Bioresearch Monitoring (BIMO) Fiscal Year 2021 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's (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) 2021.

COVID-19 Pandemic

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

- To continue supporting our mission, BIMO introduced Remote Regulatory Assessments (RRA), which are voluntary remote evaluations of data and processes conducted via video teleconference.
- RRAs allow ORA/OBIMO and center staff to continue to review study data to provide information to center review divisions to aid in marketing application review. RRAs are evaluations and do not receive classifications.
- RRAs are not equivalent to an on-site inspection, nor are they replacing inspections.
- Data for RRAs are not reflected in the inspection and final classification tables for each program area. Refer to slides 31- 32 for a 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
- OSIS: Office of Study Integrity and Surveillance
- PADE: Postmarketing Adverse Drug Experience
- PMR: Postmarketing Requirements
- RDRC: Radioactive Drug Research Committee
- REMS: Risk Evaluation and Mitigation Strategies
- S: Sponsor
- SI: Sponsor-Investigator

Inspection Classifications

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

Evaluations

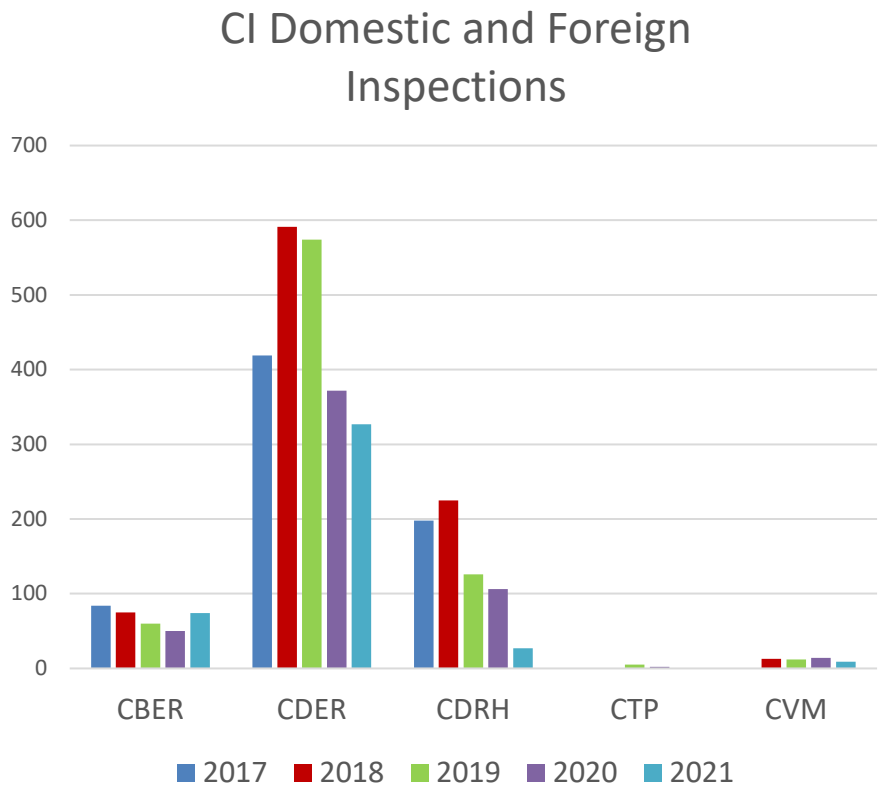
- RRA: Remote Regulatory Assessment

BIMO Inspection Final Classifications by Center – FY 2021*

Center	CI	IRB	S/CRO	S/I	GLP	BA/BE	PADE	REMS	Total
CBER	74	3	5	0	4	0	0	0	86
CDER	327	11	68	5	9	25	16	4	465
CDRH	27	15	6	0	1	0	0	0	49
CFSAN	0	0	0	0	0	0	0	0	0
CTP	0	0	0	0	0	0	0	0	0
CVM	9	0	0	0	2	0	0	0	11
Total	437	29	79	5	16	25	16	4	611

* Domestic and Foreign

Number of CI Inspections Conducted FY 2017- 2021*



Center	2017	2018	2019	2020*	2021*
CBER	84	75	60	50	74
CDER	419	591	574	372	327
CDRH	198	225	126	106	27
CTP	0	0	5	2	0
CVM	0	13	12	14	9

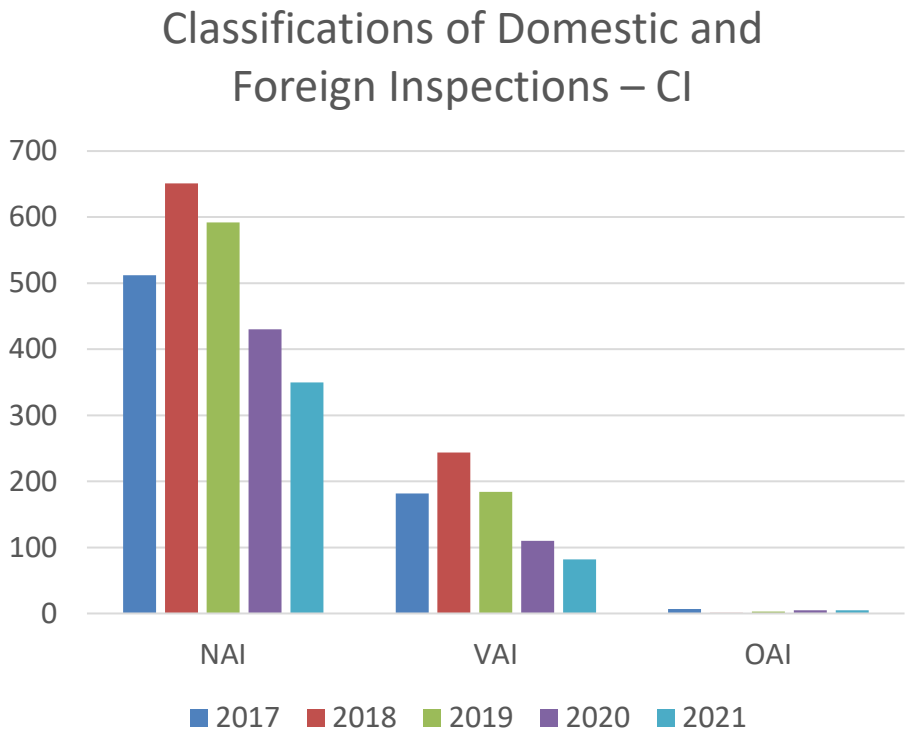
* Due to the COVID-19 pandemic, RRAs (not reflected in the above table) were conducted. See slide 31 for more details.

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.

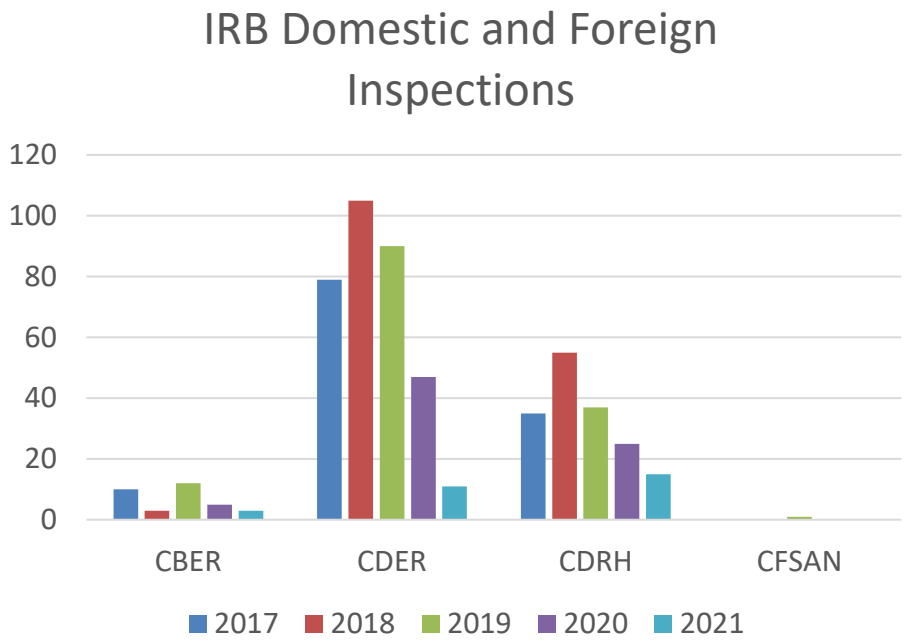
*Most common observations collected from issued FDA Form 483s

Number of CI Inspections Final Classified FY 2017-2021



	2017	2018	2019	2020	2021
NAI	512	651	592	430	350
VAI	182	244	184	110	82
OAI	7	1	3	5	5

Number of IRB and RDRC Inspections Conducted FY 2017- 2021*



Center	2017	2018	2019	2020*	2021
CBER	10	3	12	5	3
CDER	79*	105*	90*	47*	11
CDRH	35	55	37	25	15
CFSAN	0	0	1	0	0

* Includes CDER RDRC completed inspections: 4 RDRC Inspections for FY20, 2 RDRC for FY19, 4 RDRC for FY18, 2 RDRC for FY17

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

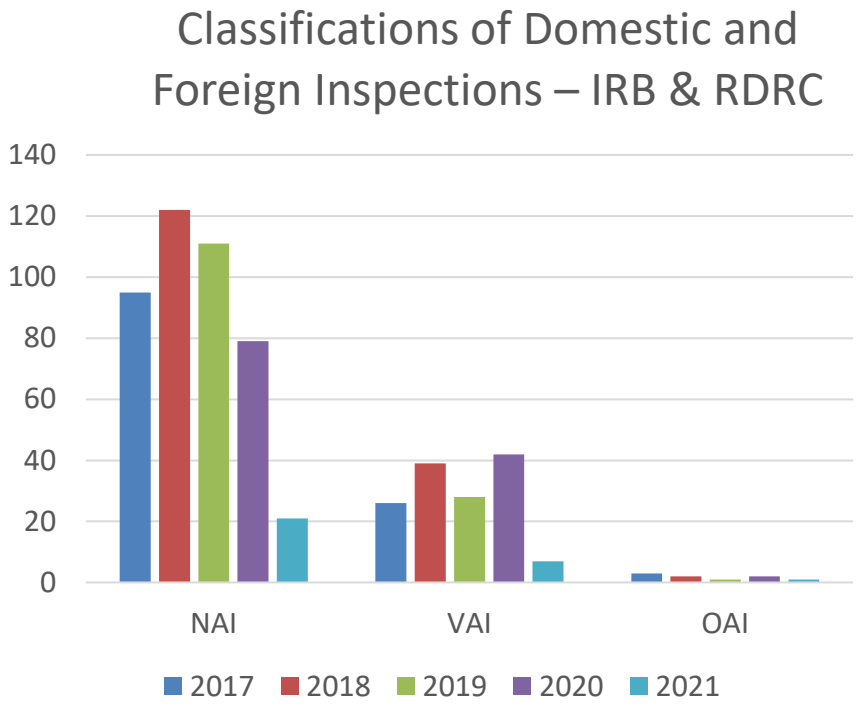
*Most common observations collected from issued FDA Form 483s

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

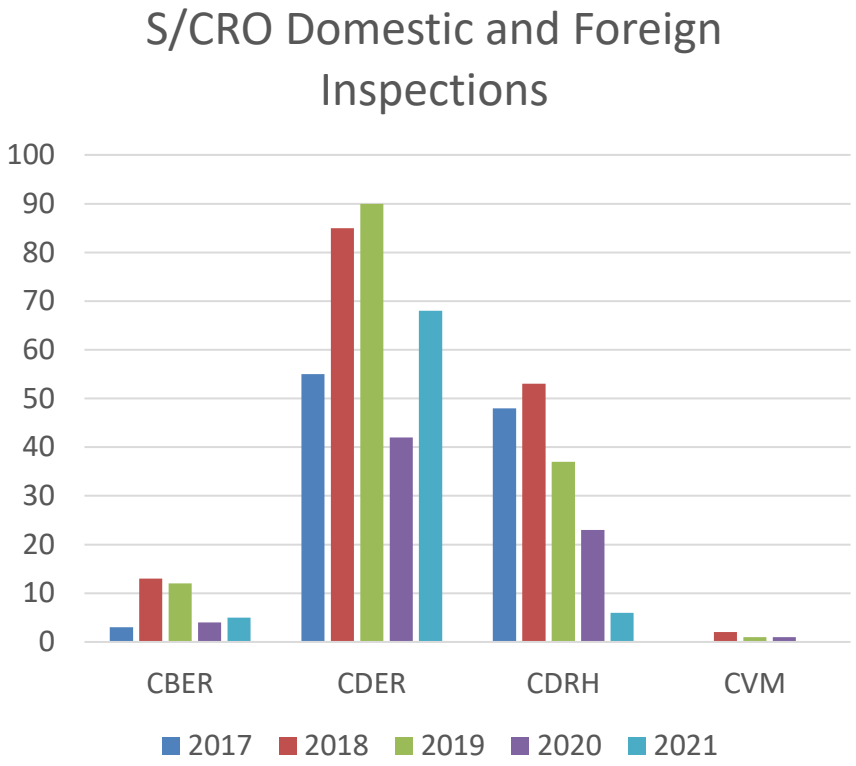
Number of IRB and RDRC Inspections Final Classified FY 2017-2021



	2017	2018	2019	2020	2021
NAI	95	122	111	45	21
VAI	26*	39*	28*	31*	7
OAI	3	2	1	1	1

* Includes 4 RDRC Inspections for FY20, 2 RDRC for FY19, 4 RDRC for FY18, 2 RDRC for FY17 completed by CDER

Number of Sponsor/CRO Inspections Conducted FY 2017-2021*



Center	2017	2018	2019	2020*	2021*
CBER	3	13	12	4	5
CDER	55	85	90	42	68
CDRH	48	53	37	23	6
CVM	0	2	1	1	0

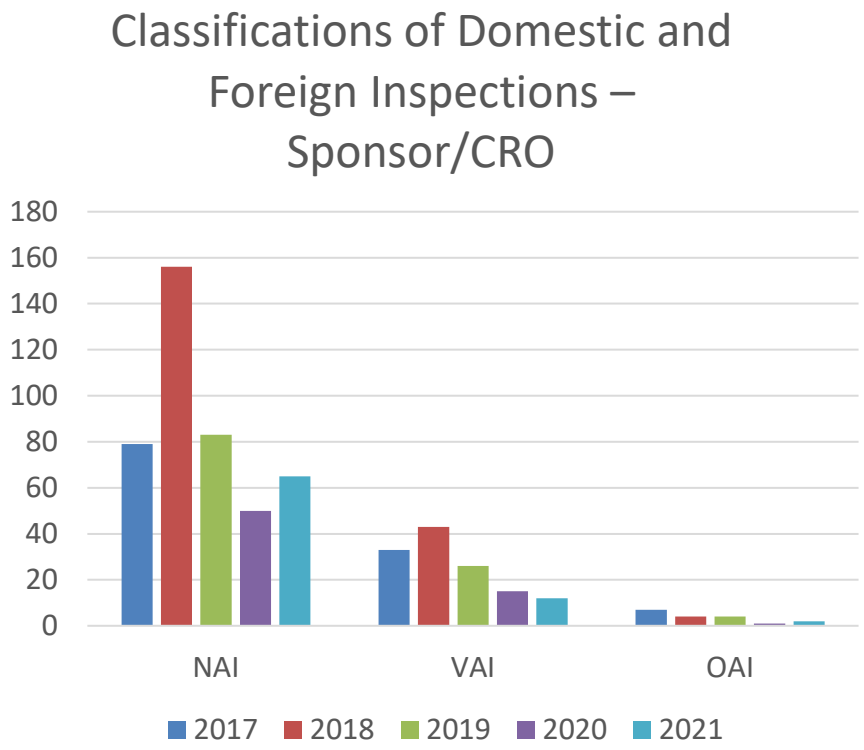
*Due to the COVID-19 pandemic, RRAs (not reflected in the above table) were conducted. See slide 31 for more details.

Common Sponsor/CRO Inspectional Observations*

- Failure to submit an Investigational New Drug (IND) application
- 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
- 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

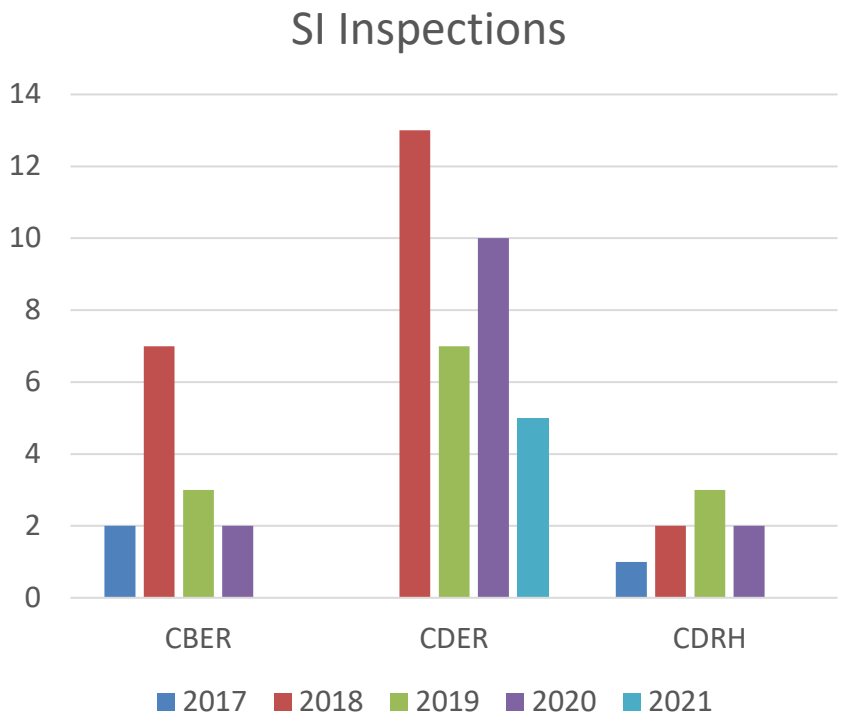
*Most common observations collected from issued FDA Form 483s

Number of Sponsor/CRO Inspections Final Classified FY 2017-2021



	2017	2018	2019	2020	2021
NAI	79	156	83	53	65
VAI	33	43	26	16	12
OAI	7	4	4	1	2

Number of Sponsor-Investigator Inspections Conducted FY 2017-2021



Center	2017	2018	2019	2020*	2021*
CBER	2	7	3	2	0
CDER	0	13	7	10	5
CDRH	1	2	3	2	0

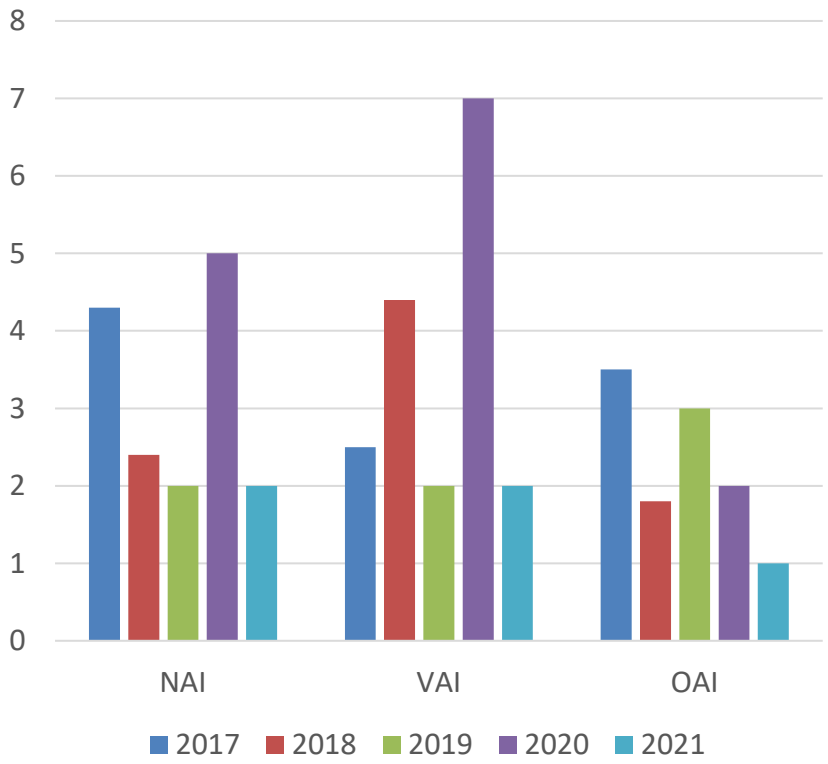
* Due to the COVID-19 pandemic, RRAs (not reflected in the above table) were conducted. See slide 31 for more details.

Common Sponsor-Investigator Inspectional Observations*

- 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.
- 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.
- Failure to submit an Investigational New Drug (IND) application
- Inadequate subject protection; informed consent issues
- Failure to notify FDA of termination of investigator

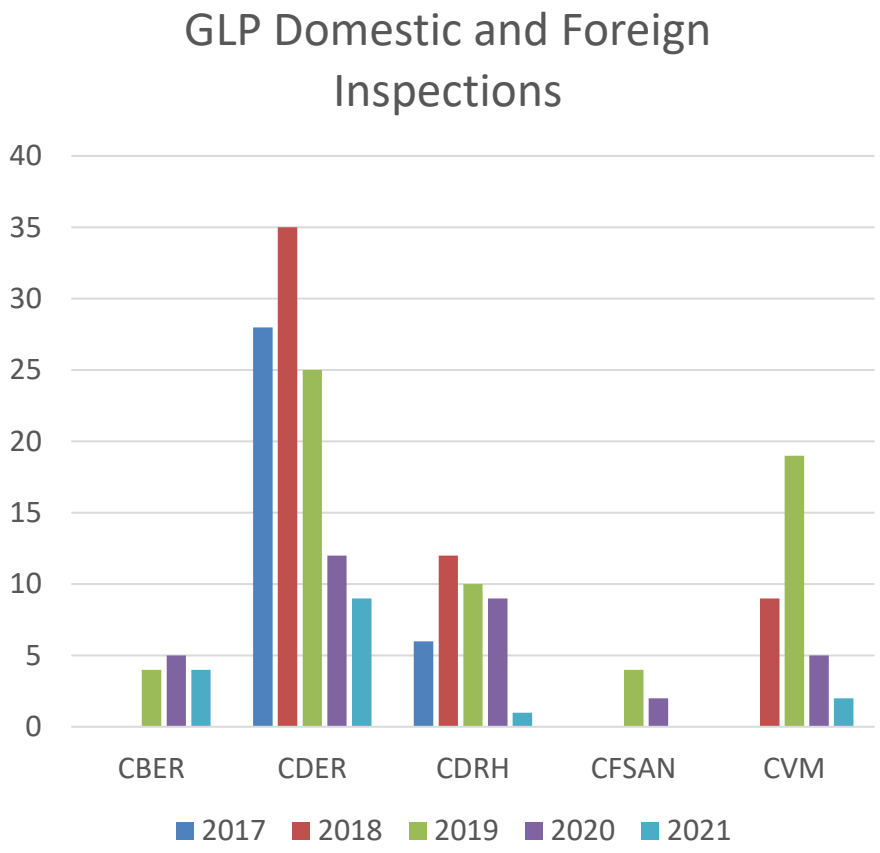
*Most common observations collected from issued FDA Form 483s

Number of Sponsor-Investigator Inspections Final Classified FY 2017-2021



	2017	2018	2019	2020	2021
NAI	1	6	7	5	2
VAI	1	5	6	7	2
OAI	1	0	0	2	1

Number of Good Laboratory Practice Inspections Conducted FY 2017-2021



Center	2017	2018	2019	2020*	2021*
CBER	0	0	4	5	4
CDER	28	35	25	12	9
CDRH	6	12	10	9	1
CFSAN	0	0	4	2	0
CVM	0	9	19	5	2

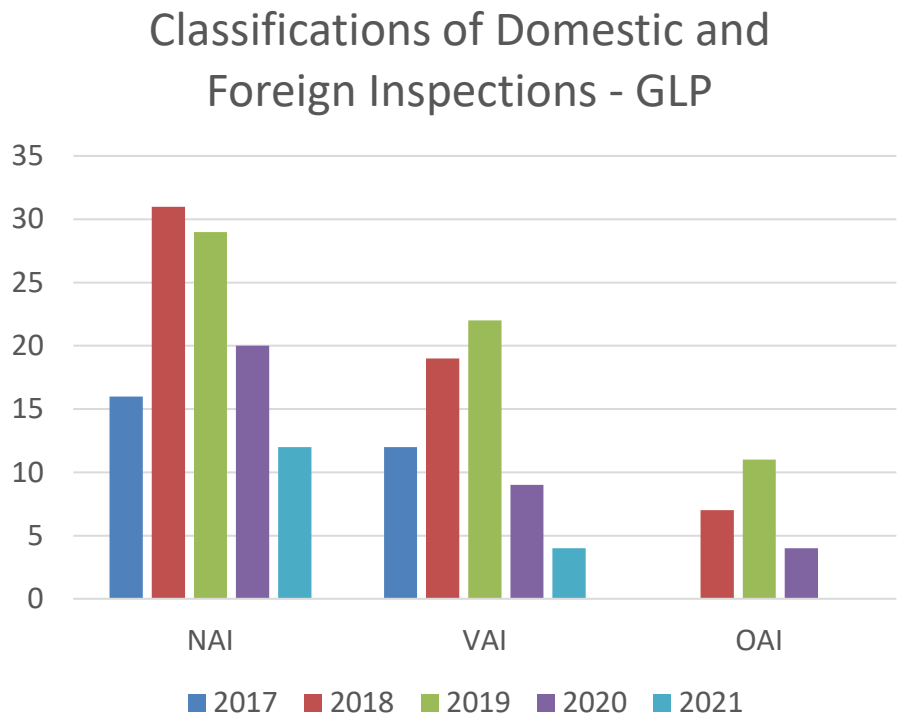
* Due to the COVID-19 pandemic, RRAs (not reflected in the above table) were conducted. See slide 31 for more details

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

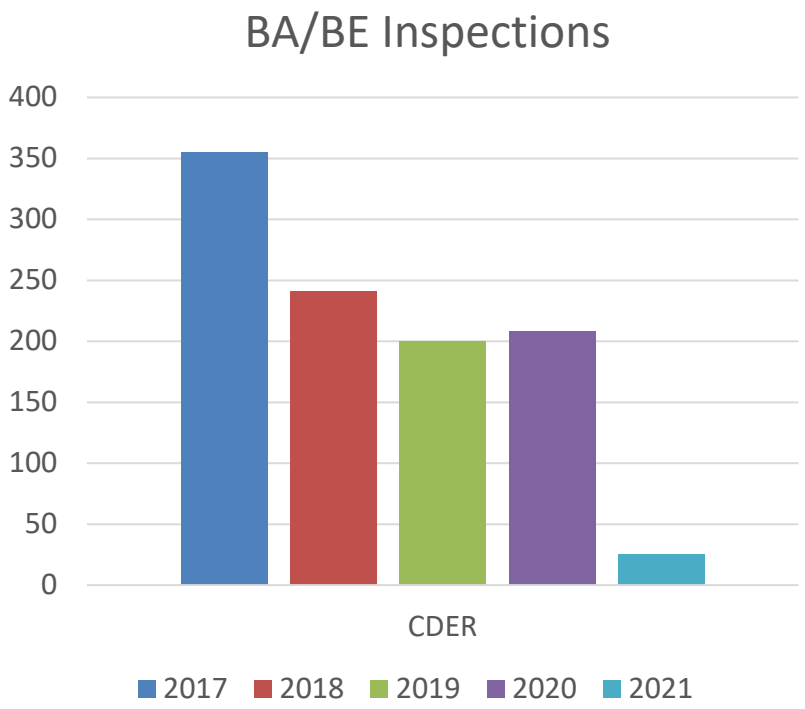
*Most common observations collected from issued FDA Form 483s

Number of Good Laboratory Practice Inspections Final Classified FY 2017-2021



	2017	2018	2019	2020	2021
NAI	16	31	29	20	12
VAI	12	19	22	9	4
OAI	0	7	11	4	0

Number of Bioavailability/Bioequivalence Inspections Conducted FY 2017-2021*



Center	2017	2018	2019	2020*	2021*
CDER	355	241	200	208	25

- CDER Specific Program

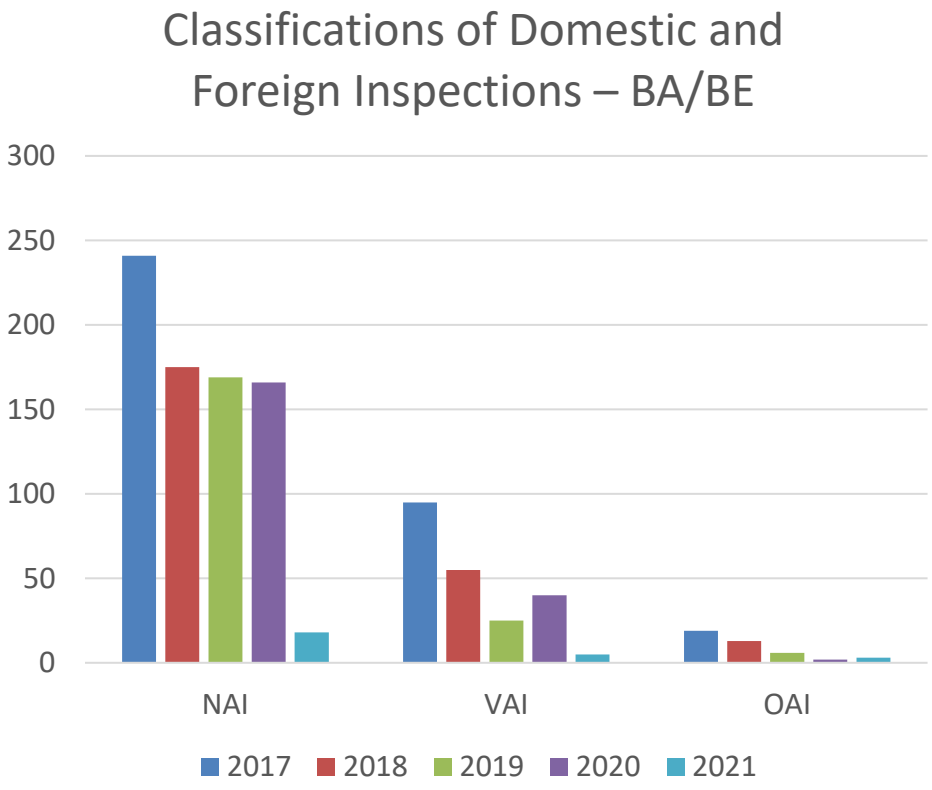
* Due to the COVID-19 pandemic, RRAs (not reflected in the above table) were conducted. See slide 31 and 32 for more details.

Common Bioavailability/Bioequivalence Inspectional Observations*

- **Analytical**
  - Validation
  - Quality Control
  - Stability
- **Clinical**
  - Reserve Samples
  - Inclusion/Exclusion Criteria
  - Recordkeeping

*Most common observations collected from issued FDA Form 483s

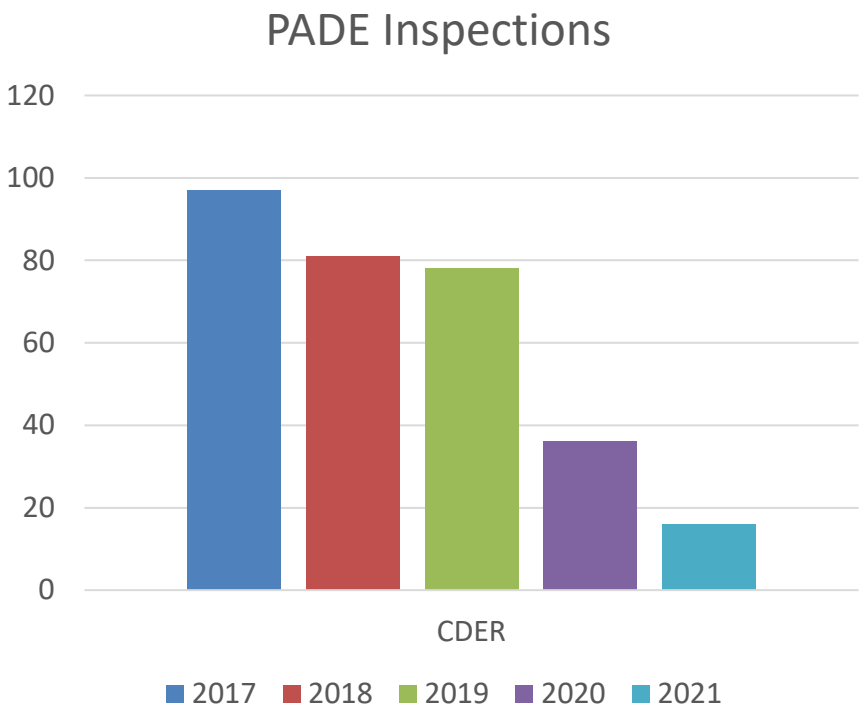
Number of Bioavailability/Bioequivalence Inspections Final Classified FY 2017-2021



	2017	2018	2019	2020	2021
NAI	241	175	169	166	18
VAI	95	55	25	40	5
OAI	19	13	6	2	2

- CDER Specific Program

Number of Postmarketing Adverse Drug Experience (PADE) Inspections Conducted FY 2017-2021*



Center	2017	2018	2019	2020*	2021*
CDER	97	81	78	36	16

- CDER Specific Program

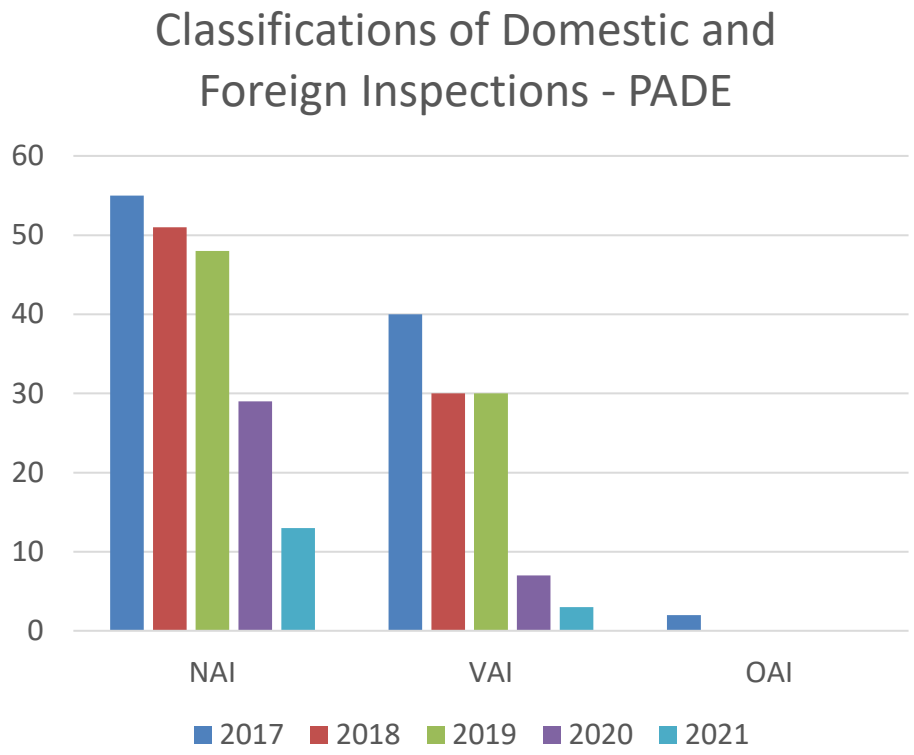
* Due to the COVID-19 pandemic, RRAs (not reflected in the above table) were conducted. See slide 31 for more details.

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

*Most common observations collected from issued FDA Form 483s

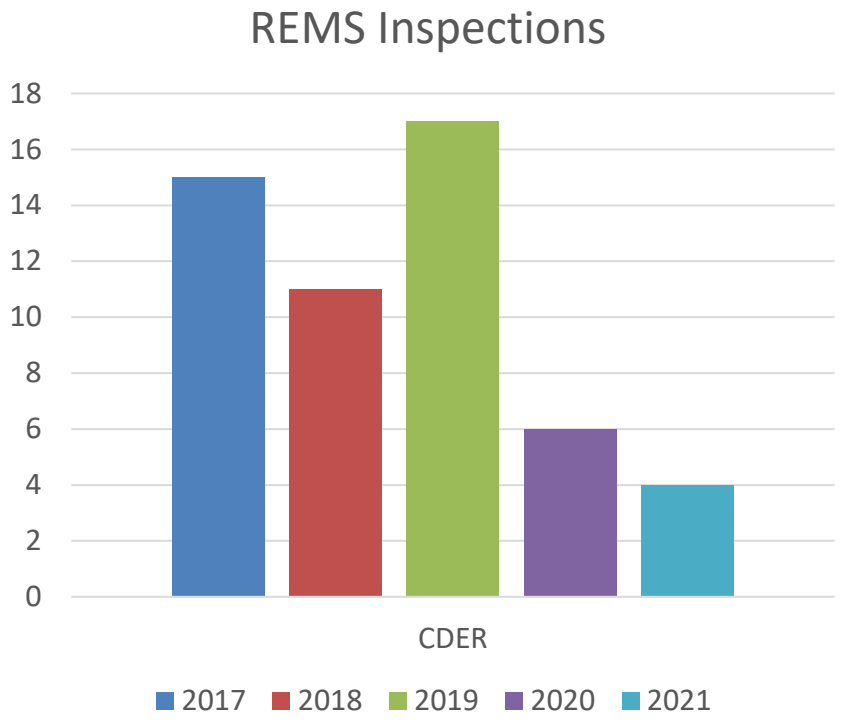
Number of Postmarketing Adverse Drug Experience Inspections Final Classified FY 2017-2021



	2017	2018	2019	2020	2021
NAI	55	51	48	29	13
VAI	40	30	30	7	3
OAI	2	0	0	0	0

- CDER Specific Program

Number of Risk Evaluation and Mitigation Strategies Inspections Conducted FY 2017-2021*



Center	2017	2018	2019	2020*	2021*
CDER	15	11	17	6	4

- CDER Specific Program

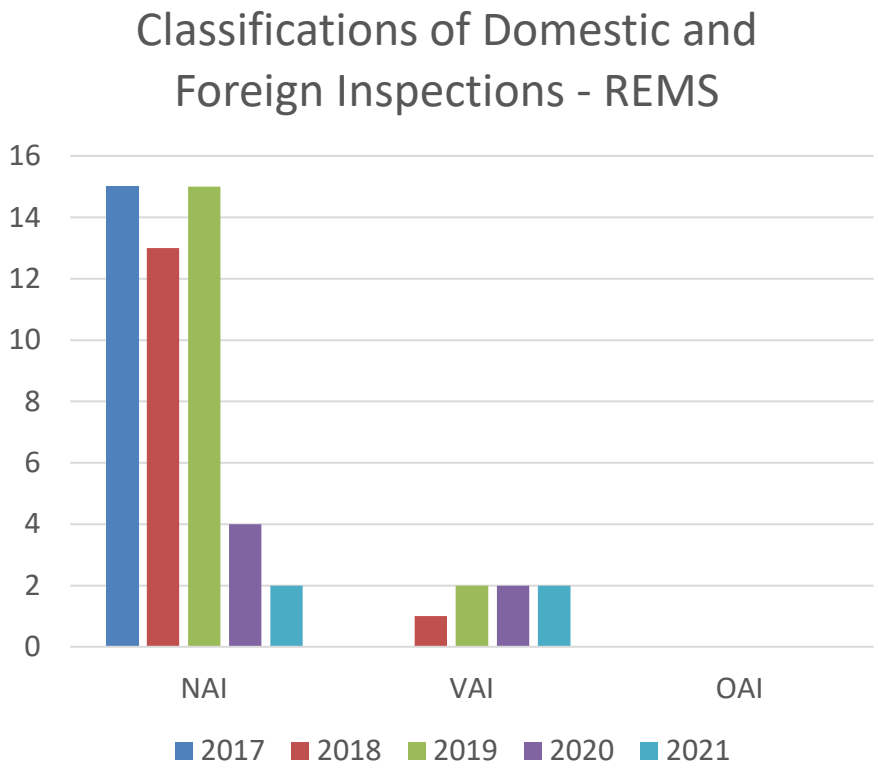
* Due to the COVID-19 pandemic, RRAs were conducted. See slide 31 for more details.

Common Risk Evaluation and Mitigation Strategies Inspectional Observations*

- Failure to comply with REMS Implementation System
  - -Audits
  - -Website
  - -Database

*Most common observations collected from issued FDA Form 483s

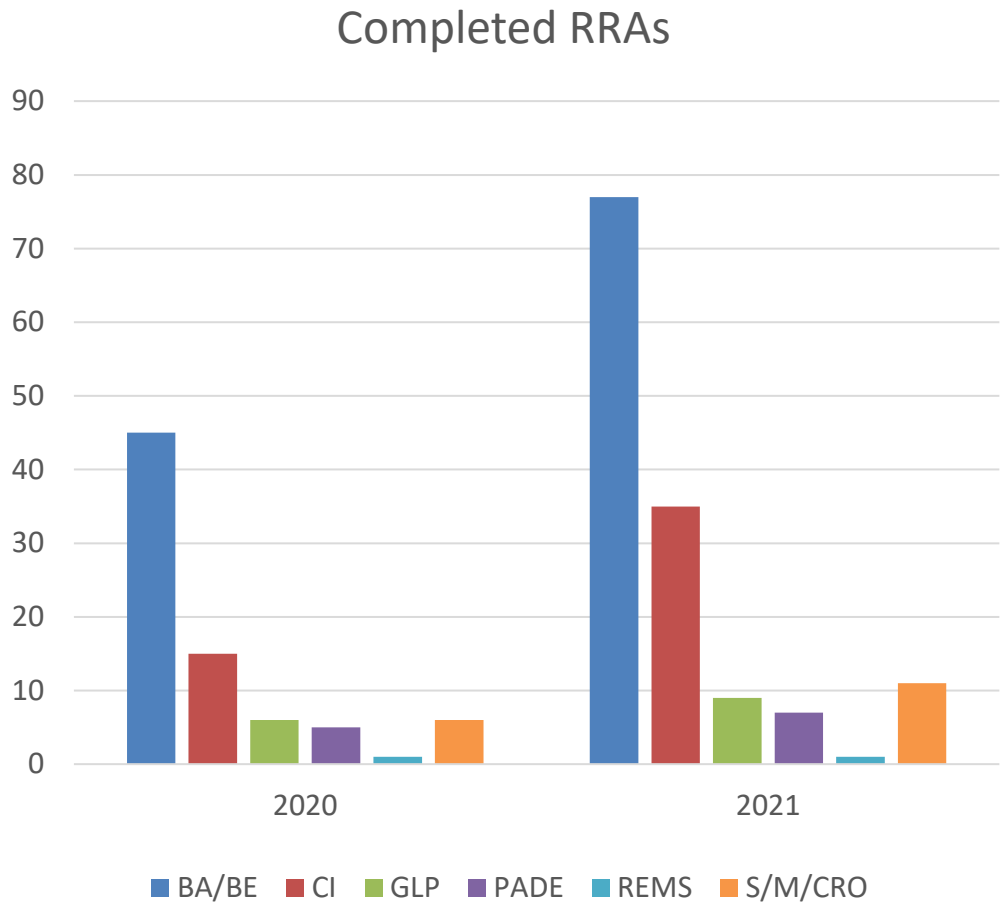
Number of REMS Inspections Final Classified FY 2017-2021



	2017	2018	2019	2020	2021
NAI	15	13	15	4	2
VAI	0	1	2	2	2
OAI	0	0	0	0	0

- CDER Specific Program

Number of Remote Regulatory Assessments Completed FY 2020-2021



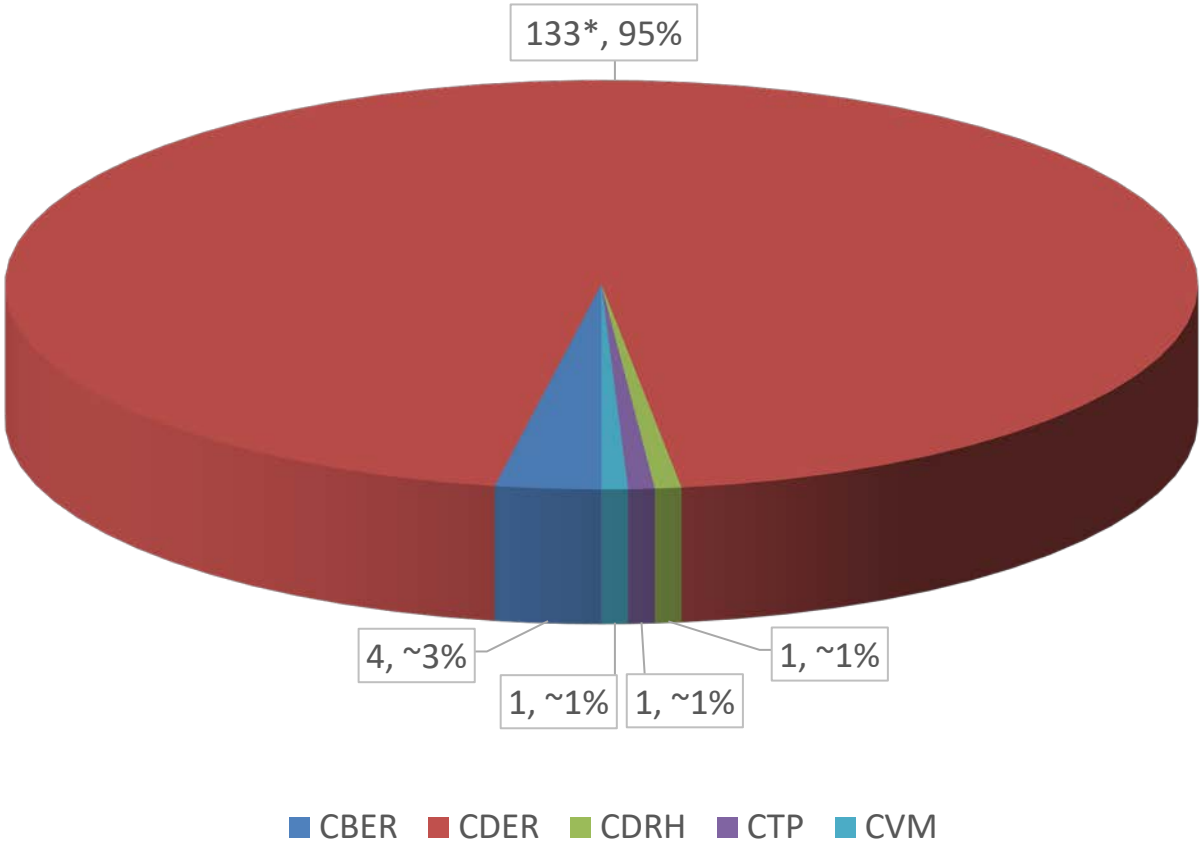
Program area	2020	2021
Bioavailability/Bioequivalence	45*	77*
Clinical Investigator	15	35
Good Laboratory Practice	6	9*
Postmarketing Adverse Drug Experience	5	7
Risk Evaluation and Mitigation Strategies	1	1
Sponsor/Contract Research Organization	6	11

*CDER/OSIS Completed RRAs:

- 40 BA/BE RRAs in FY20 (18 Clinical, 22 Analytical)
- 68 BA/BE RRAs in FY21 (18 Clinical, 50 Analytical)
- 7 GLP RRAs in FY21

OSIS: Office of Study Integrity and Surveillance

Number of Remote Regulatory Assessments Completed per Center FY2021



*CDER/OSIS conducted 75 of the 133 RRAs completed for CDER in FY2021

References

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


FDA
U.S. FOOD & DRUG
ADMINISTRATION