

# Bioresearch Monitoring (BIMO) Fiscal Year 2020 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) 2020.

# COVID-19 Pandemic



Due to the COVID-19 pandemic, FDA paused on-site surveillance inspections in March 2020 to protect the safety of our staff and stakeholders. During this timeframe we only conducted on-site inspections deemed mission-critical by both the product center and ORA.

- To continue supporting our mission, BIMO introduced Remote Regulatory Assessments (RRA), which were voluntary remote evaluations of data and processes conducted via video teleconference. RRAs allowed ORA/BIMO staff to continue to review study data and information and provide an evaluation to center staff to aid in marketing application review. RRAs are evaluations and will not receive an inspection classification.
- The Remote Record Review (RRR) is an alternative to inspection involving a voluntary interaction with a site of interest. Records from the site are evaluated by Center staff, which are followed by a series of remote video and teleconference meetings with the site of interest to discuss questions, concerns and findings. It is different from the RRA.
- RRAs and RRRs are not equivalent to on-site inspection, nor are they replacing inspections.
- Data for RRAs and RRRs are not reflected in the inspection and final classification tables for each program area. Refer to slides 31 and 32 for complete breakdown.

# Metrics Terms

## Organizations and Programs

- BA/BE or BEQ: Bioavailability/Bioequivalence - clinical and analytical
- BIMO: Bioresearch Monitoring
- CI or Clin: Clinical Investigator
- CRO: Contract Research Organization
- 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
- S or S/I: Sponsor or Sponsor-Investigator

## Inspection Classifications

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

## Evaluations

- RRA: Remote Regulatory Assessment
- RRR: Remote Record Review

# BIMO Inspection Classifications by Center – FY 2020\*

| <u>Center</u> | <u>CI</u>  | <u>IRB</u> | <u>S/M/CRO</u> | <u>S/I</u> | <u>GLP</u> | <u>BEQ</u> | <u>PADE</u> | <u>REMS</u> | <u>Total</u> |
|---------------|------------|------------|----------------|------------|------------|------------|-------------|-------------|--------------|
| <b>CBER</b>   | 50         | 5          | 4              | 2          | 5          | 0          | 0           | 0           | <b>66</b>    |
| <b>CDER</b>   | 372        | 47         | 42             | 10         | 12         | 208        | 36          | 6           | <b>733</b>   |
| <b>CDRH</b>   | 106        | 25         | 23             | 2          | 9          | 0          | 0           | 0           | <b>165</b>   |
| <b>CFSAN</b>  | 0          | 0          | 0              | 0          | 2          | 0          | 0           | 0           | <b>2</b>     |
| <b>CTP</b>    | 2          | 0          | 0              | 0          | 0          | 0          | 0           | 0           | <b>2</b>     |
| <b>CVM</b>    | 14         | 0          | 1              | 0          | 5          | 0          | 0           | 0           | <b>20</b>    |
| <b>Total</b>  | <b>544</b> | <b>77</b>  | <b>70</b>      | <b>14</b>  | <b>33</b>  | <b>208</b> | <b>36</b>   | <b>6</b>    | <b>988</b>   |

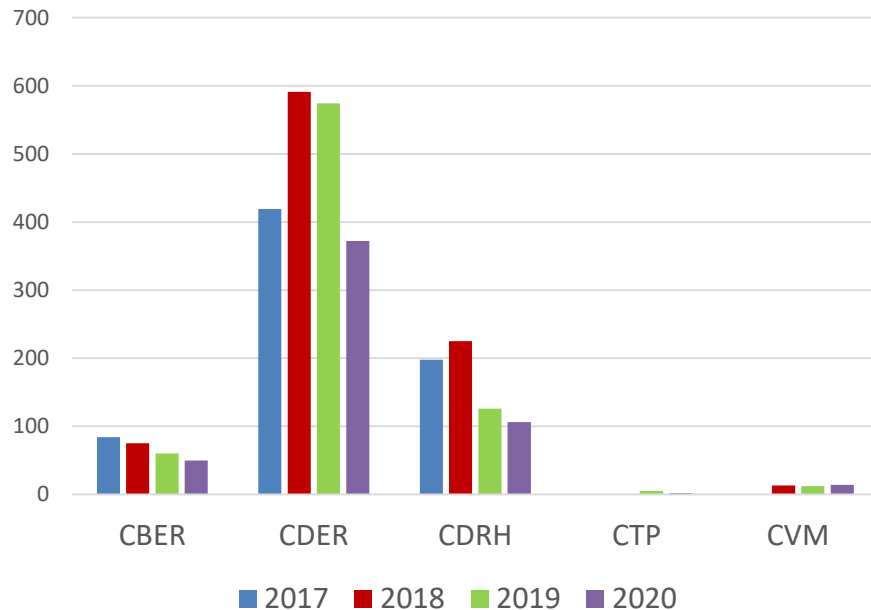
\* Domestic and Foreign

[www.fda.gov](http://www.fda.gov)

# Clinical Investigator Inspections by Center FY 2017- 2020\*



CI Inspections



| Center | 2017 | 2018 | 2019 | 2020* |
|--------|------|------|------|-------|
| CBER   | 84   | 75   | 60   | 50    |
| CDER   | 419  | 591  | 574  | 372   |
| CDRH   | 198  | 225  | 126  | 106   |
| CTP    | 0    | 0    | 5    | 2     |
| CVM    | 0    | 13   | 12   | 14    |

\* Due to the COVID-19 pandemic, RRAs (not reflected in the above table) were conducted. See slide 31 for more details.

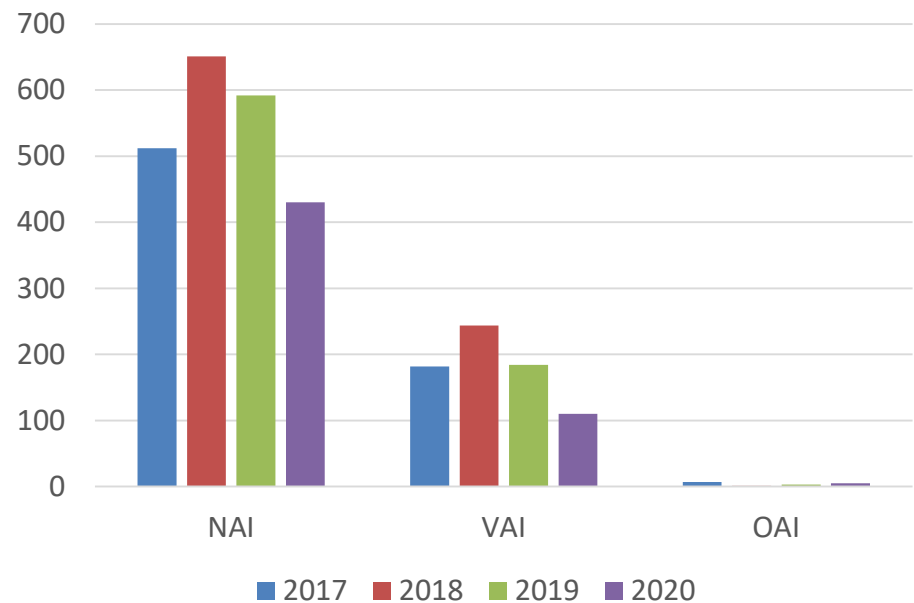
# Common Clinical Investigator Inspectional Observations\*

- Failure to follow the investigational plan; protocol deviations
- Inadequate and/or inaccurate case history records; inadequate study records
- Inadequate accountability and/or control of the investigational product
- Failure to comply with Form FDA 1572 requirements
- 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.

\*Most common observations collected from issued FDA Form 483s

# Final Classifications for Clinical Investigator Inspections FY 2017-2020

Classifications of Domestic and Foreign Inspections

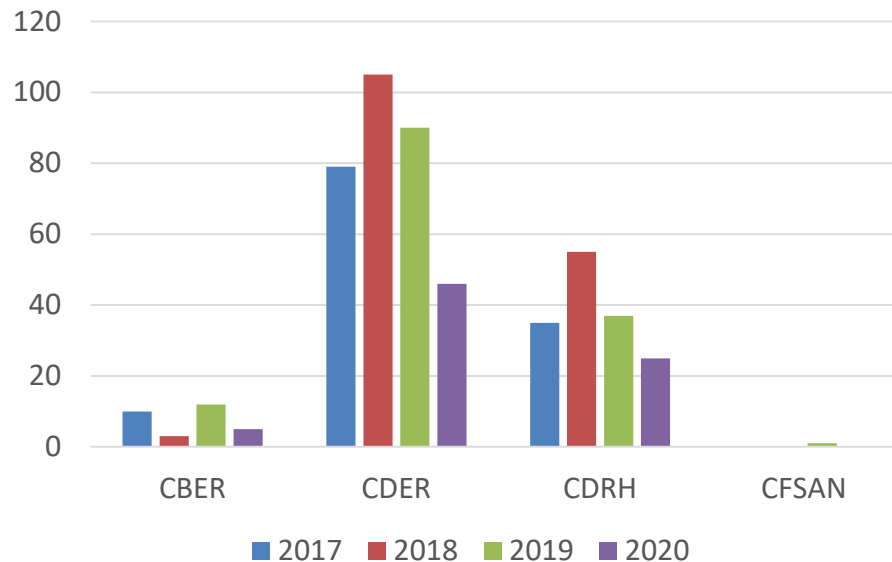


|     | 2017 | 2018 | 2019 | 2020 |
|-----|------|------|------|------|
| NAI | 512  | 651  | 592  | 430  |
| VAI | 182  | 244  | 184  | 110  |
| OAI | 7    | 1    | 3    | 5    |

# Institutional Review Board and Radioactive Drug Research Center Inspections by Center FY 2017- 2020\*



IRB Inspections



| Center | 2017 | 2018 | 2019 | 2020* |
|--------|------|------|------|-------|
| CBER   | 10   | 3    | 12   | 5     |
| CDER   | 79   | 105  | 90   | 47*   |
| CDRH   | 35   | 55   | 37   | 25    |
| CFSAN  | 0    | 0    | 1    | 0     |

\* Includes 4 RDRC Inspections

# Common Institutional Review Board Inspectional Observations\*



- Failure to conduct initial and/or continuing review of research
- 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 follow FDA regulations regarding expedited review procedures
- 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

\*Most common observations collected from issued FDA Form 483s

# Radioactive Drug Research Committee Inspectional Observations\*



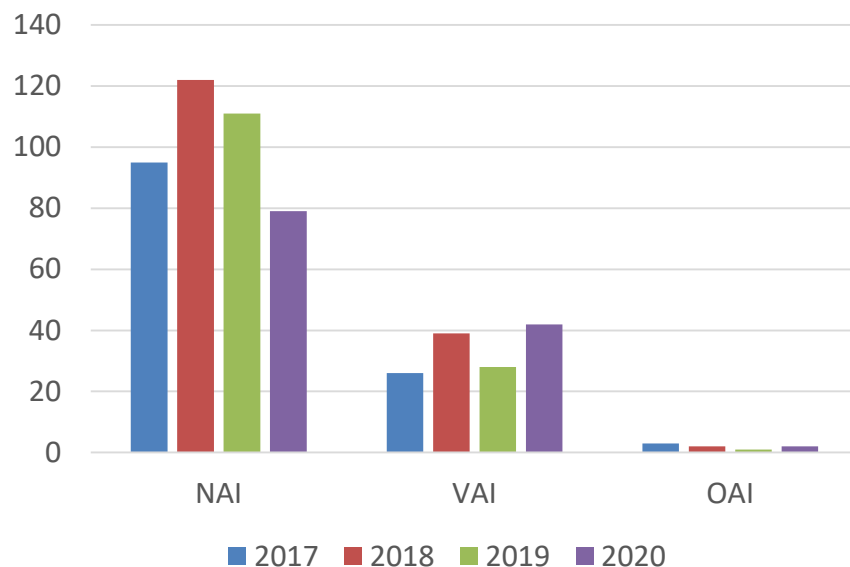
- Failure to comply with the requirements of 21 CFR 361.1(c)(2);
  - Quorum and appropriate representation at meeting
  - RDRC Chair signature on application, meeting minutes and RDRC reports
  - Minutes of RDRC meeting did not include the numerical results of votes on protocols involving use in human subjects
- Failure to comply with the requirements of 21 CFR 361.1(f);
  - Labelling of radioactive drug product

\*Most common observations collected from issued FDA Form 483s

# Final Classifications for Institutional Review Board and Radioactive Drug Research Committee Inspections FY 2017-2020



Classifications of Domestic and Foreign Inspections



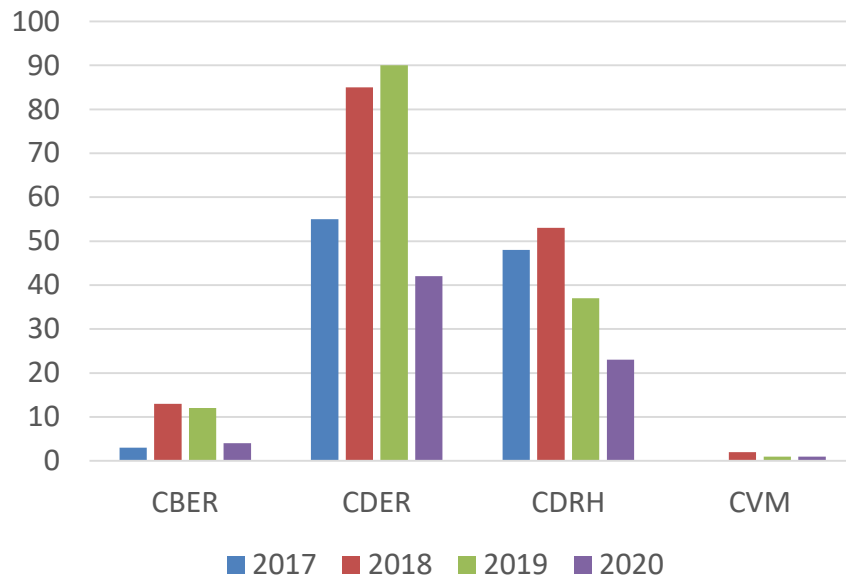
|     | 2017 | 2018 | 2019 | 2020 |
|-----|------|------|------|------|
| NAI | 95   | 122  | 111  | 45   |
| VAI | 26   | 39   | 28   | 31*  |
| OAI | 3    | 2    | 1    | 1    |

\* Includes 4 RDRC Inspections classified as VAI for FY20

# Sponsor/Monitor/Contract Research Organization Inspections by Center FY 2017-2020\*



S/M/CRO Inspections



| Center | 2017 | 2018 | 2019 | 2020* |
|--------|------|------|------|-------|
| CBER   | 3    | 13   | 12   | 4     |
| CDER   | 55   | 85   | 90   | 42    |
| CDRH   | 48   | 53   | 37   | 23    |
| CVM    | 0    | 2    | 1    | 1     |

- Due to the COVID-19 pandemic, RRAs (not reflected in the above table) were conducted. See slide 31 for more details.

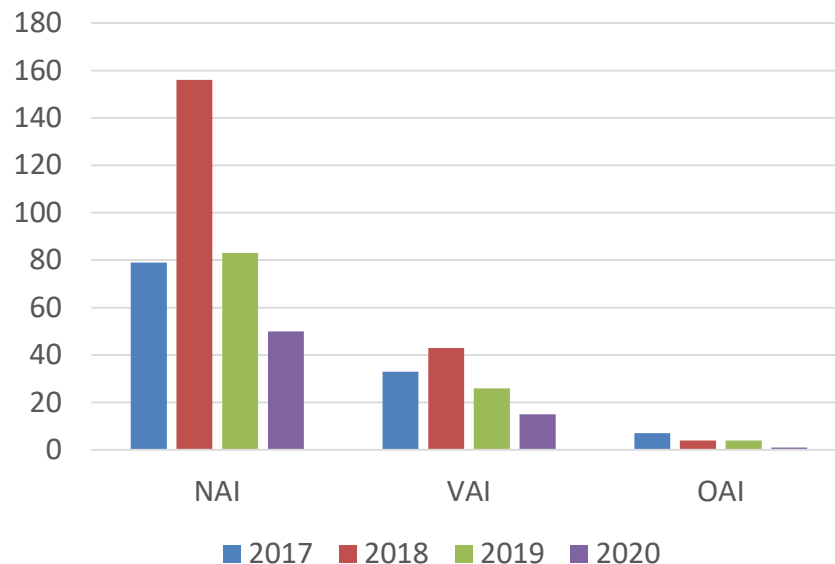
# Common Sponsor/Monitor/Contract Research Organization Inspectional Observations\*



- 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; Investigator Statement (Form FDA 1572); Financial disclosures.
- Failure to submit and Investigational New Drug (IND) application

# Final Classifications for Sponsor/Monitor/Contract Research Organization Inspections FY 2017-2020

Classifications of Domestic and  
Foreign Inspections

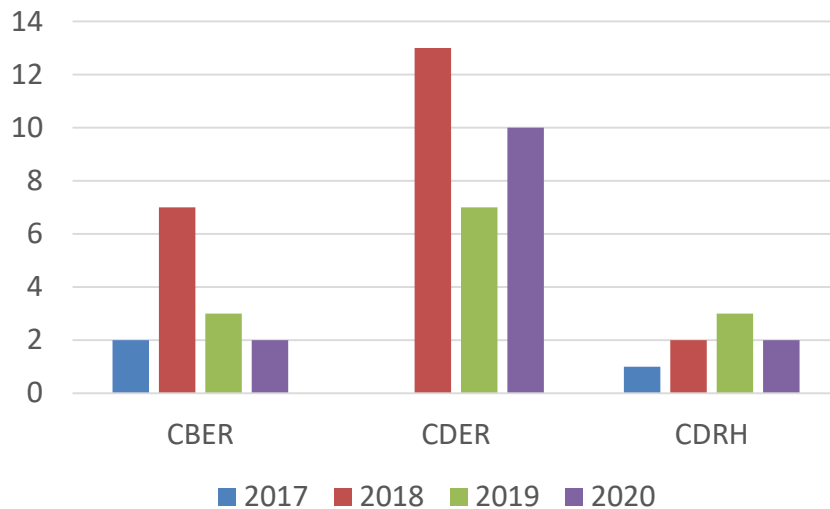


|     | 2017 | 2018 | 2019 | 2020 |
|-----|------|------|------|------|
| NAI | 79   | 156  | 83   | 53   |
| VAI | 33   | 43   | 26   | 16   |
| OAI | 7    | 4    | 4    | 1    |

# Sponsor-Investigator Inspections by Center FY 2017-2020



SI Inspections



| Center | 2017 | 2018 | 2019 | 2020 |
|--------|------|------|------|------|
| CBER   | 2    | 7    | 3    | 2    |
| CDER   | 0    | 13   | 7    | 10   |
| CDRH   | 1    | 2    | 3    | 2    |

# Common Sponsor-Investigator Inspectional Observations\*

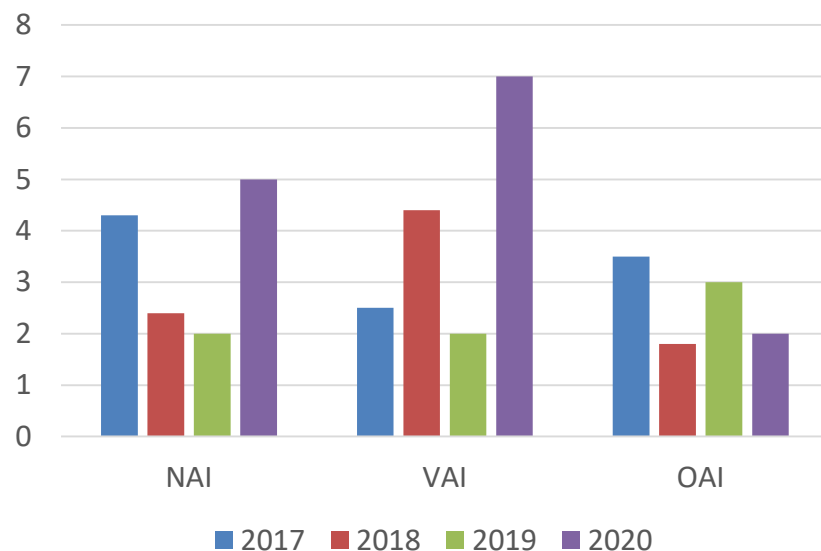
- Failure to select qualified investigators and/or monitors, ensure proper monitoring of the study and ensure the study is conducted in accordance with the protocol and/or investigational plan. (General responsibilities of sponsors)
- Failure to submit an Investigational New Drug (IND) application
- Failure to maintain and/or retain adequate records in accordance with 21 CFR 312.57; accountability for the investigational product; Investigator Statement (FDA 1572); Financial disclosures.
- Inadequate subject protection; informed consent issues
- Failure to notify FDA of termination of investigator

\*Most common observations collected from issued FDA Form 483s

# Final classifications for Sponsor-Investigator Inspections FY 2017-2020

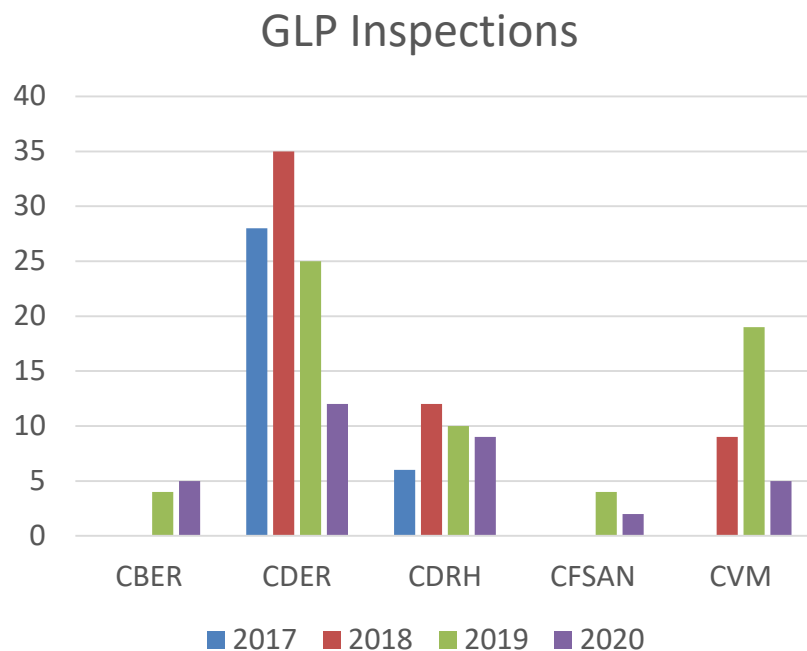


Classifications of Domestic and  
Foreign Inspections



|     | 2017 | 2018 | 2019 | 2020 |
|-----|------|------|------|------|
| NAI | 1    | 6    | 7    | 5    |
| VAI | 1    | 5    | 6    | 7    |
| OAI | 1    | 0    | 0    | 2    |

# Good Laboratory Practice Inspections by Center FY 2017-2020



| Center | 2017 | 2018 | 2019 | 2020 |
|--------|------|------|------|------|
| CBER   | 0    | 0    | 4    | 5    |
| CDER   | 28   | 35   | 25   | 12   |
| CDRH   | 6    | 12   | 10   | 9    |
| CFSAN  | 0    | 0    | 4    | 2    |
| CVM    | 0    | 9    | 19   | 5    |



# Common Good Laboratory Practice Inspectional Observations\*

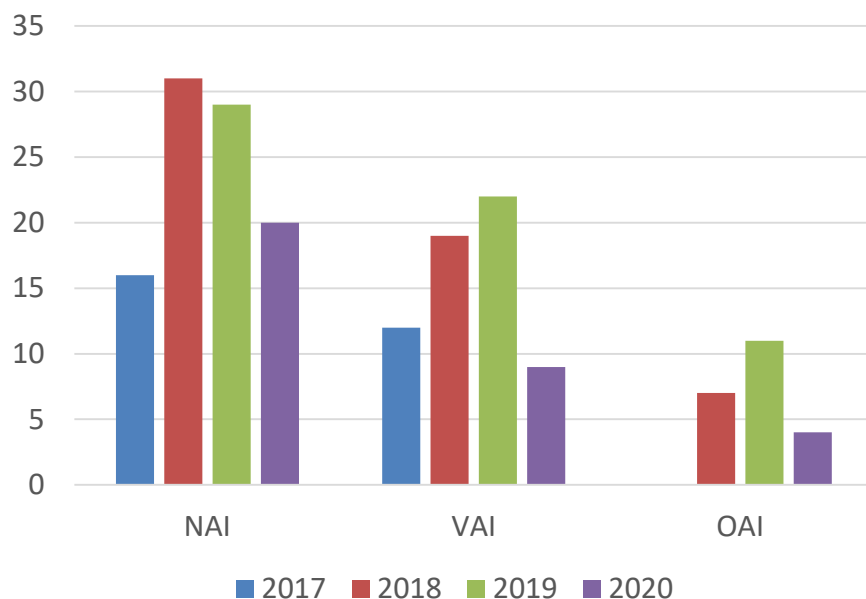
- Final report; circumstances affecting data quality and integrity
- Study Director requirements; failure to transfer data to archives, document unforeseen circumstances, assure data is accurately recorded and verified
- Conduct; not all studies were conducted in accordance with the protocol
- Missing standard operating procedures (SOPs)
- Equipment; appropriate design and adequate capacity; inspection, cleaning and maintenance

\*Most common observations collected from issued FDA Form 483s

# Final classifications for Good Laboratory Practice Inspections FY 2017-2020



Classifications of Domestic and Foreign Inspections

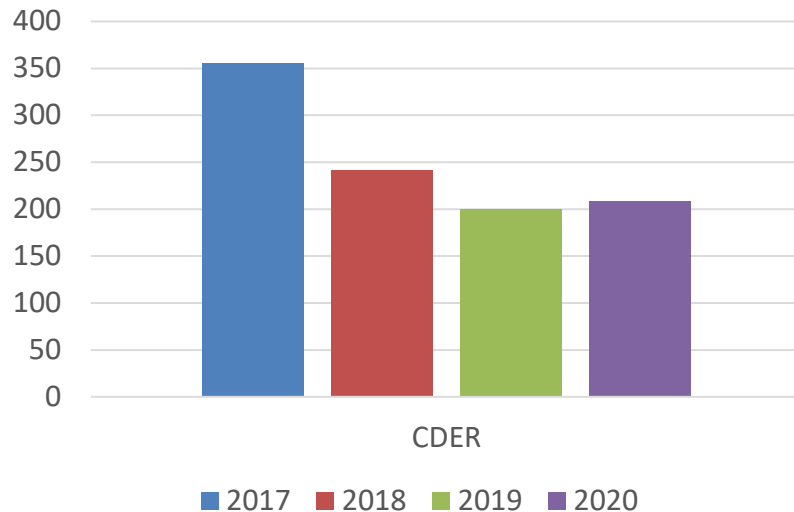


|     | 2017 | 2018 | 2019 | 2020 |
|-----|------|------|------|------|
| NAI | 16   | 31   | 29   | 20   |
| VAI | 12   | 19   | 22   | 9    |
| OAI | 0    | 7    | 11   | 4    |

# Bioavailability/Bioequivalence Inspections FY 2017-2020\*



BEQ Inspections



| Center | 2017 | 2018 | 2019 | 2020* |
|--------|------|------|------|-------|
| CDER   | 355  | 241  | 200  | 208   |

- CDER Specific Program

\* Due to the COVID-19 pandemic, RRAs and RRRs (not reflected in the above table) were conducted. See slide 31 and 32 for more details.

# Common Bioavailability/Bioequivalence Inspectional Observations\*



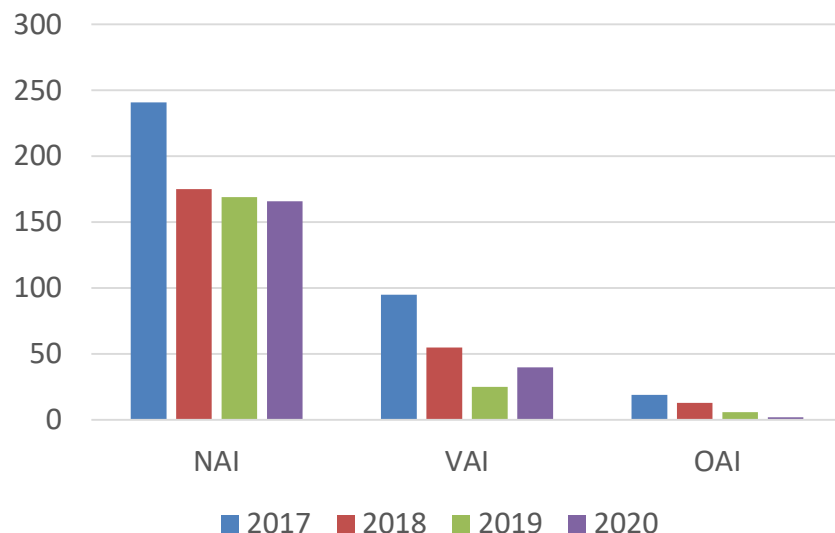
- **Analytical**
  - Validation
  - Reserve Samples
- **Clinical**
  - Blinding Codes
  - Recordkeeping

\*Most common observations collected from issued FDA Form 483s

# Final Classifications for Bioavailability/Bioequivalence Inspections FY 2017-2020



Classifications of Domestic and Foreign Inspections



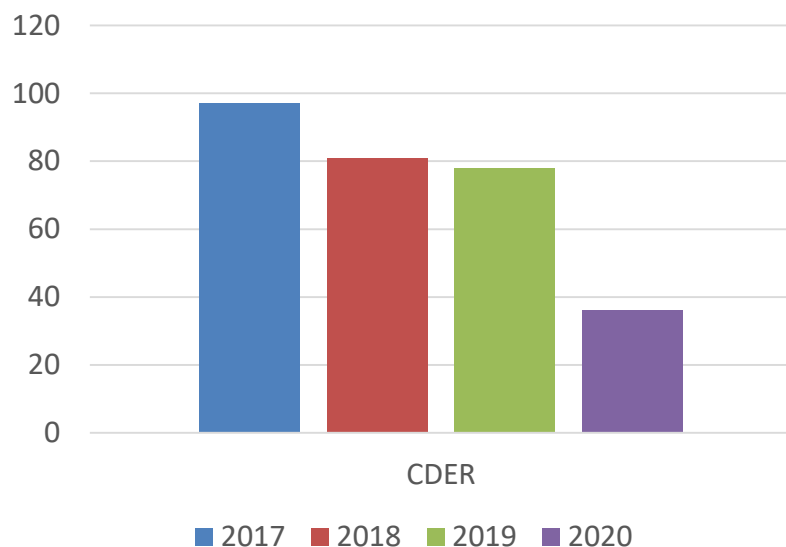
|     | 2017 | 2018 | 2019 | 2020 |
|-----|------|------|------|------|
| NAI | 241  | 175  | 169  | 166  |
| VAI | 95   | 55   | 25   | 40   |
| OAI | 19   | 13   | 6    | 2    |

- CDER Specific Program

# Postmarketing Adverse Drug Experience Inspections FY 2017-2020\*



PADE Inspections



| Center | 2017 | 2018 | 2019 | 2020* |
|--------|------|------|------|-------|
| CDER   | 97   | 81   | 78   | 36    |

- CDER Specific Program

\* Due to the COVID-19 pandemic, RRAs (not reflected in the above table) were conducted. See slide 31 for more details.

# Common Postmarketing Adverse Drug Experience Inspectional Observations\*

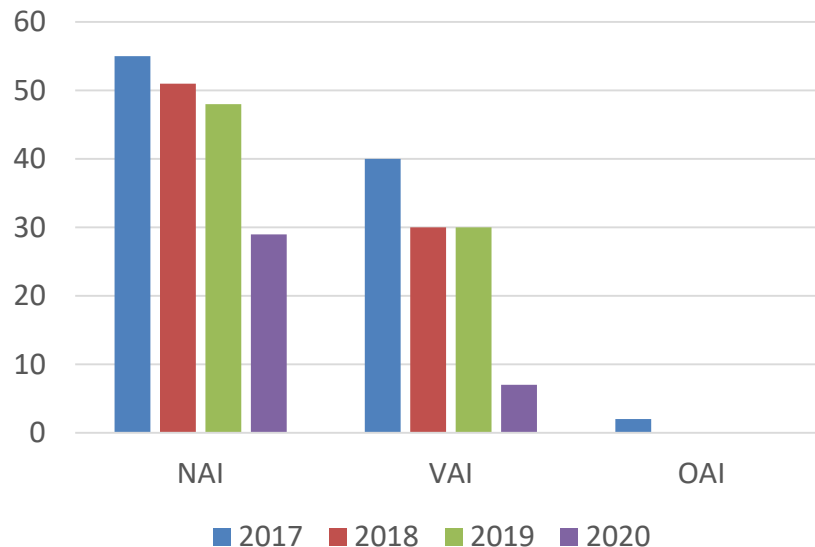
- Failure to develop written procedures for the surveillance, receipt, evaluation, and reporting of post-marketing adverse drug experiences
- Late submission of 15-day Alert reports
- Late submission of annual safety report
- Failure to maintain or submit records; compliant records for marketed drugs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

\*Most common observations collected from issued FDA Form 483s

# Final Classifications for Postmarketing Adverse Drug Experience Inspections FY 2017-2020



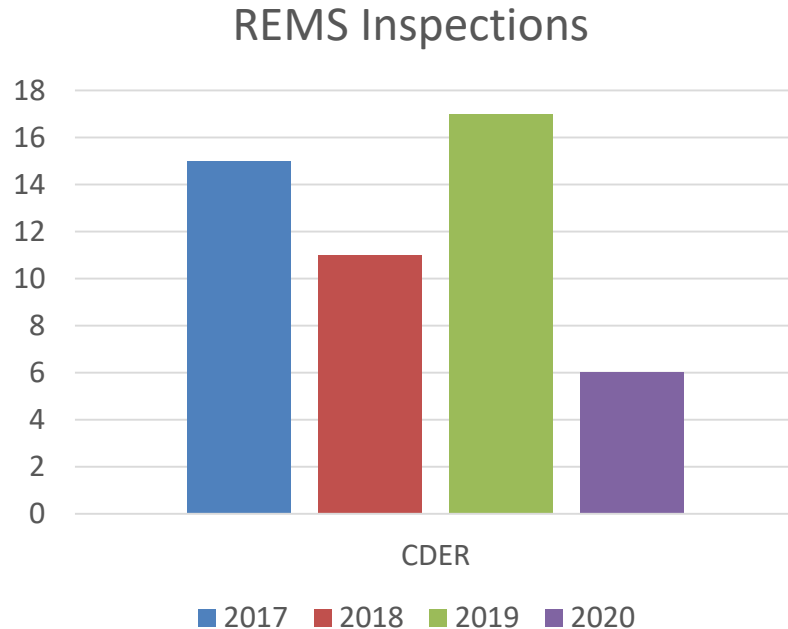
Classifications of Domestic and Foreign Inspections



|     | 2017 | 2018 | 2019 | 2020 |
|-----|------|------|------|------|
| NAI | 55   | 51   | 48   | 29   |
| VAI | 40   | 30   | 30   | 7    |
| OAI | 2    | 0    | 0    | 0    |

- CDER Specific Program

# Risk Evaluation and Mitigation Strategies Inspections FY 2017-2020\*



| Center | 2017 | 2018 | 2019 | 2020* |
|--------|------|------|------|-------|
| CDER   | 15   | 11   | 17   | 6     |

- CDER Specific Program

\* Due to the COVID-19 pandemic, RRAs (not reflected in the above table) were conducted. See slide 31 for more details.

# Common Risk Evaluation and Mitigation Strategies Inspectional Observations\*

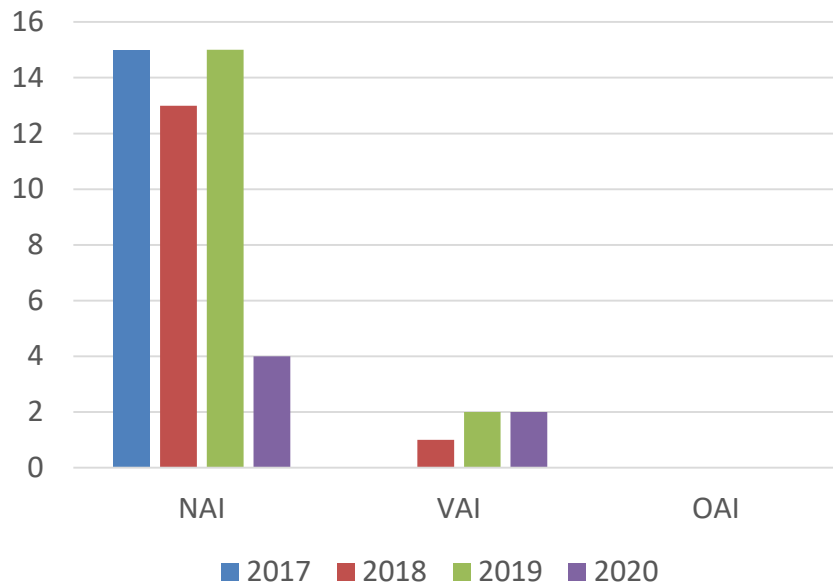
- Failure to comply with the REMS Communication Plan
- Failure to comply with REMS Elements to Assure Safe Use
  - Element B- Certified Pharmacies
- Failure to comply with REMS Implementation System
  - Audits
  - Website
  - Database

\*Most common observations collected from issued FDA Form 483s

# Final classifications for Risk Evaluation Mitigation Strategies Inspections FY 2017-2020



Classifications of Domestic and  
Foreign Inspections



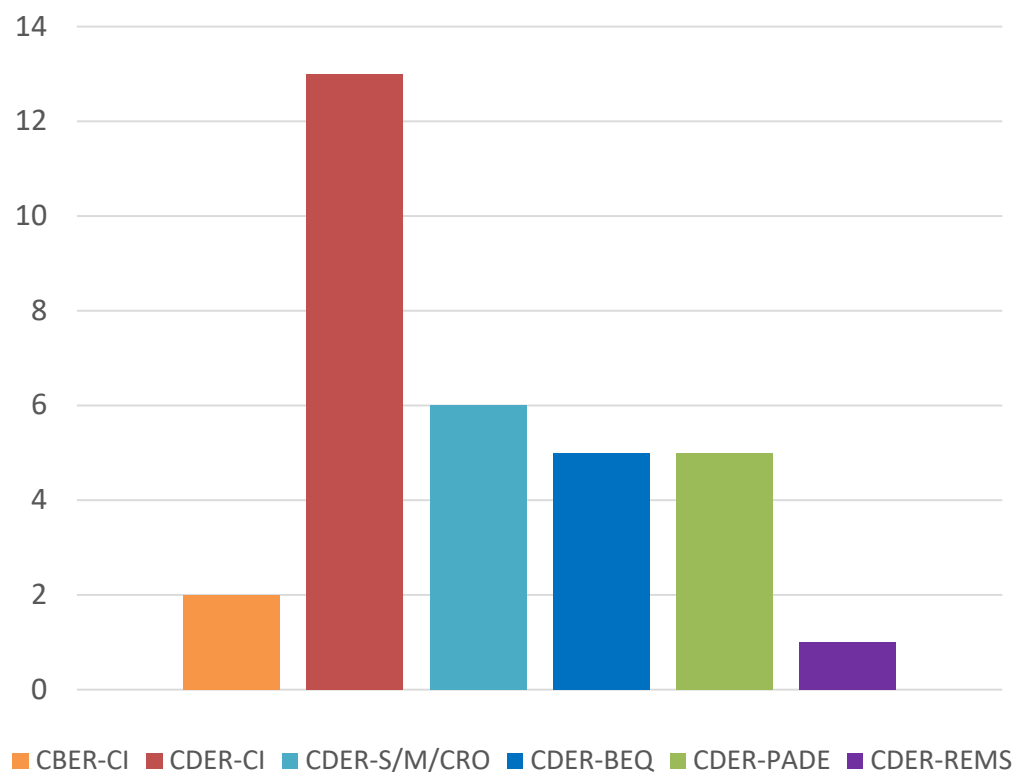
|     | 2017 | 2018 | 2019 | 2020 |
|-----|------|------|------|------|
| NAI | 15   | 13   | 15   | 4    |
| VAI | 0    | 1    | 2    | 2    |
| OAI | 0    | 0    | 0    | 0    |

- CDER Specific Program

# Remote Regulatory Assessments Completed during FY20 COVID-19 Pandemic

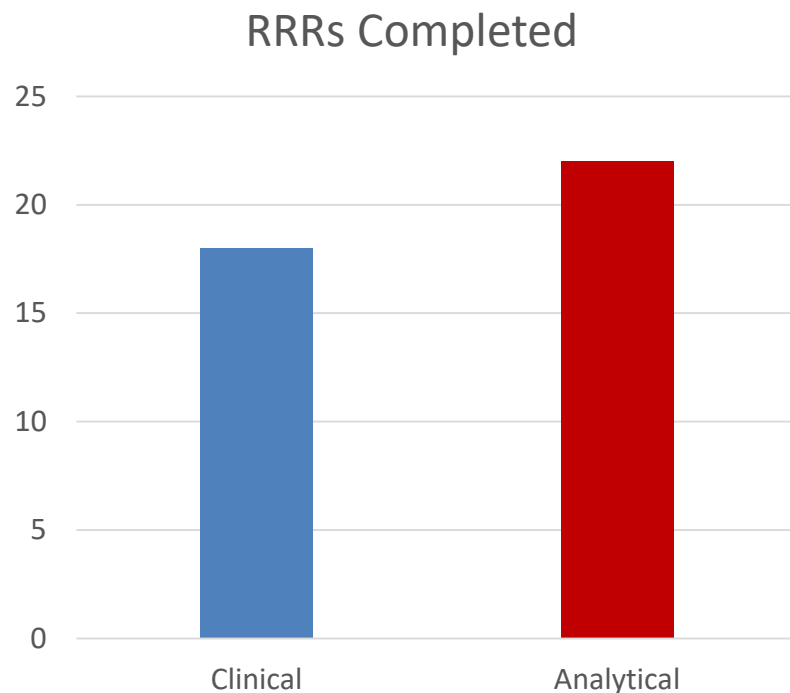


Completed RRAs



| Center | Program area                                   | 2020 |
|--------|------------------------------------------------|------|
| CBER   | Clinical Investigator                          | 2    |
| CDER   | Clinical Investigator                          | 13   |
| CDER   | Sponsor/Monitor/Contract Research Organization | 6    |
| CDER   | Bioavailability/Bioequivalence                 | 5    |
| CDER   | Postmarketing Adverse Drug Experience          | 5    |
| CDER   | Risk Evaluation Mitigation Strategies          | 1    |

# Bioavailability/Bioequivalence Remote Record Reviews Completed during FY20 COVID-19 Pandemic



| Center | Program area            | 2020 |
|--------|-------------------------|------|
| CDER   | BA/BE – Clinical RRRs   | 18   |
| CDER   | BA/BE – Analytical RRRs | 22   |

- CDER Specific Program

# Reference

- FDA's BIMO Compliance Programs:
  - Clinical Investigator ([CP 7348.811](#))
  - Institutional Review Board ([CP 7348.809](#))
  - Sponsor, 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](#))

