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

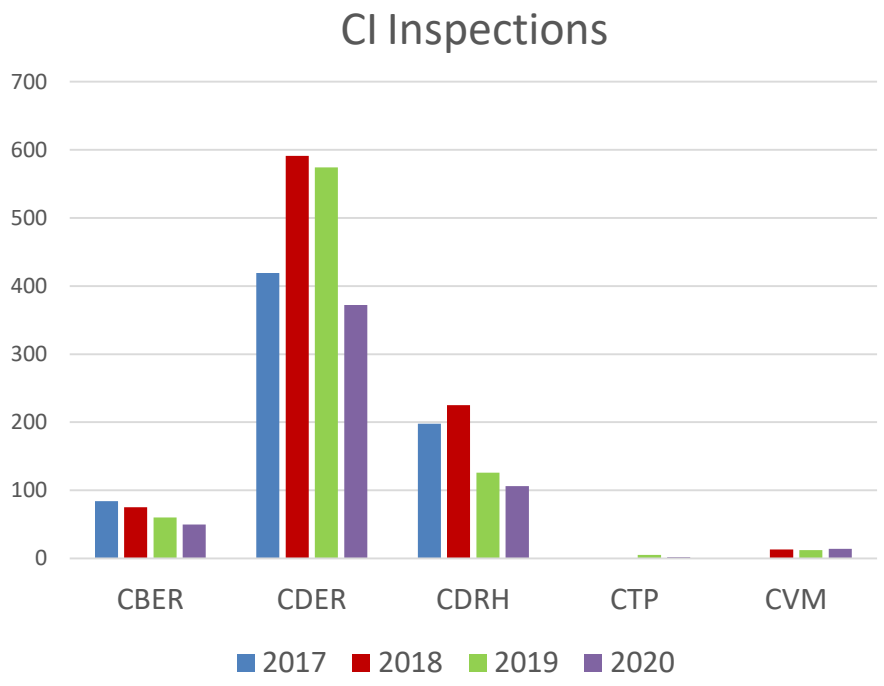
- RRA: Remote Regulatory Assessment
- RRR: Remote Record Review

BIMO Inspection Classifications by Center – FY 2020*

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

* Domestic and Foreign

Clinical Investigator Inspections by Center FY 2017- 2020*



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

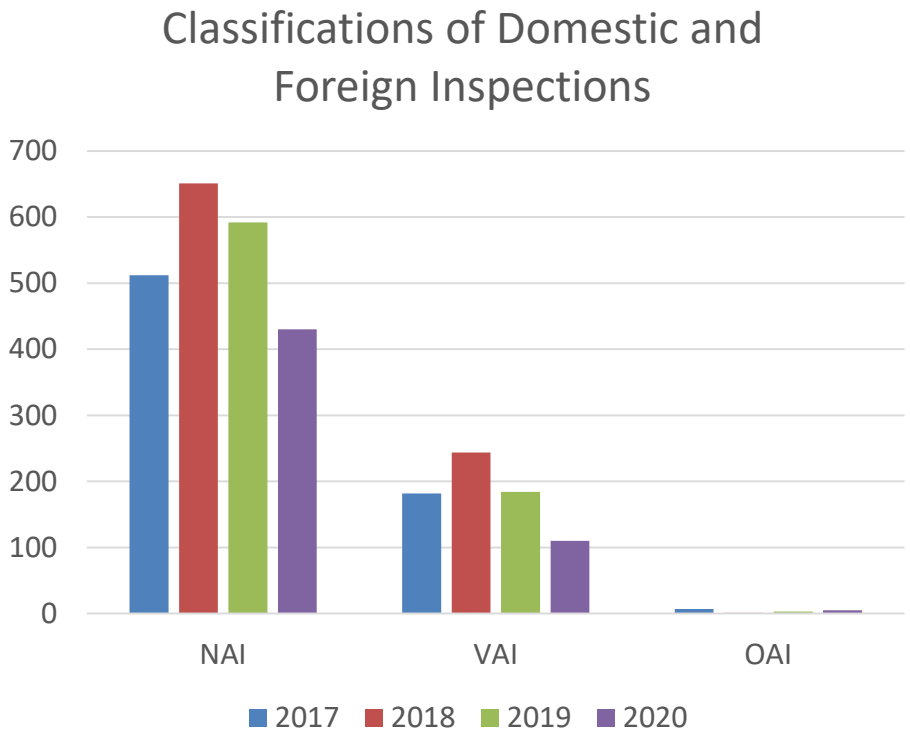
* Due to the COVID-19 pandemic, RRAs (not reflected in the above table) were conducted. See slide 31 for more details.

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.

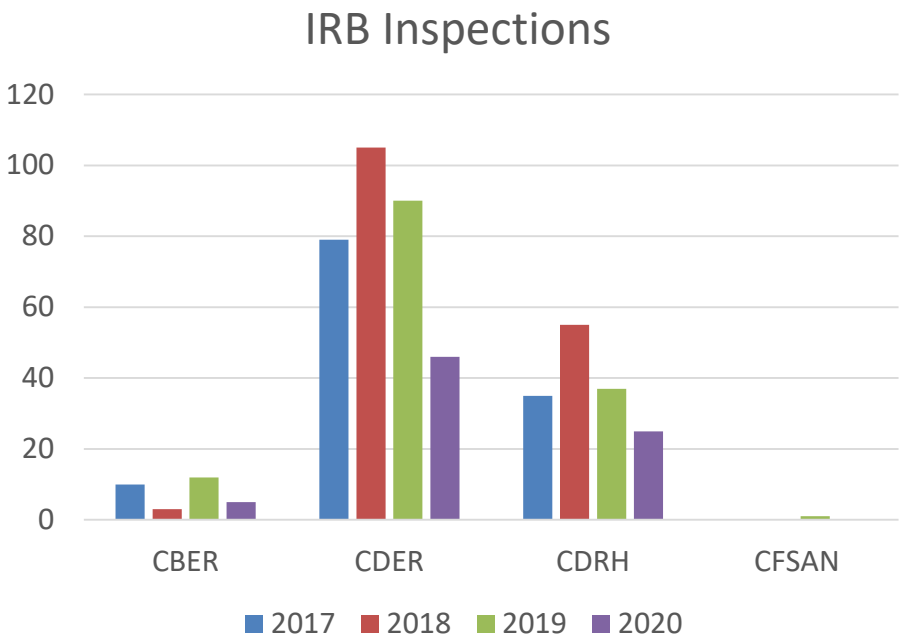
*Most common observations collected from issued FDA Form 483s

Final Classifications for Clinical Investigator Inspections FY 2017-2020



	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*



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

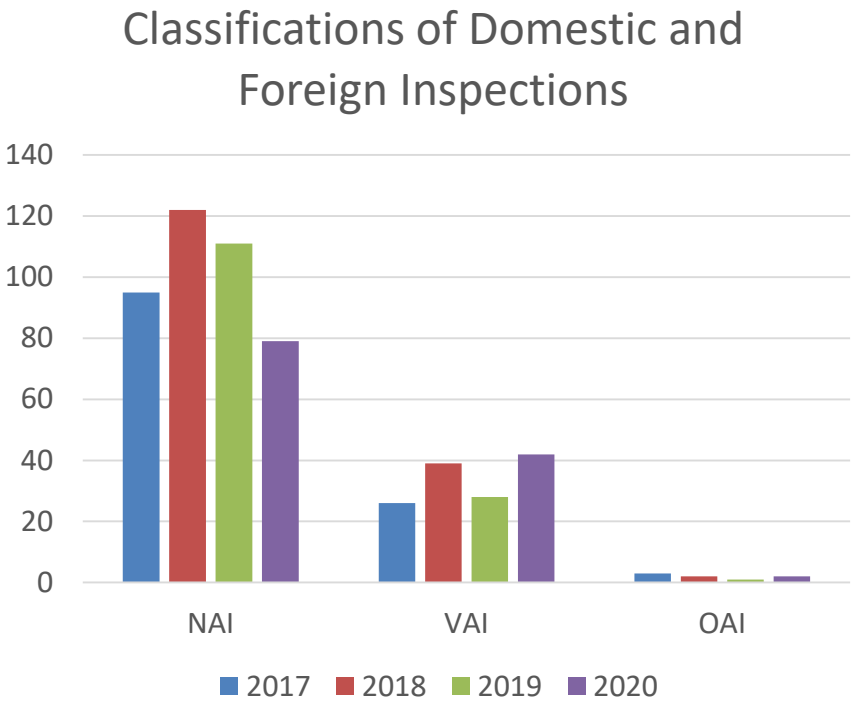
*Most common observations collected from issued FDA Form 483s

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

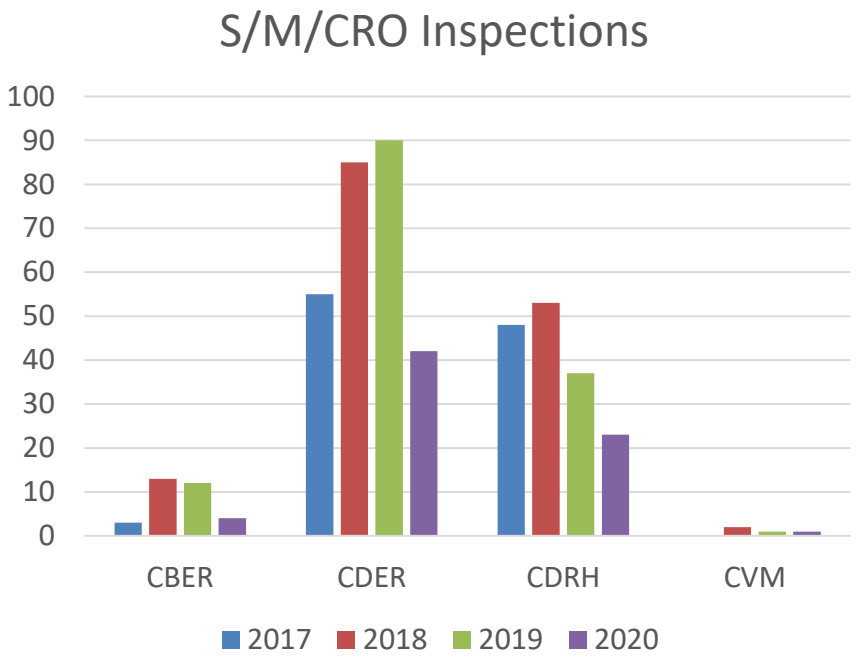
Final Classifications for Institutional Review Board and Radioactive Drug Research Committee Inspections FY 2017-2020



	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*



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

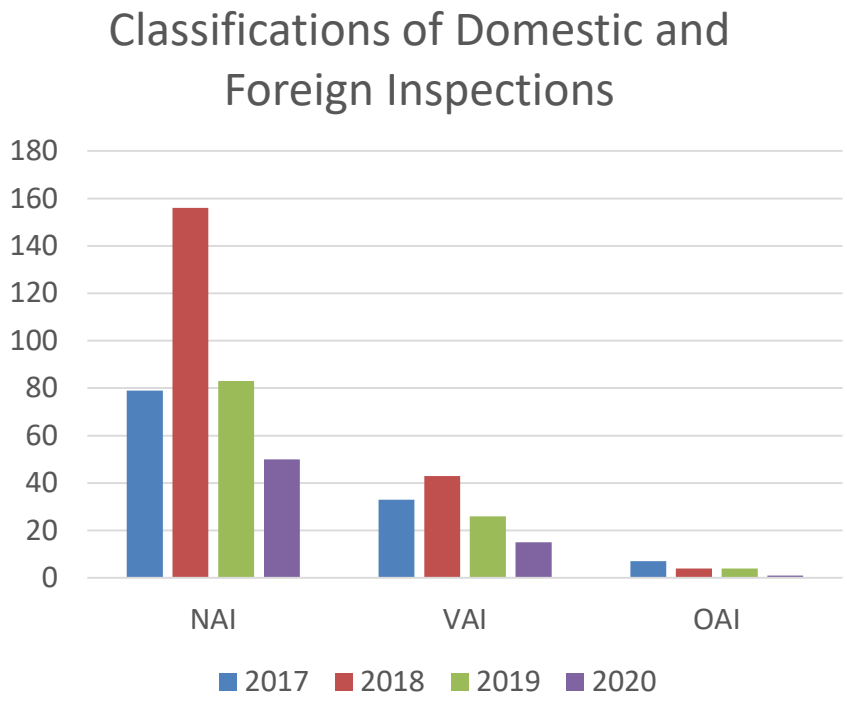
- Due to the COVID-19 pandemic, RRAs (not reflected in the above table) were conducted. See slide 31 for more details.

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

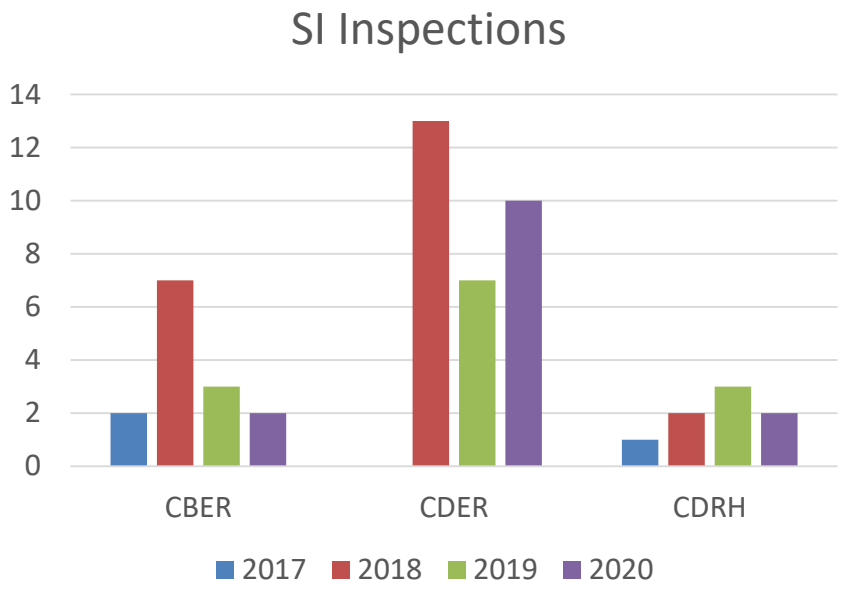
*Most common observations collected from issued FDA Form 483s

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



	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



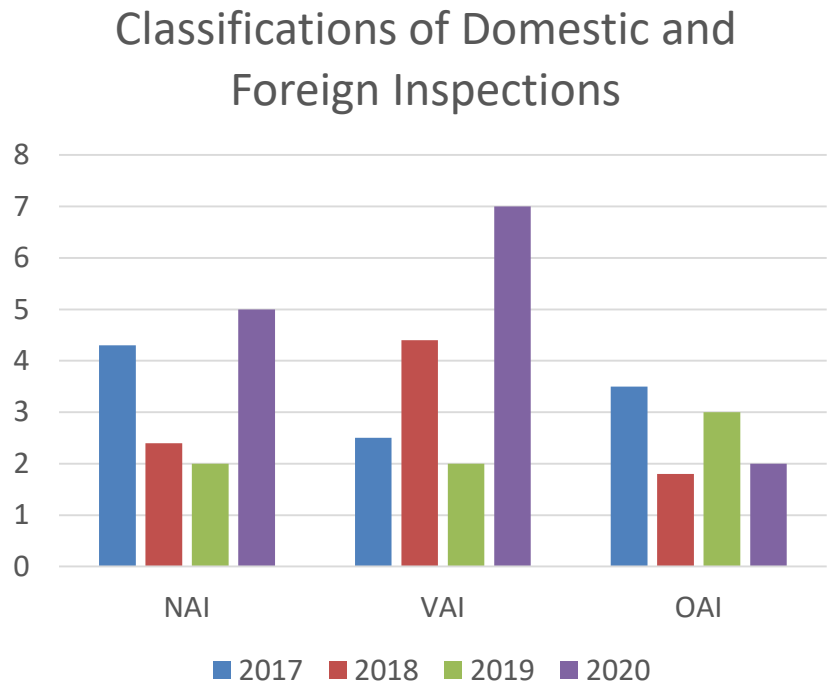
Center	2017	2018	2019	2020
CBER	2	7	3	2
CDER	0	13	7	10
CDRH	1	2	3	2

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

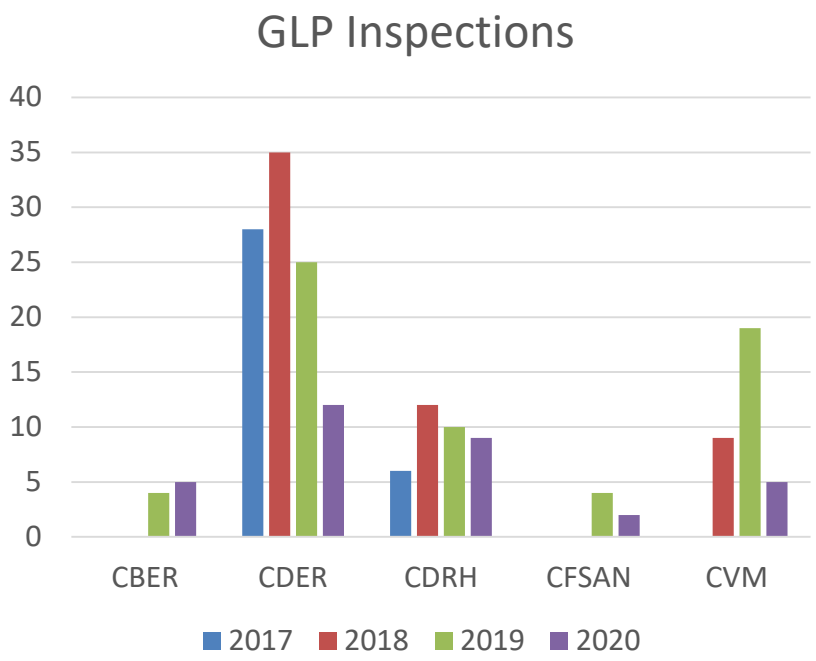
*Most common observations collected from issued FDA Form 483s

Final classifications for Sponsor-Investigator Inspections FY 2017-2020



	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



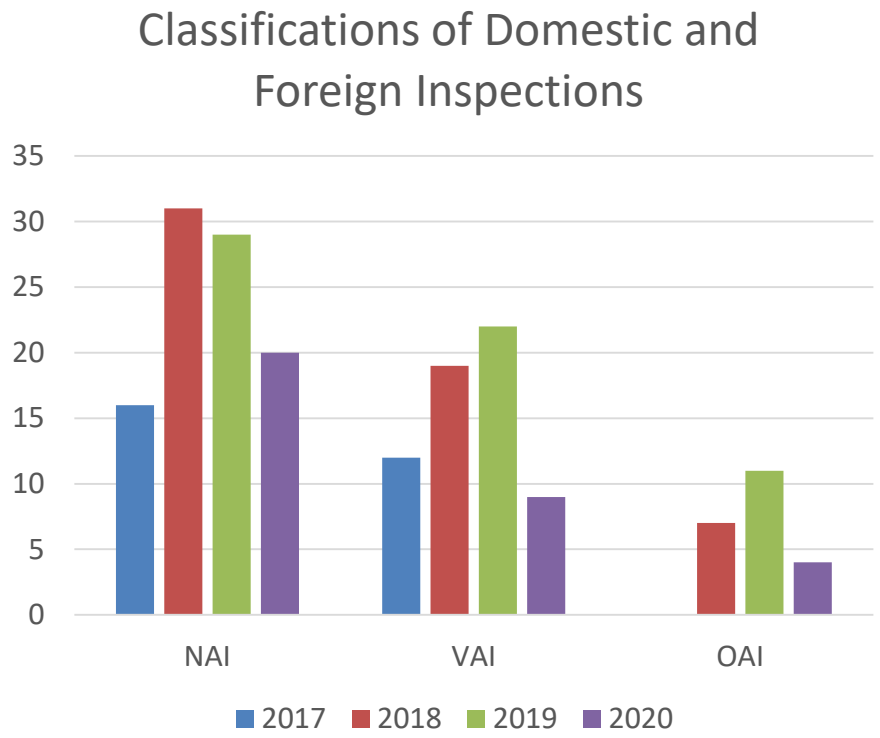
Center	2017	2018	2019	2020
CBER	0	0	4	5
CDER	28	35	25	12
CDRH	6	12	10	9
CFSAN	0	0	4	2
CVM	0	9	19	5

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

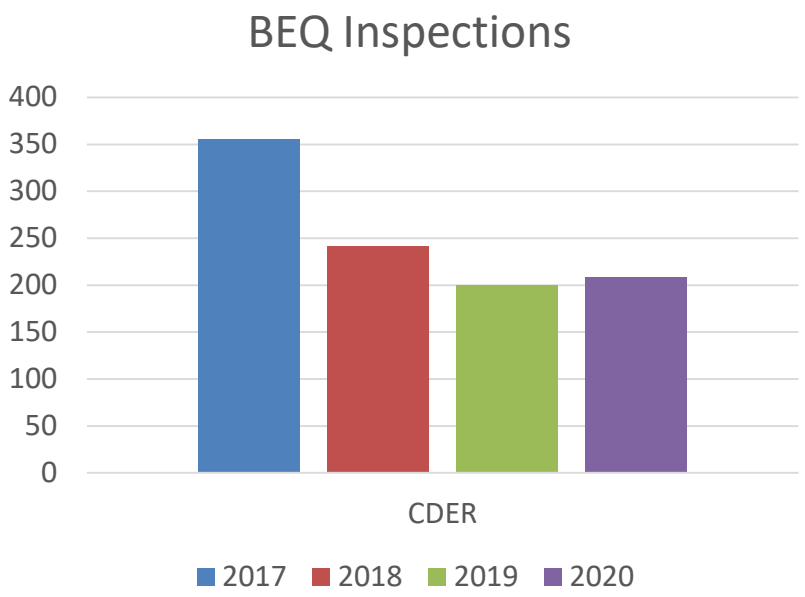
*Most common observations collected from issued FDA Form 483s

Final classifications for Good Laboratory Practice Inspections FY 2017-2020



	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*



Center	2017	2018	2019	2020*
CDER	355	241	200	208

- CDER Specific Program

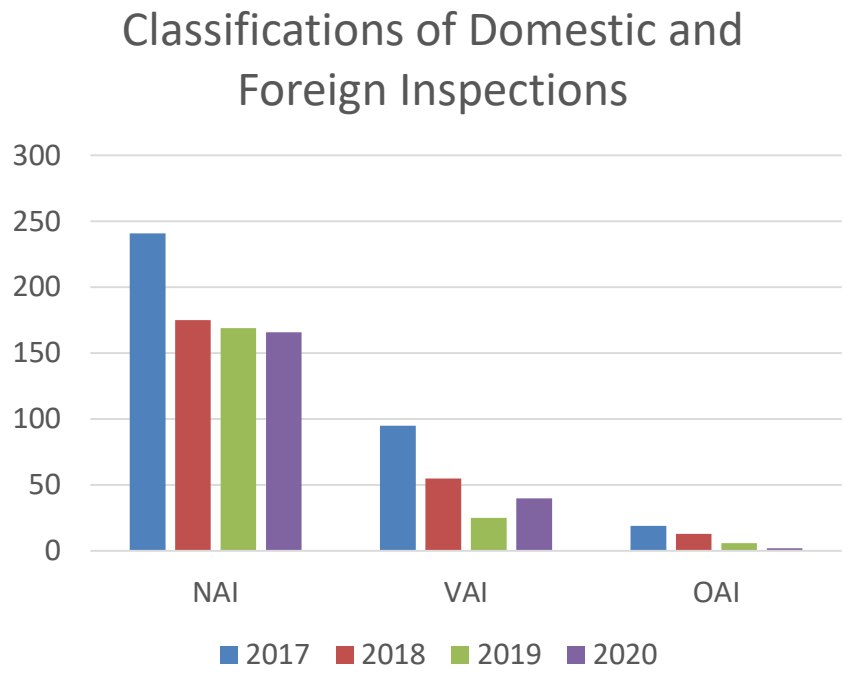
* Due to the COVID-19 pandemic, RRAs and RRRs (not reflected in the above table) were conducted. See slide 31 and 32 for more details.

Common Bioavailability/Bioequivalence Inspectional Observations*

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

*Most common observations collected from issued FDA Form 483s

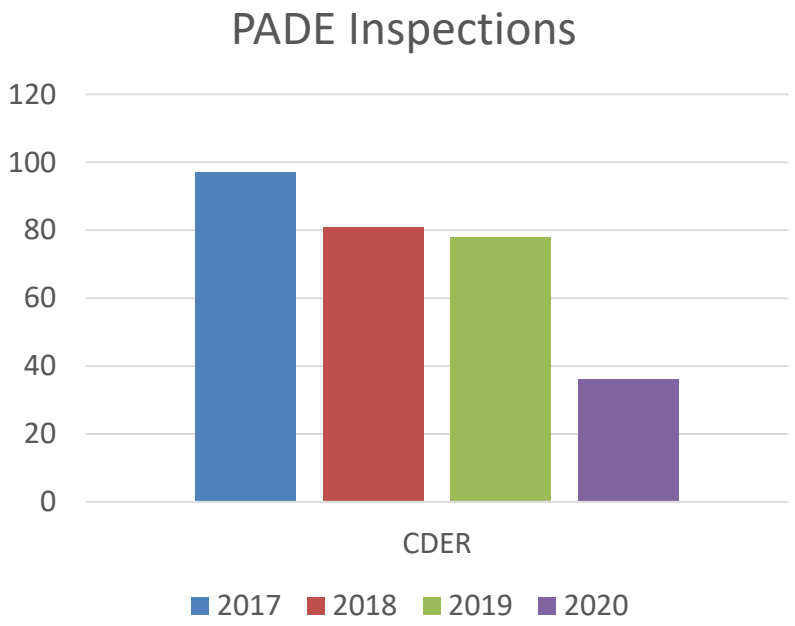
Final Classifications for Bioavailability/Bioequivalence Inspections FY 2017-2020



	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*



Center	2017	2018	2019	2020*
CDER	97	81	78	36

- CDER Specific Program

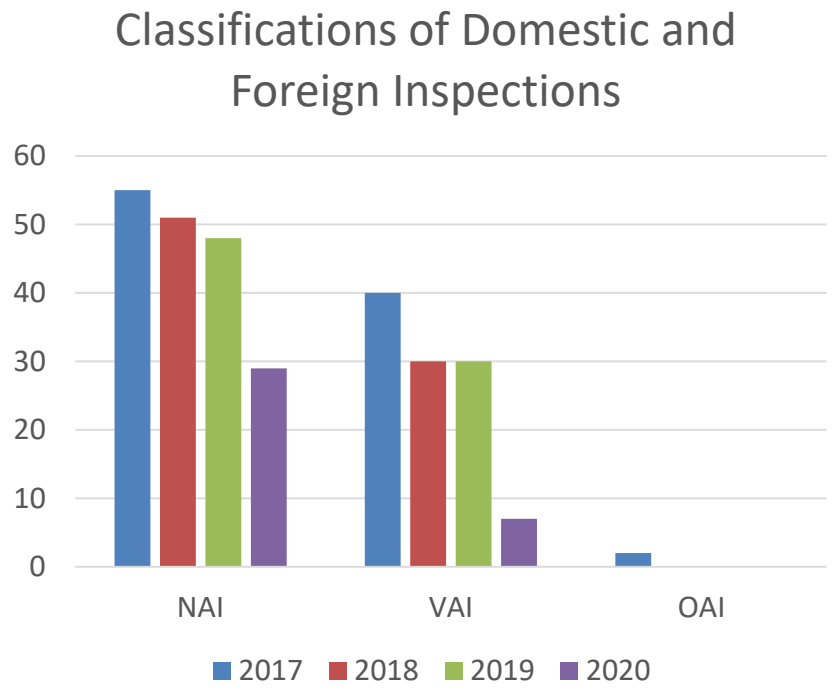
* Due to the COVID-19 pandemic, RRAs (not reflected in the above table) were conducted. See slide 31 for more details.

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

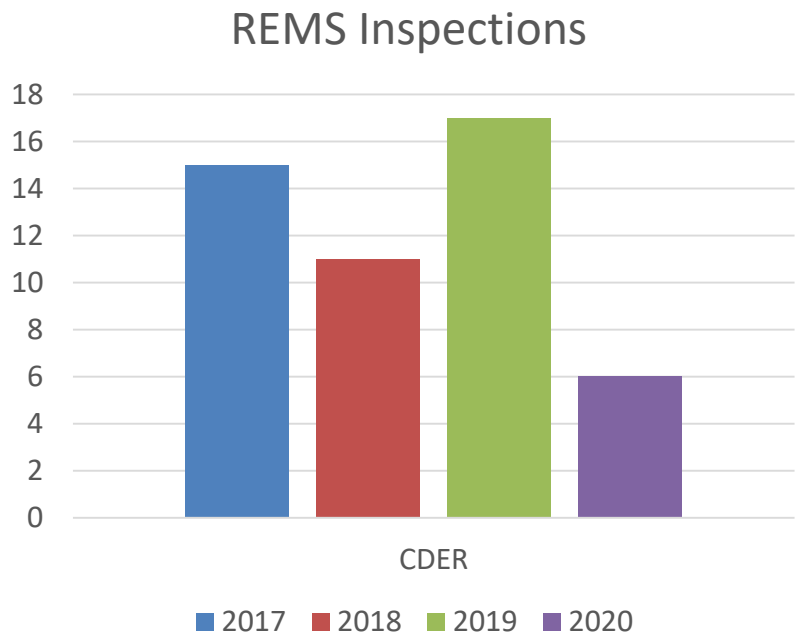
Final Classifications for Postmarketing Adverse Drug Experience Inspections FY 2017-2020



	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

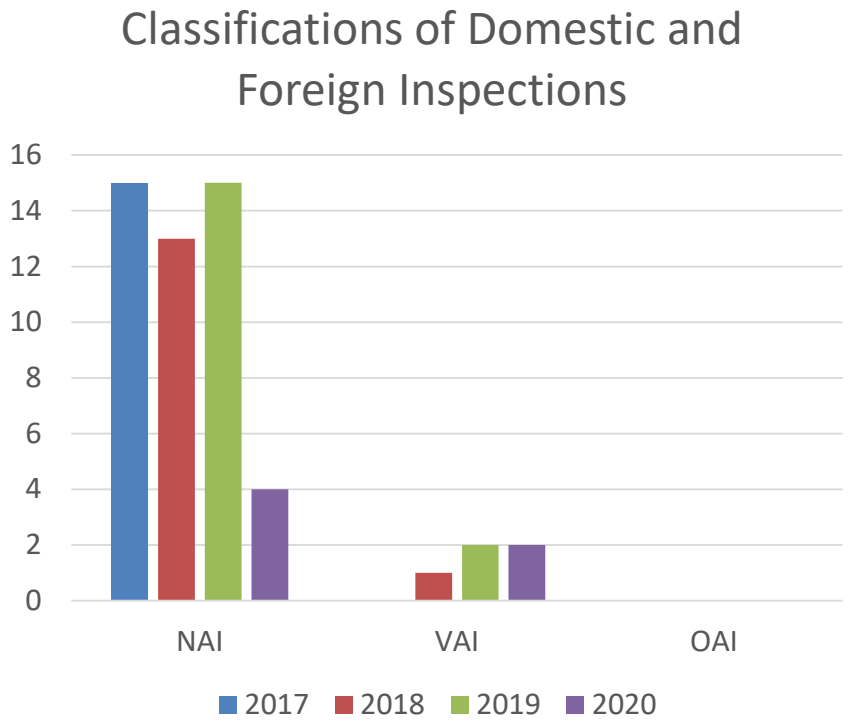
* Due to the COVID-19 pandemic, RRAs (not reflected in the above table) were conducted. See slide 31 for more details.

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

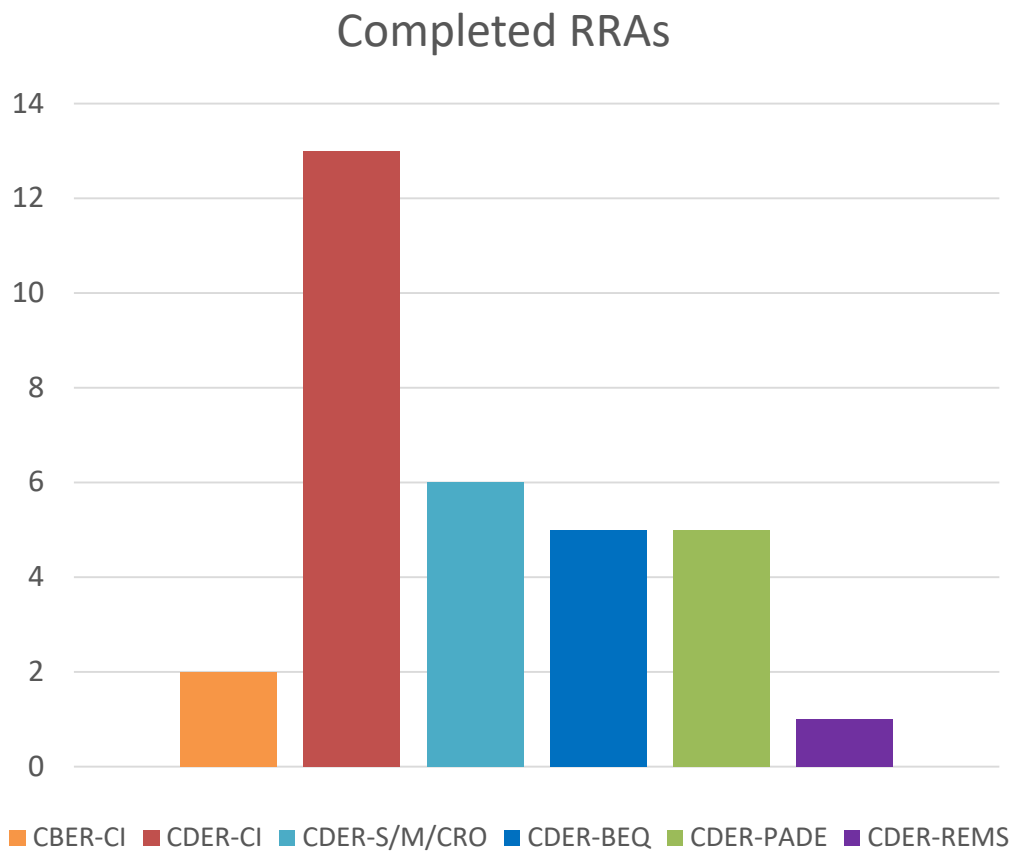
Final classifications for Risk Evaluation Mitigation Strategies Inspections FY 2017-2020



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

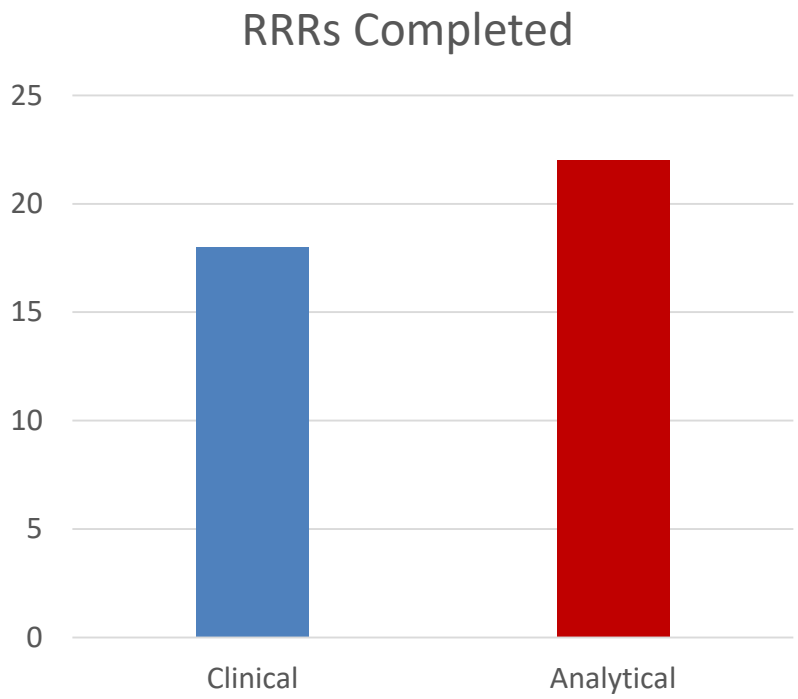
- CDER Specific Program

Remote Regulatory Assessments Completed during FY20 COVID-19 Pandemic



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)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