Bioresearch Monitoring (BIMO)
Fiscal Year 2019
Metrics

Inspection Metrics Overview

- The following slides provide annual inspection metrics for the compliance programs within the Bioresearch Monitoring (BIMO) Program overseen by the Food and Drug Administration (FDA) six product centers:
  - Center for Biologics Evaluation and Research (CBER)
  - Center for Devices and Radiological Health (CDRH)
  - Center for Drug Evaluation and Research (CDER)
  - Center for Food Safety and Applied Nutrition (CFSAN)
  - Center for Tobacco Products (CTP)
  - Center for Veterinary Medicine (CVM)

- The inspections (domestic and foreign) were conducted by FDA's Office of Regulatory Affairs (ORA). A portion of the CDER bioequivalence inspections were conducted independently by CDER subject matter experts.

- Metrics are based on the Center final classification determined in fiscal year (FY) 2019.

Metrics Terms

Organizations and Programs

- BE or BEQ: Bioequivalence - clinical and analytical
- BIMO: Bioresearch Monitoring
- CBER: Center for Biologics Evaluation and Research
- CDER: Center for Drug Evaluation and Research
- CDRH: Center for Devices and Radiological Health
- CFSAN: Center for Food Safety and Applied Nutrition
- CI or Clin: Clinical Investigator
- CRO: Contract Research Organization
- CTP: Center for Tobacco Products
- CVM – Center for Veterinary Medicine
- FDA: Food and Drug Administration
- GLP: Good Laboratory Practice
- IRB: Institutional Review Board
- M: Monitors
- PADE: Postmarketing Adverse Drug Experience
- PMR: Postmarketing Requirements
- RDRC: Radioactive Drug Research Committee
- REMS: Risk Evaluation and Mitigation Strategy
- Sponsor: Sponsor or Sponsor-Investigator

Classifications

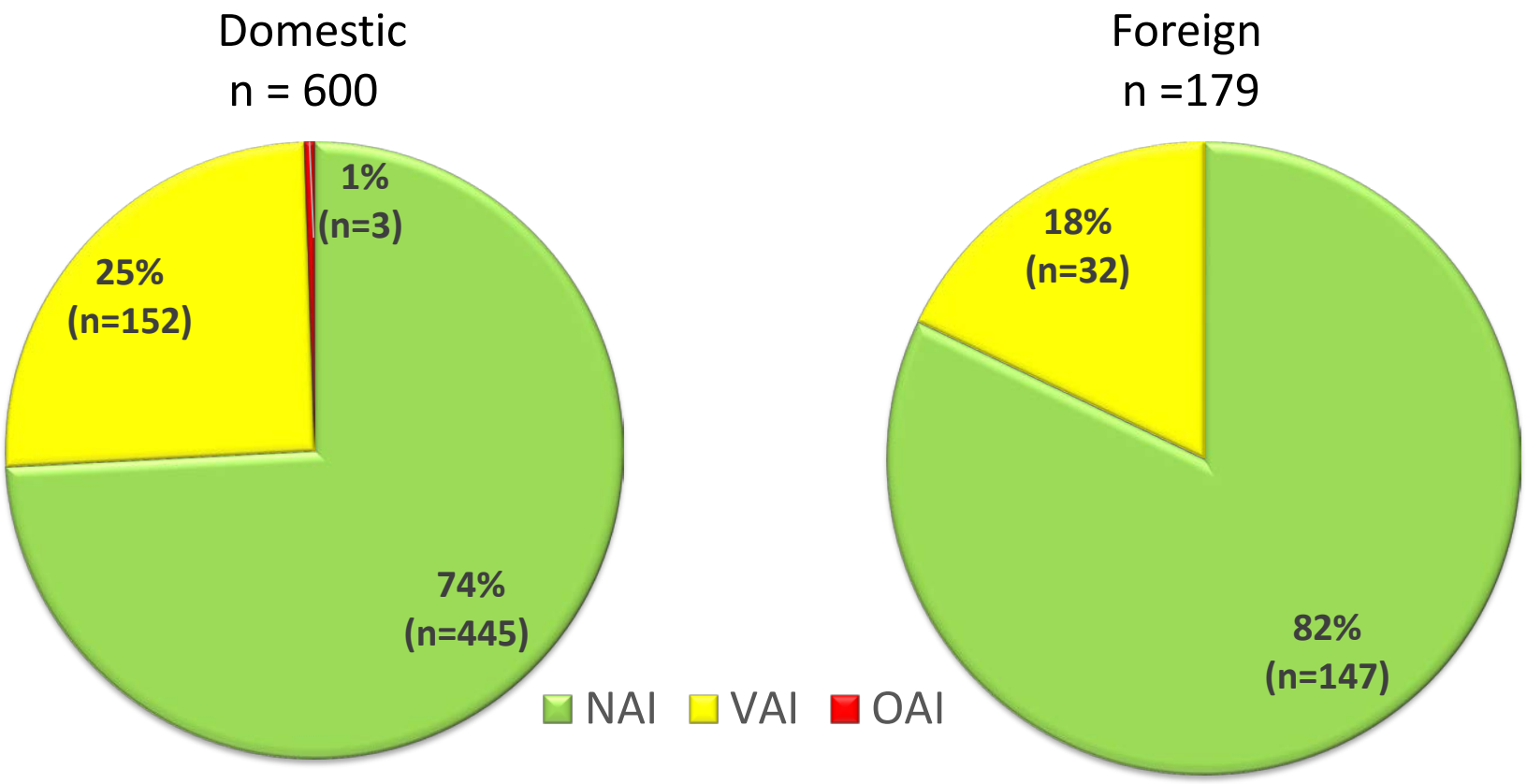
- NAI: No Action Indicated
- OAI: Official Action Indicated
- VAI: Voluntary Action Indicated

BIMO Inspection Classifications by Center – FY 2019*

Center	CI	IRB	S/M/CRO	S/I	GLP	BEQ	PADE	REMS	Total
CBER	60	12	9	3	4	0	0	0	**88**
CDER	574	90	62	7	25	200	78	17	**1053**
CDRH	126	37	39	3	10	0	0	0	**215**
CFSAN	2	1	0	0	4	0	0	0	**7**
CTP	5	0	0	0	0	0	0	0	**5**
CVM	12	0	3	0	19	0	0	0	**34**
Totals	**779**	**140**	**113**	**13**	**62**	**200**	**78**	**17**	**1402**

* Domestic and Foreign

Clinical Investigator Inspection Classifications
(FY 2019)



Common Clinical Investigator Inspectional Observations

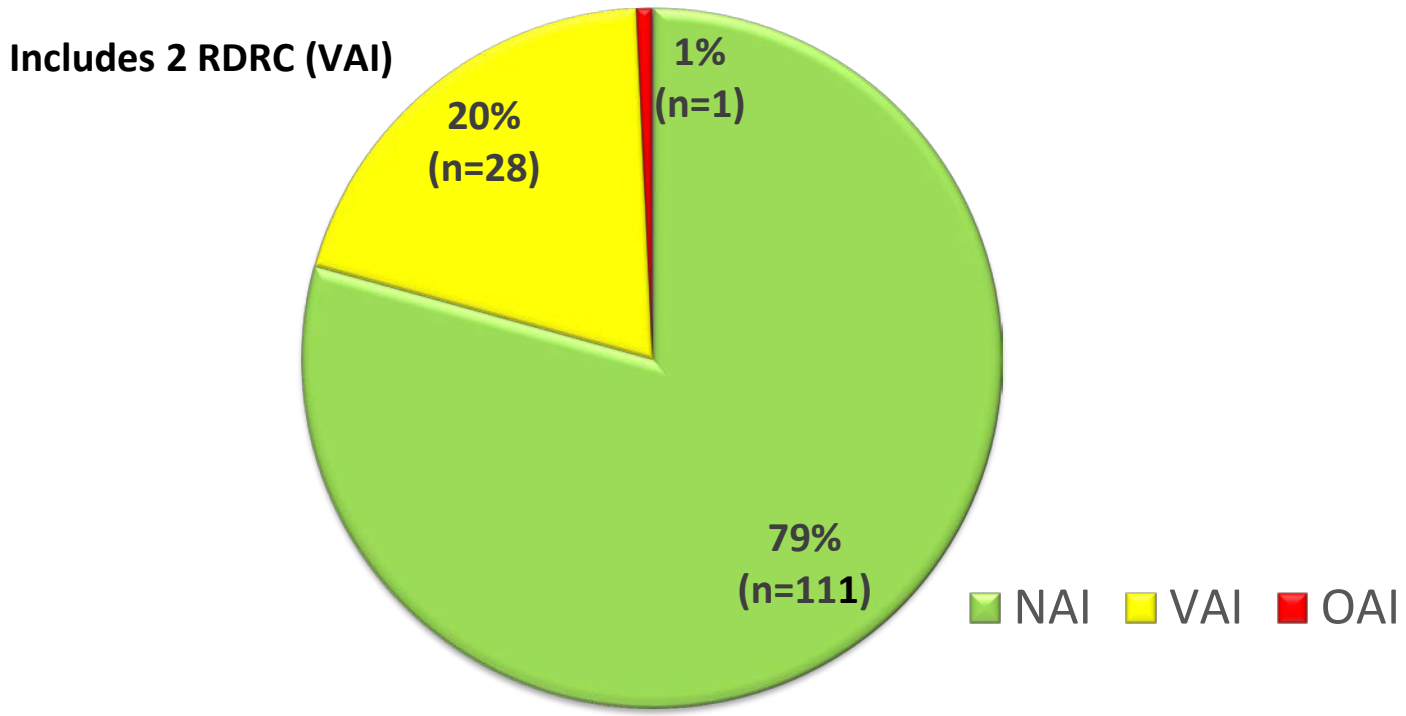
- Failure to follow the investigational plan; protocol deviations
- Failure to comply with Form FDA 1572 requirements
- Inadequate and/or inaccurate case history records; inadequate study records
- Inadequate accountability for the investigational product
- Inadequate subject protection; informed consent issues
- Safety reporting; failure to report and/or record adverse events
- Failure to comply with 21 CFR part 56 (IRB) requirements.

Institutional Review Board Inspections Classifications

(FY 2019)

Domestic

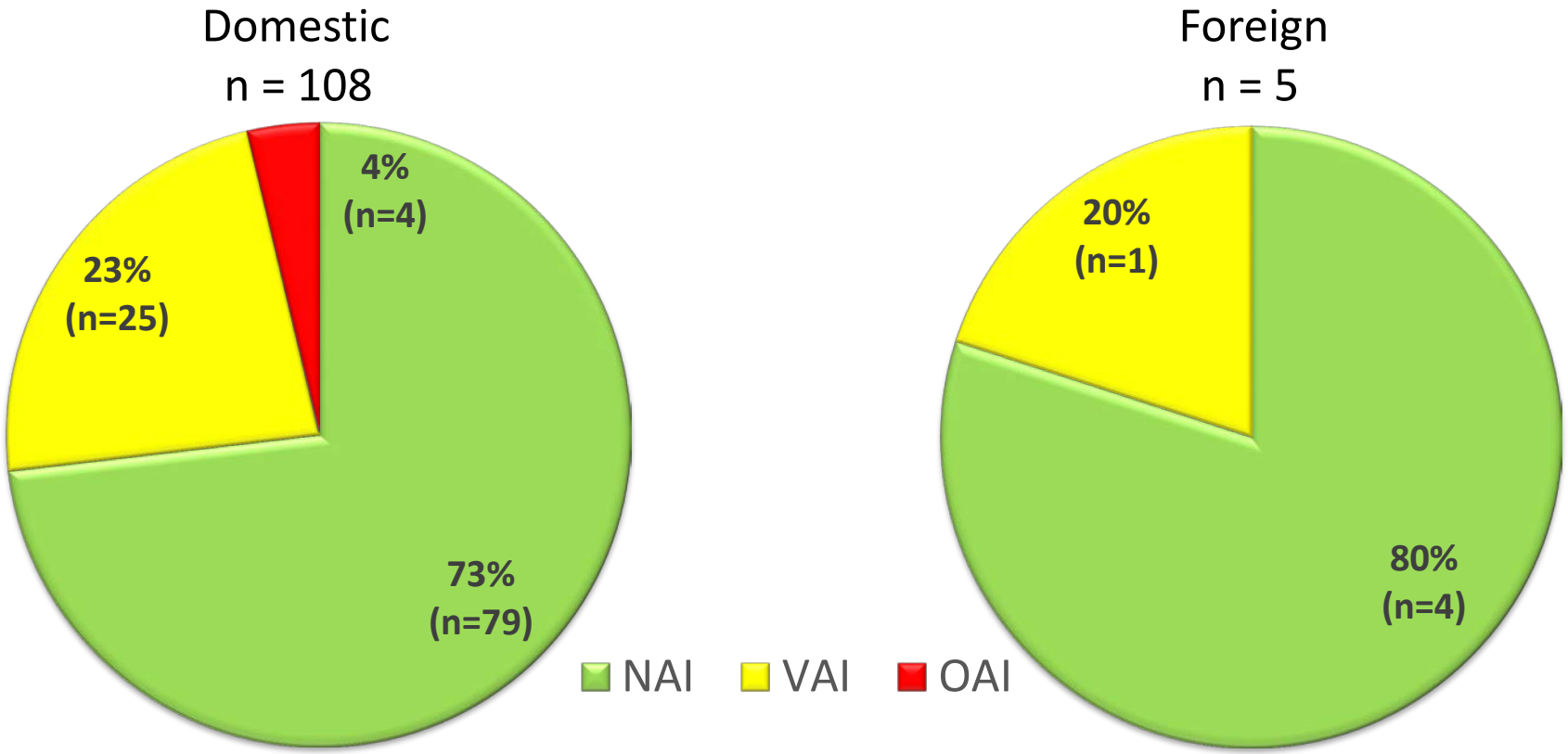
n = 140



Common Institutional Review Board Inspectional Observations

- Failure to have minutes of IRB meetings in sufficient detail to show attendance at the meeting; vote actions, quorum issues
- Failure to conform to membership criteria listed in 21 CFR 56.107; membership list
- Failure to conduct initial and/or continuing review of research
- Inadequate written procedures for prompt reporting of non-compliance, suspension or termination
- Failure to prepare and maintain documentation of IRB activities; inadequate copies of research proposals and related documents

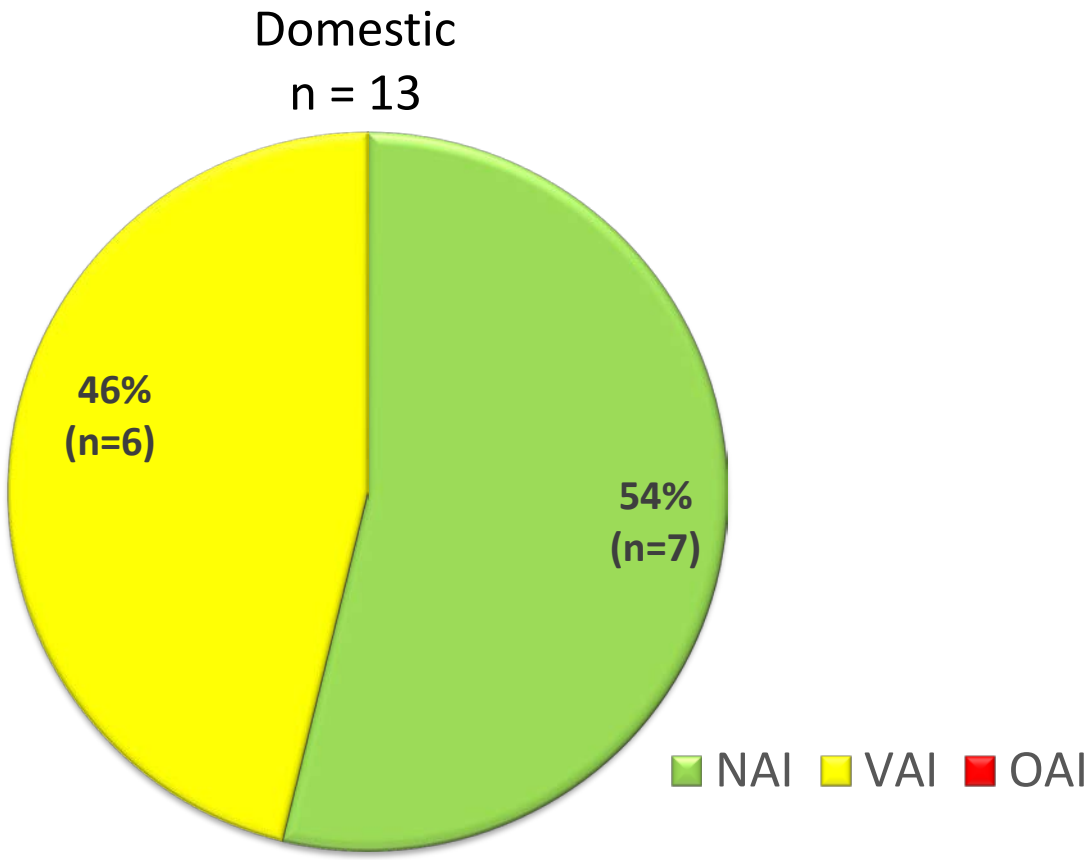
Sponsor/Monitor/CRO Inspections Classifications
(FY 2019)



Common Sponsor/Monitor/CRO Inspectional Observations

- Failure to select qualified investigators and/or monitors, ensure proper monitoring of the study and ensure the study is conducted in accordance with the protocol and/or investigational plan. (General responsibilities of sponsors)
- Failure to maintain and/or retain adequate records in accordance with 21 CFR 312.57; accountability for the investigational product.
- Failure to bring non-compliant investigators into compliance

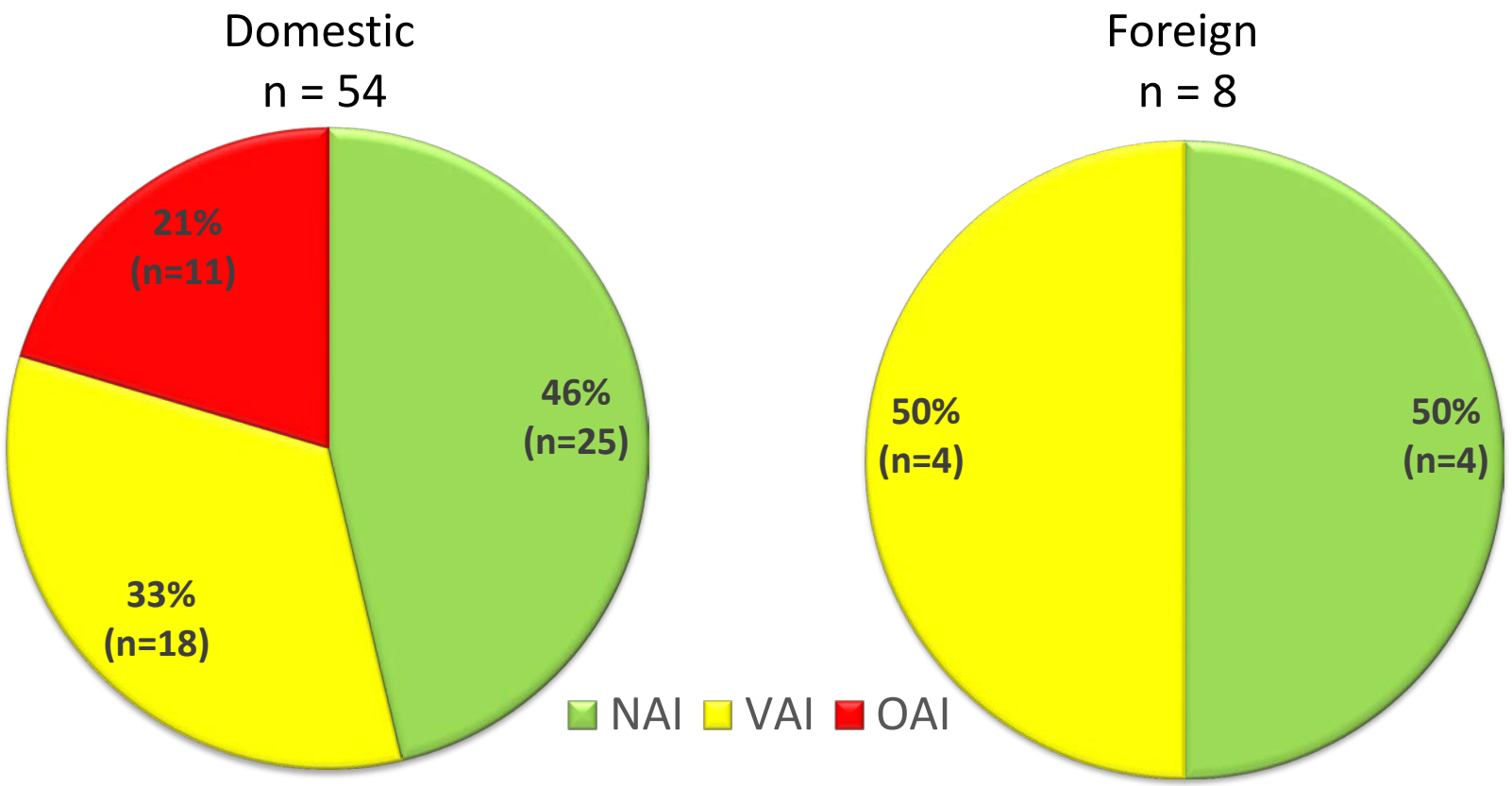
Sponsor-Investigator Inspections Classifications
(FY 2019)



Common Sponsor-Investigator Inspectional Observations

- Failure to submit an Investigational New Drug (IND) application
- Failure to ensure proper monitoring of the clinical investigation
- Failure to follow the investigational plan
- Failure to comply with Form FDA 1572 requirements
- Inadequate and/or inaccurate case history records; inadequate study records
- Inadequate accountability for the investigational product
- Inadequate subject protection; informed consent issues
- Failure to comply with 21 CFR part 56 (IRB) requirements.

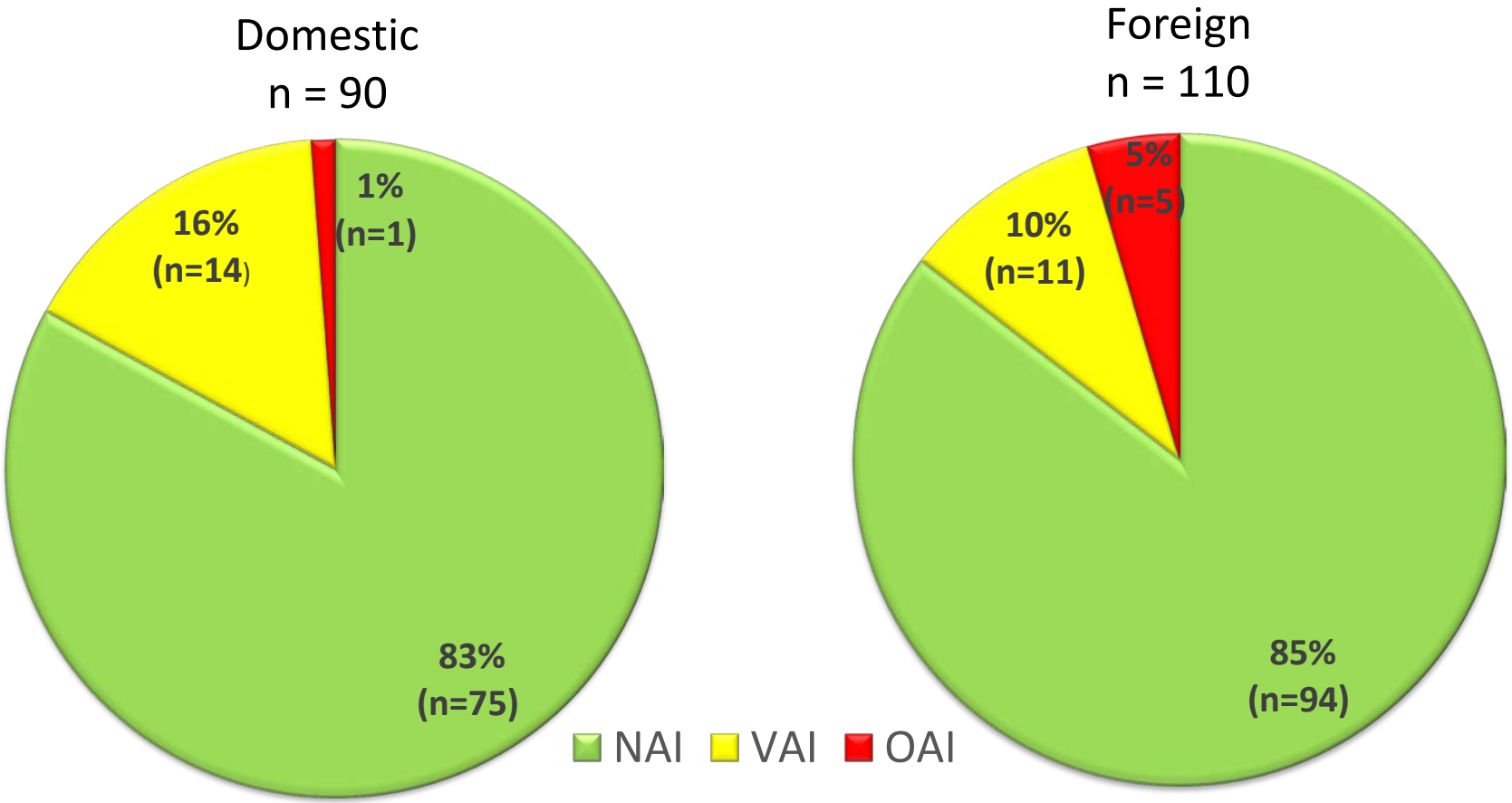
Good Laboratory Practice Inspections Classifications
(FY 2019)



Common Good Laboratory Practice Inspectional Observations

- Inadequate labeling; test article, reagent
- Study Director requirements; failure to transfer data to archives, document unforeseen circumstances, assure data is accurately recorded and verified
- Missing standard operating procedures (SOPs)
- Conduct; not all studies were conducted in accordance with the protocol
- Final report; circumstances affecting data quality and integrity

Bioequivalence Inspections Classifications
(FY 2019)

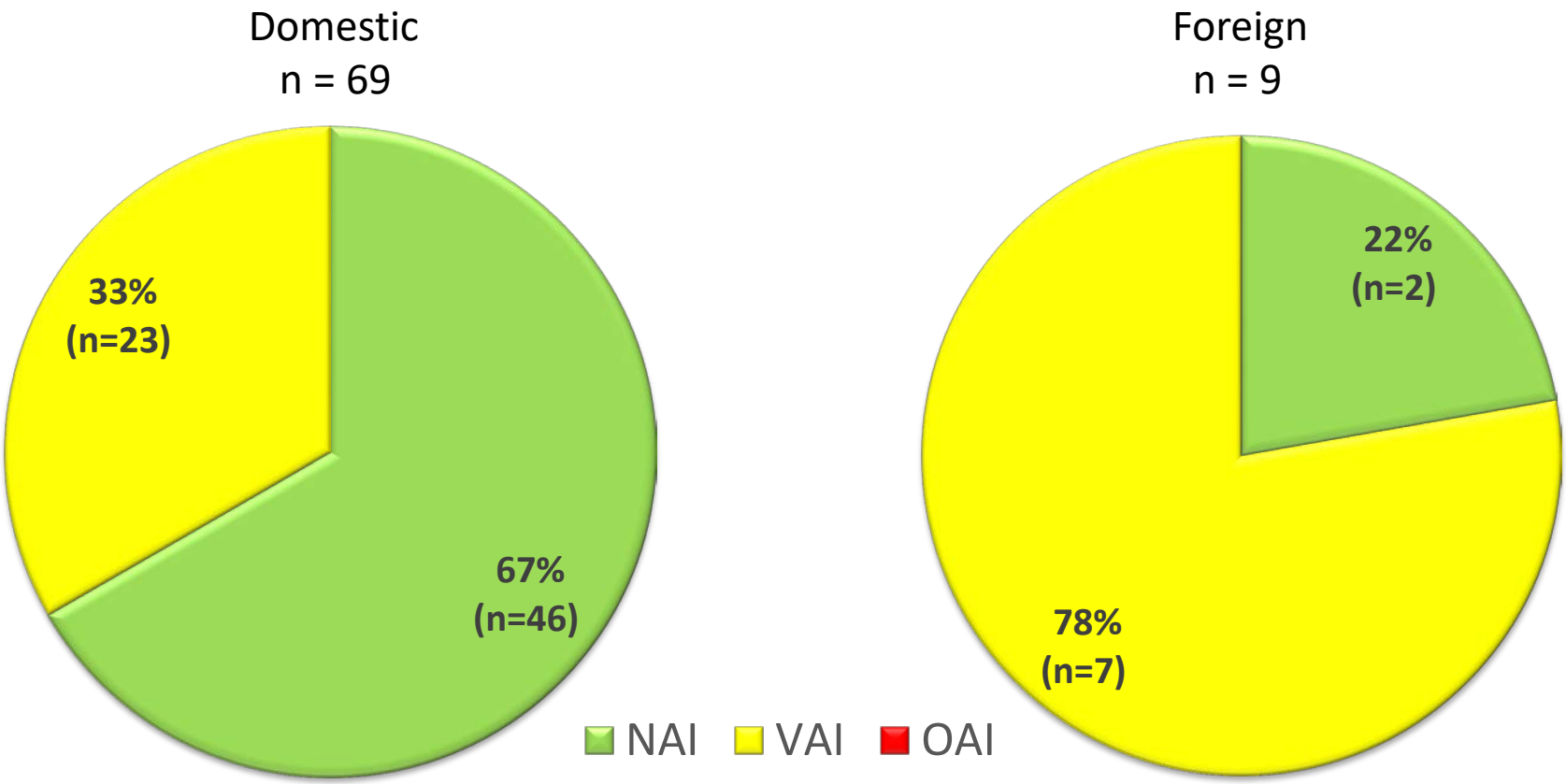


Common Bioequivalence Inspectional Observations

- **Analytical**
  - Validation
  - Reserve Samples
- **Clinical**
  - Blinding Codes
  - Recordkeeping

Postmarketing Adverse Drug Experience Inspections Classifications

(FY 2019)

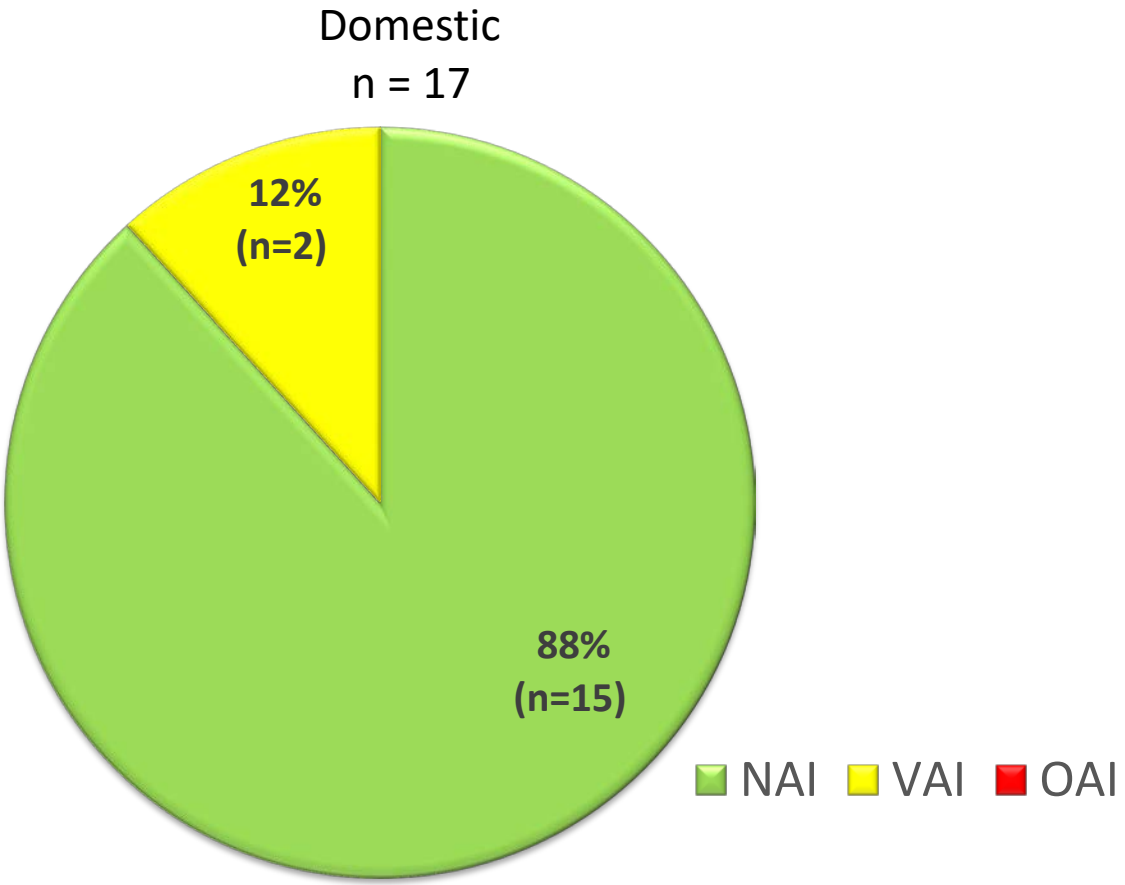


Common Postmarketing Adverse Drug Experience Inspectional Observations

- Failure to develop written procedures for the surveillance, receipt, evaluation, and reporting of post-marketing adverse drug experiences
- Late submission of 15-day Alert reports
- Late submission of annual safety report
- Late submission of quarterly safety reports
- Failure to maintain records; compliant records for marketed drugs and/or PADE reports

Risk Evaluation Mitigation Strategies Inspections Classifications

(FY 2019)



Common Risk Evaluation Mitigation Strategies Inspectional Observations

- Failure to comply with REMS elements to assure safe use (ETASU) B
- Failure to comply with REMS medication guide
- Late submission of 15-day report
- Failure to comply with REMS Implementation System

Reference

- FDA's BIMO Compliance Programs:
  - Clinical Investigator (CP 7348.811)
  - Institutional Review Board (CP 7348.809)
  - Sponsors, Contract Research Organizations, Monitors (CP 7348.810)
  - Sponsor-Investigator (CP 7348.810, CP 7348.811)
  - Good Laboratory Practice (CP 7348.808)
  - Bioequivalence (CP 7348.003, CP 7348.004, CP 7348.007, CP 7348.808)
  - Postmarketing Adverse Drug Experience (CP 7353.001)
  - Risk Evaluation Mitigation Strategies (CP 7353.001c)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