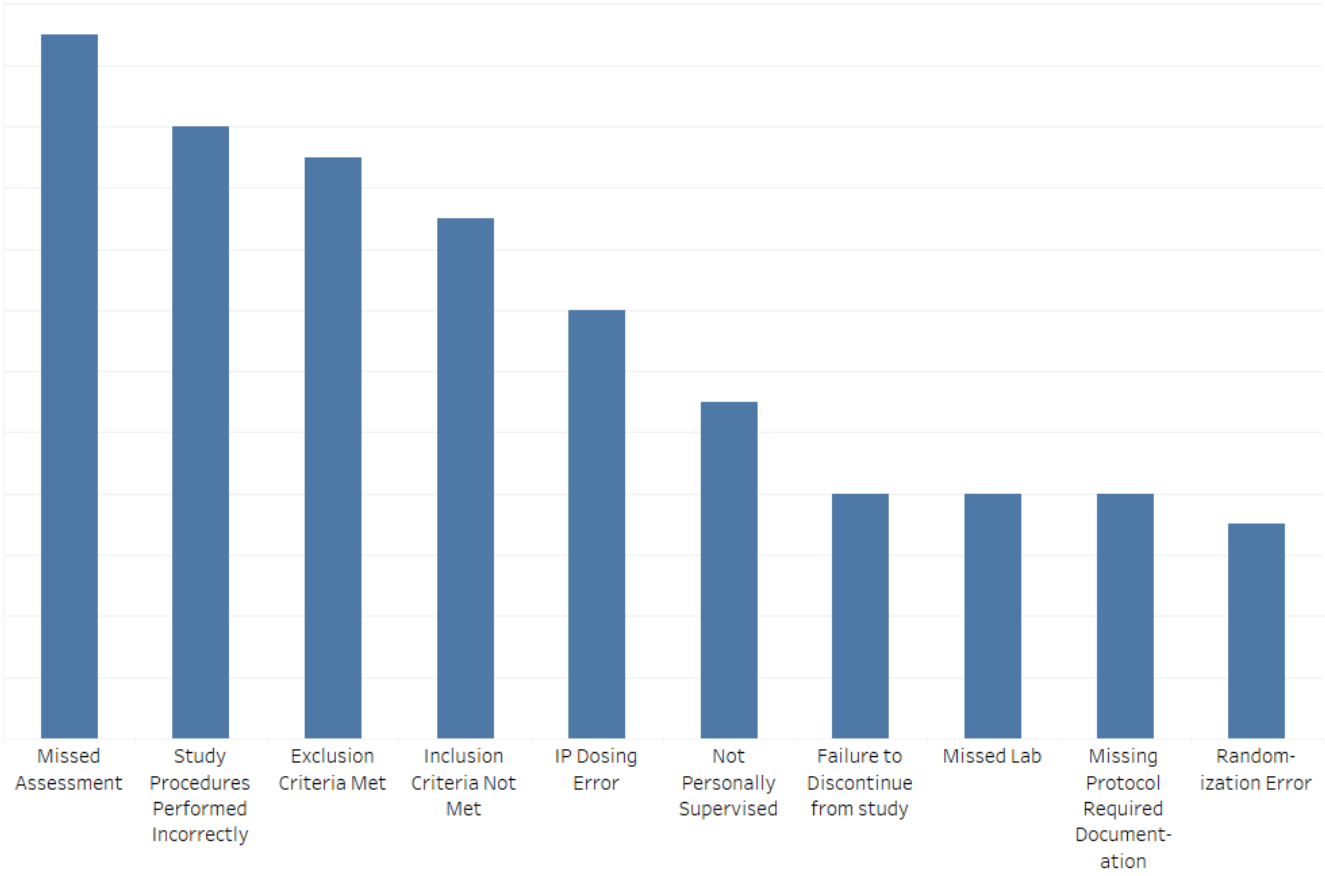


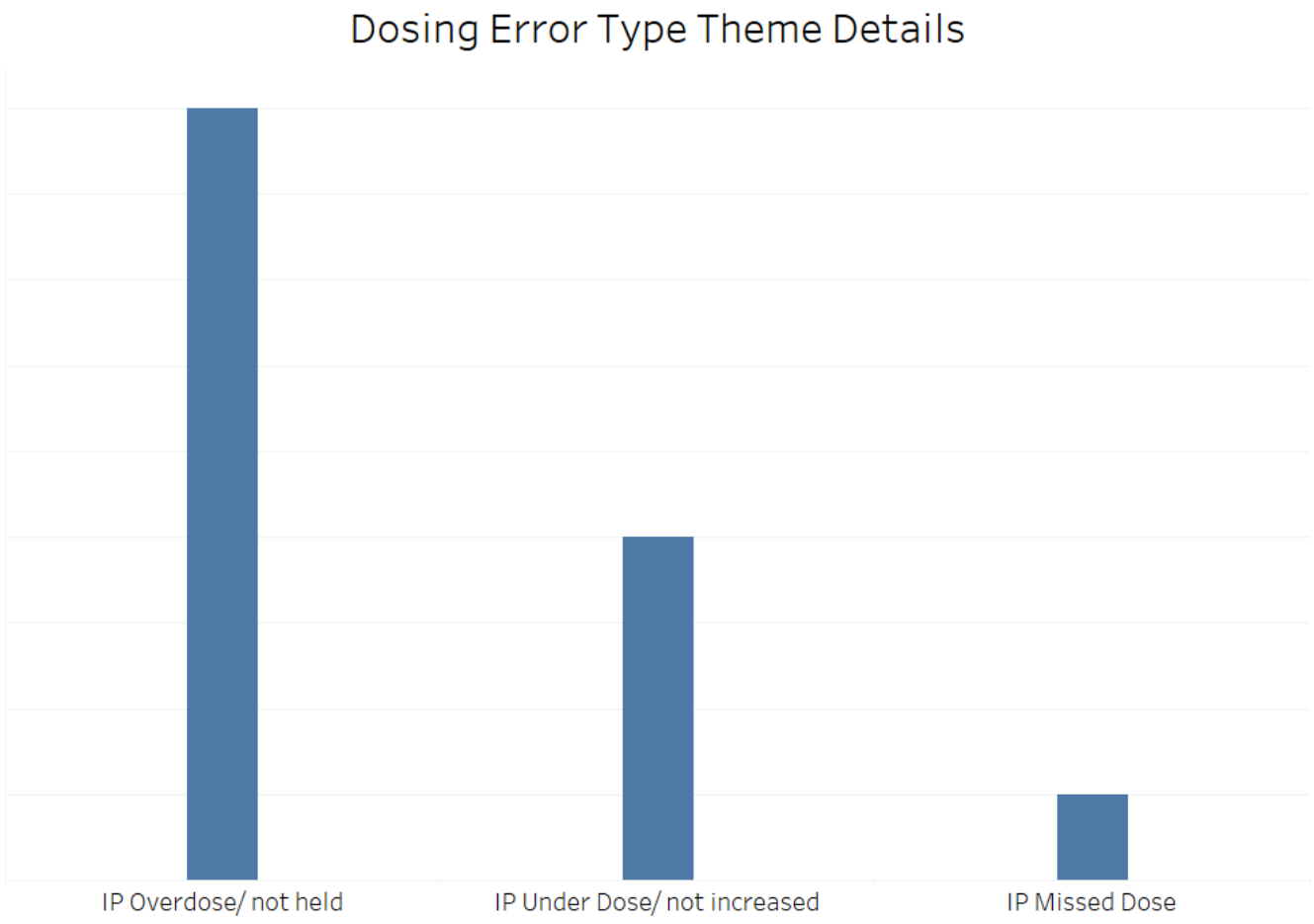
Short Cite Description

- Informed consent
- Non-compliance w/ agreement/plan/regulations
- FD-1572, protocol compliance
- Investigator adverse effect records inadequate
- Investigator's subject records inadequate
- Case history records- inadequate or inadequate
- Investigator device accountability inadequate
- Records of disposition of devices inadequate
- Accountability records
- Initial and continuing review
- Changes in research
- Unanticipated problems
- Safety reports
- ClincialTrials.gov statement
- No statement of experimental procedures
- Understandable language
- Circumstances of obtaining consent
- Consent form not approved/signed/dated

FDA U.S. FOOD & DRUG ADMINISTRATION

1572-Protocol Compliance Theme Details



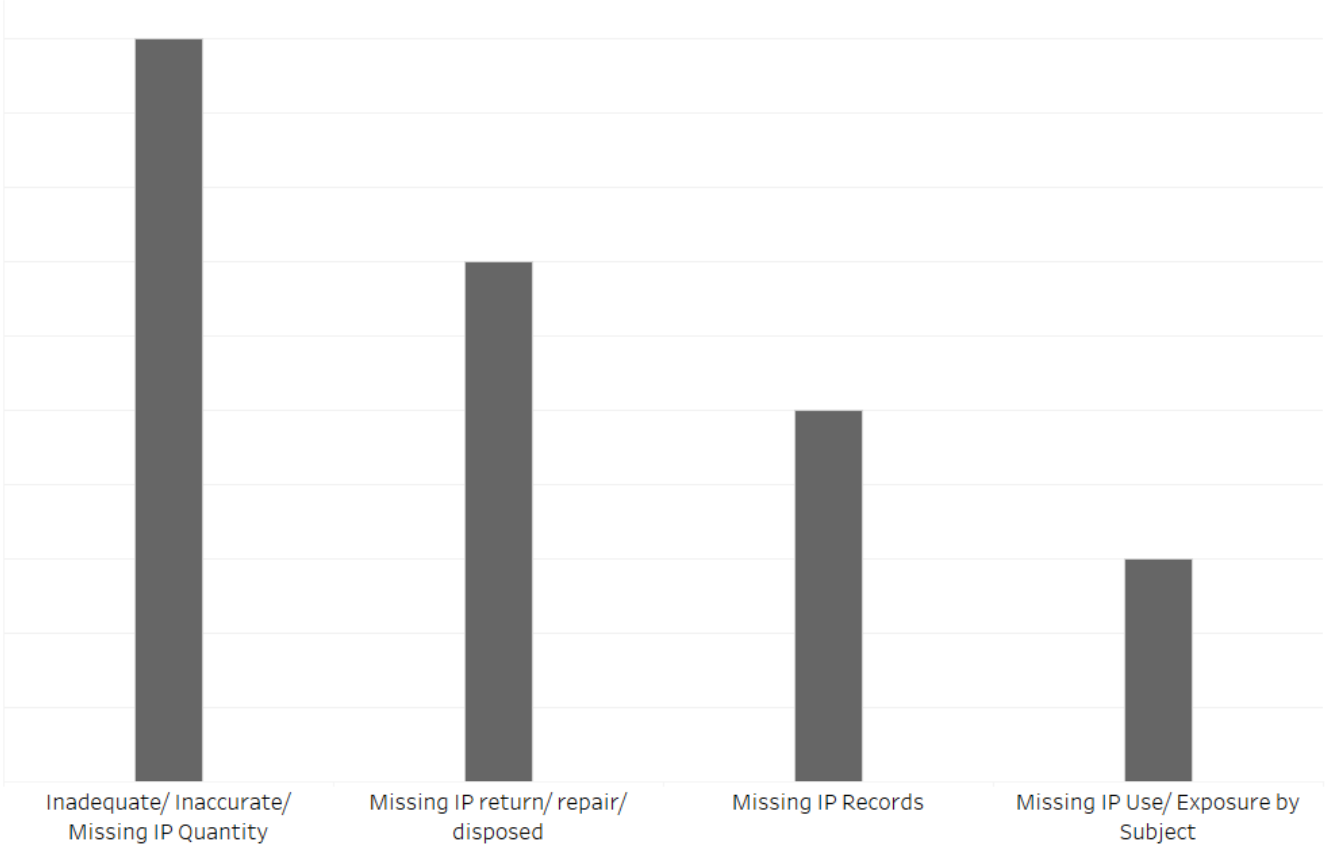

Dosing Error Type Theme Details
IP Overdose/ not held
IP Under Dose/ not increased
IP Missed Dose

U.S. FOOD & DRUG ADMINISTRATION

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

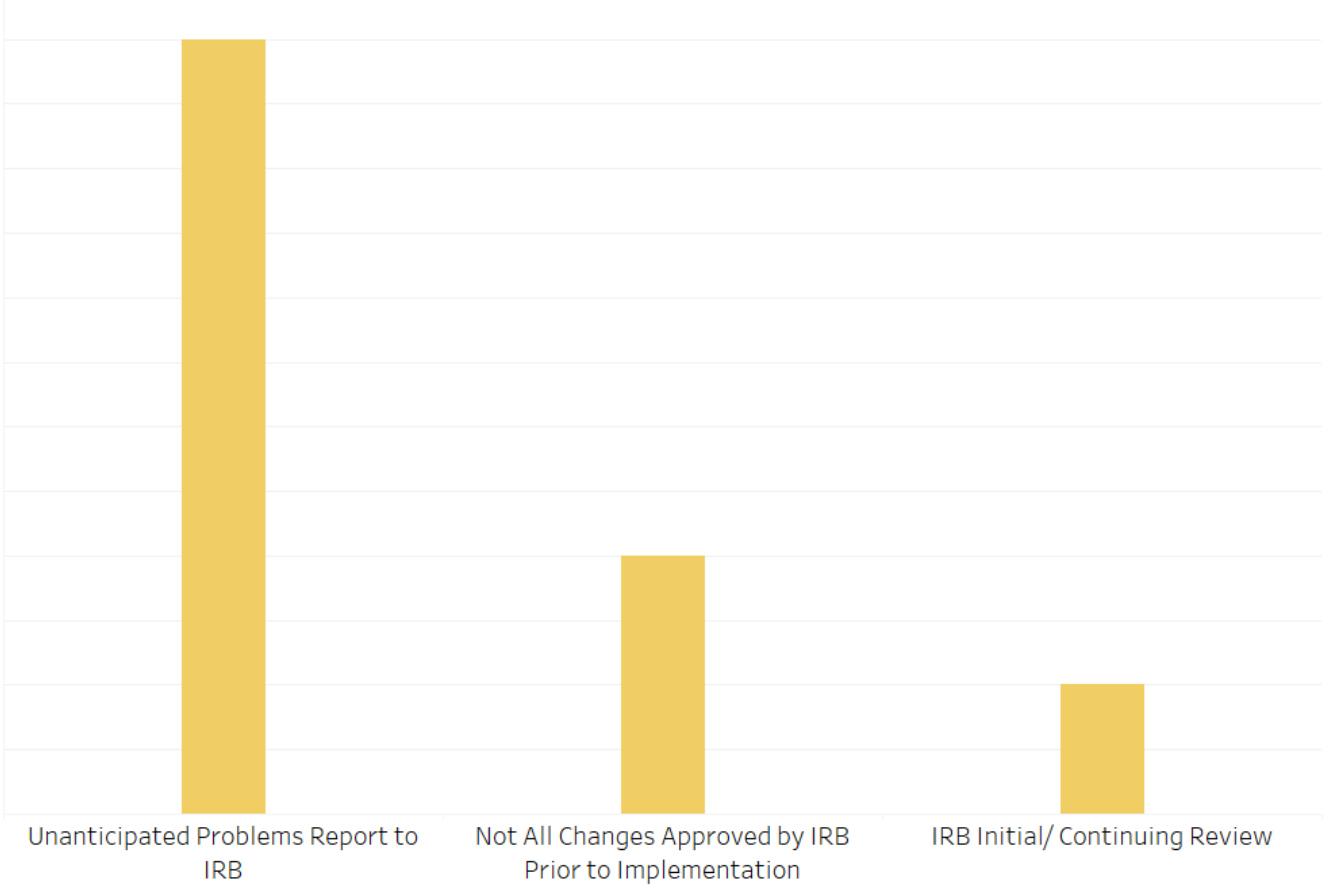
FDA U.S. FOOD & DRUG ADMINISTRATION

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



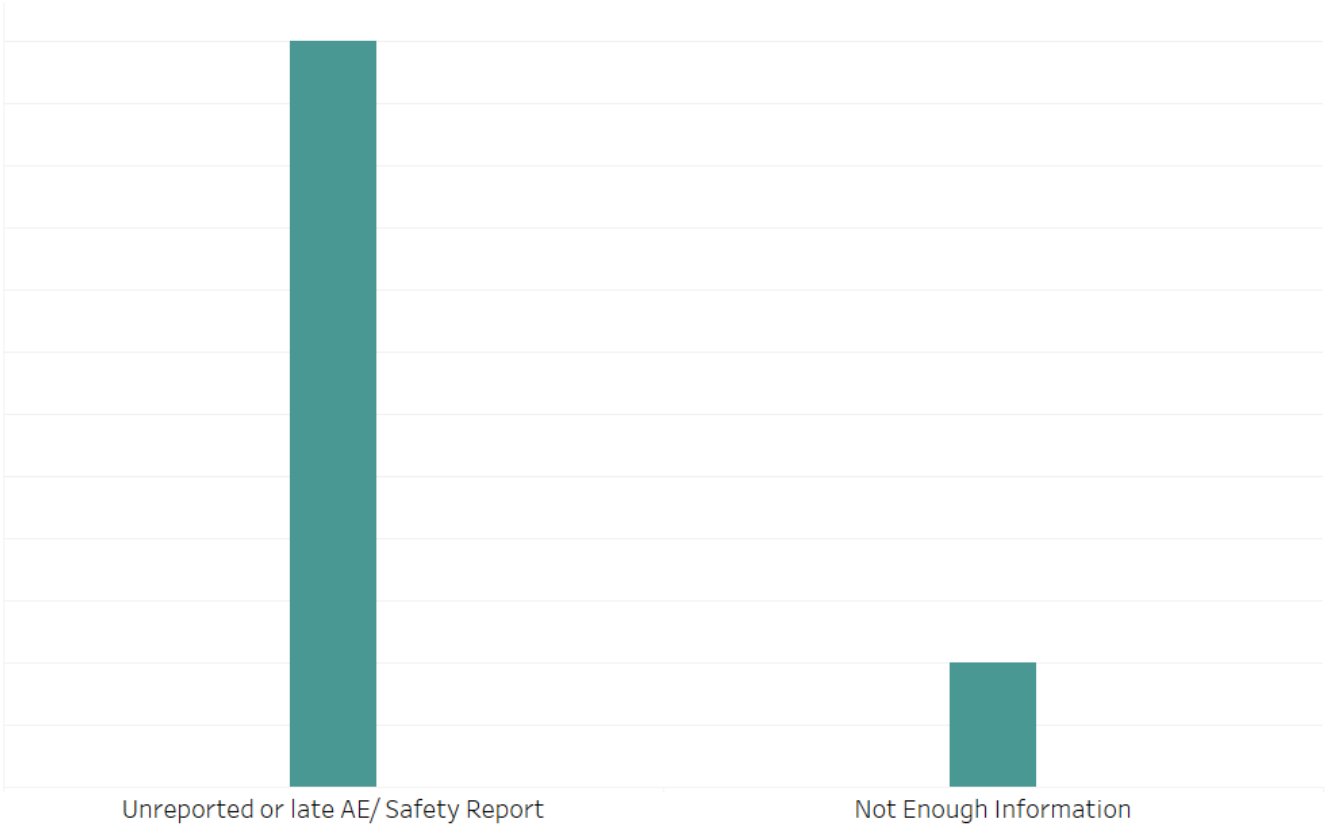
U.S. FOOD & DRUG ADMINISTRATION

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



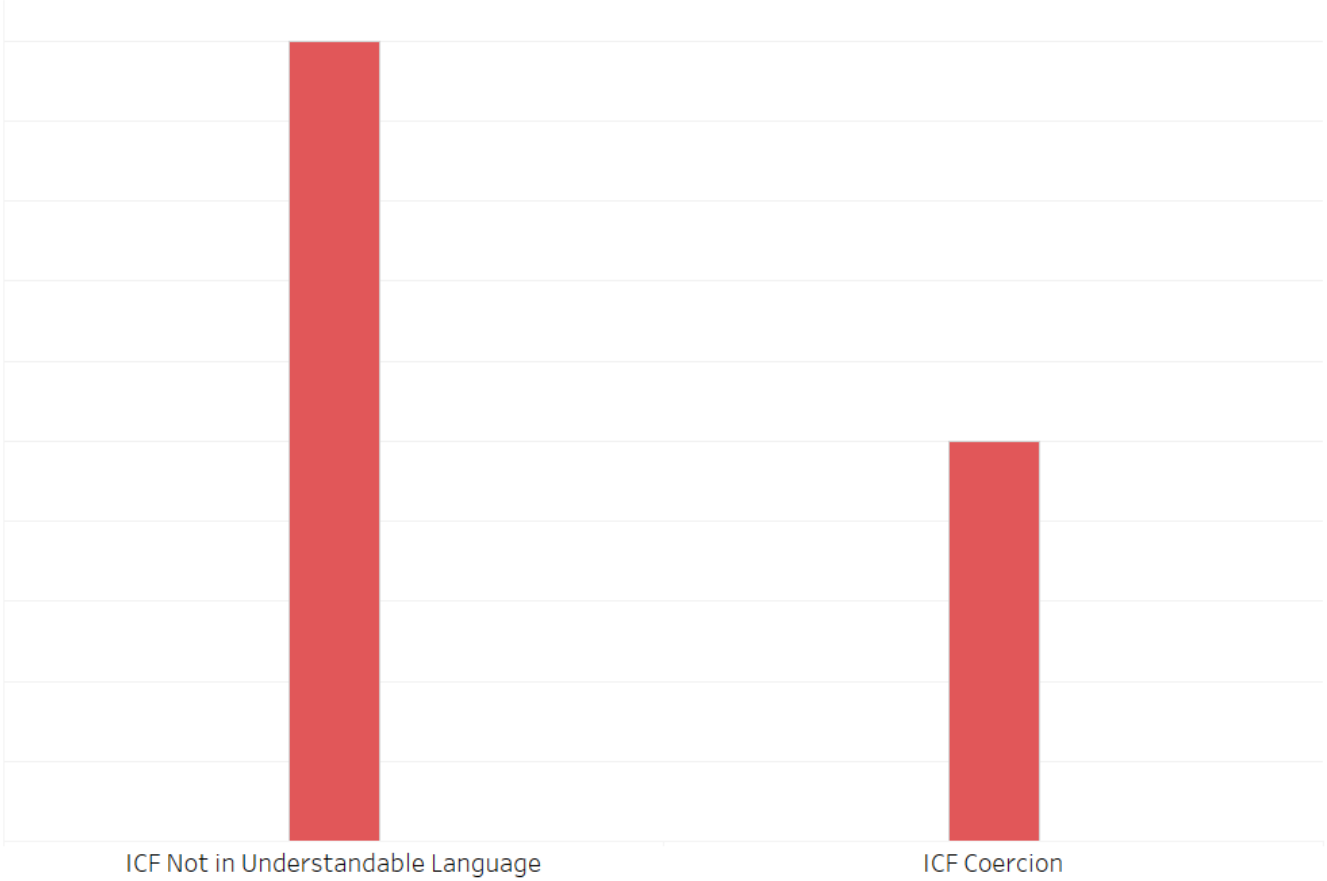
U.S. FOOD & DRUG ADMINISTRATION

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



U.S. FOOD & DRUG ADMINISTRATION

ICF 50.20 Theme Details




FDA
U.S. FOOD & DRUG
ADMINISTRATION