Bioresearch Monitoring (BIMO) Fiscal Year 2023 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) 2023.
- Inspections conducted during the fiscal year represent the number of completed assignments with the center providing final classification by the end of that fiscal year.

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 currently 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 slide 31 for a complete breakdown.

Remote Interactive Evaluations of Drug Manufacturing and Bioresearch Monitoring Facilities | FDA

Conducting Remote Regulatory Assessments Questions and Answers | FDA

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
- ETASU: Elements to Assure Safe Use
- 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 Strategy
- S: Sponsor
- SI: Sponsor-Investigator

Inspection Classifications

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

Remote Interactive Evaluations

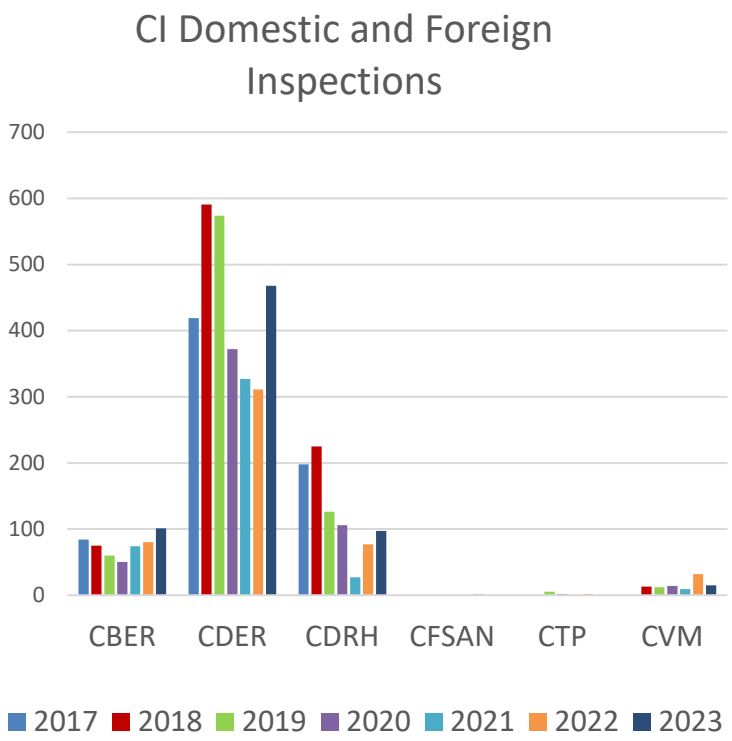
- RRA: Remote Regulatory Assessment

BIMO Inspection Final Classifications by Center – FY 2023*

Center	CI	IRB	S/CRO	S/I	GLP	BEQ	PADE	REMS	Total
CBER	101	7	10	2	6	0	0	0	126
CDER	468	47	65	9	14	133	35	8	779
CDRH	97	16	24	2	2	0	0	0	141
CFSAN	0	1	0	0	0	0	0	0	1
CVM	15	0	4	0	7	0	0	0	26
Total	681	71	103	13	29	133	35	8	1073

* Includes both Domestic and Foreign inspections. CTP did not have any FY2023 inspections

Clinical Investigator Inspections Final Classified FY 2017-2023*



Center	2017	2018	2019	2020*	2021*	2022	2023
CBER	84	75	60	50	74	80	101
CDER	419	591	574	372	327	311	468
CDRH	198	225	126	106	27	77	97
CFSAN	0	0	2	0	0	2	0
CTP	0	0	5	2	0	2	0
CVM	0	13	12	14	9	32	15

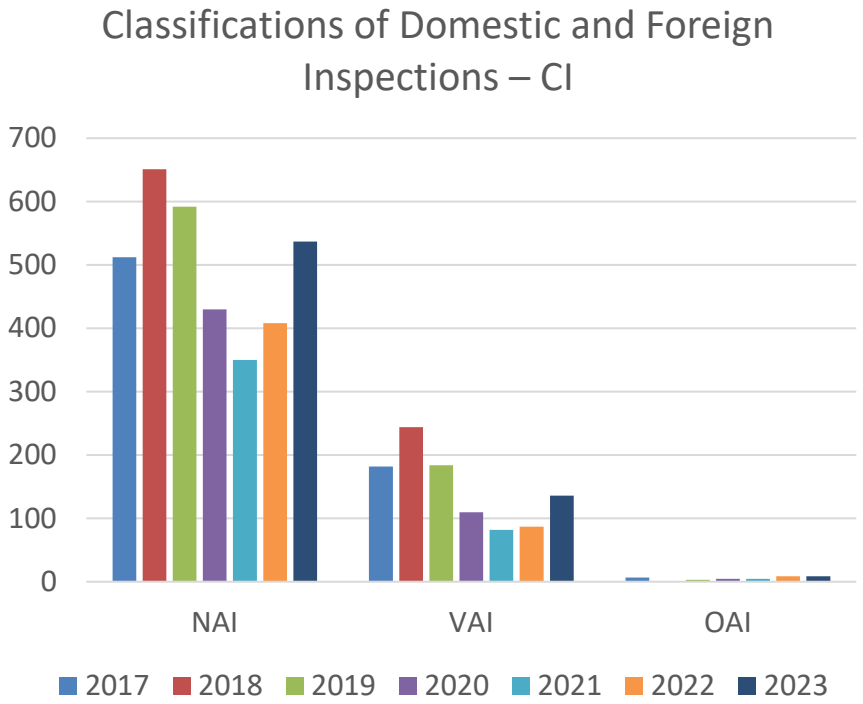
*RRAs conducted are not reflected in the above table. See slide 31 for more details.

Common Clinical Investigator Inspectional Observations*

- Failure to comply with Form FDA 1572 requirements, failure to follow the investigational plan
- Inadequate and/or inaccurate case history records; inadequate study records
- Inadequate subject protection; informed consent issues
- Inadequate accountability and/or control of the investigational product
- Safety reporting; failure to report and/or record adverse events

*Most common observations collected from issued FDA Form 483s

Clinical Investigator Inspection Final Classifications FY 2017-2023

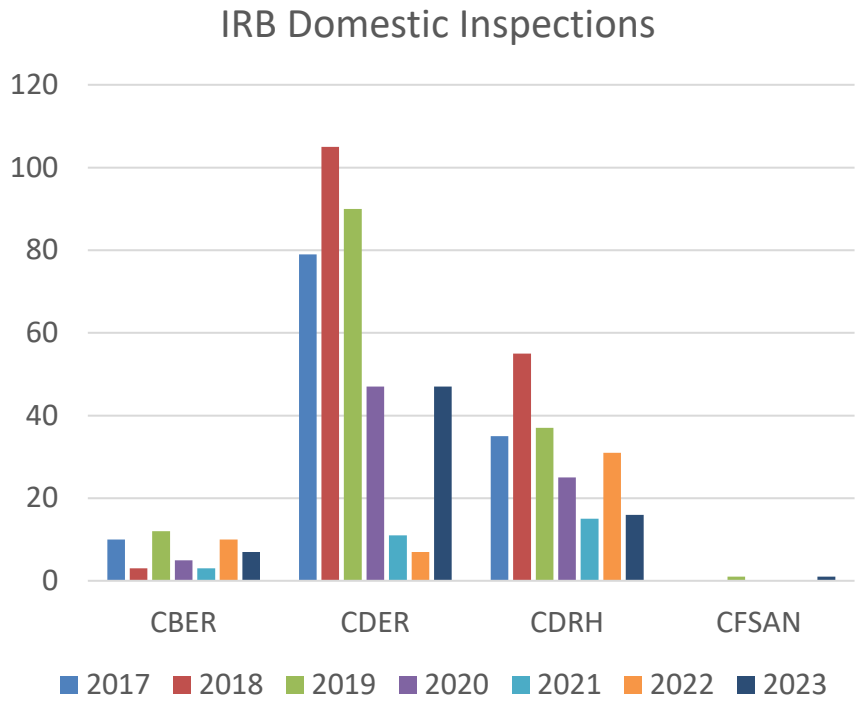


	2017	2018	2019	2020	2021	2022	2023
NAI	512	651	592	430	350	408	537
VAI	182	244	184	110	82	87	136
OAI	7	1	3	5	5	9	9

This data is inclusive of all centers' inspections.

Return to the inspections conducted slide

IRB and RDRC Inspections
Final Classified FY 2017- 2023*



Center	2017	2018	2019	2020	2021	2022	2023
CBER	10	3	12	5	3	10	7
CDER	79*	105*	90*	47*	11	7	47
CDRH	35	55	37	25	15	31	16
CFSAN	0	0	1	0	0	1	1

* Includes CDER completed RDRC inspections:
FY20: 4; FY19: 2; FY18: 4; FY17: 2

Terms

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 conduct initial and/or continuing review of research
- Failure to have a majority of IRB members present for review of proposed research for other than expedited reviews
- Failure to keep members of the IRB advised of research proposals that have been approved under an expedited review procedure
- Failure to follow FDA regulations regarding expedited review procedures
- 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

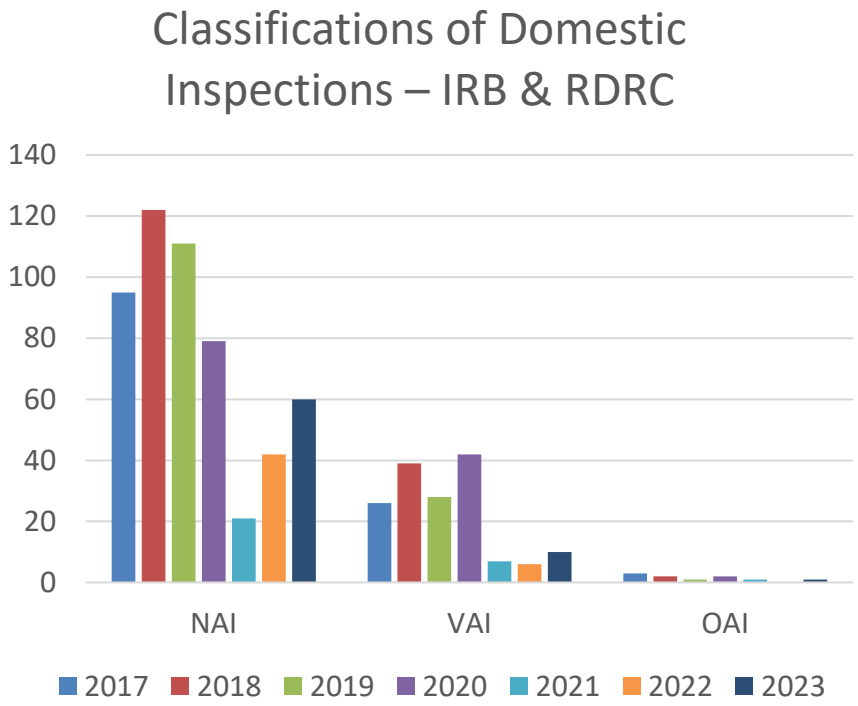
Radioactive Drug Research Committee Inspectional Observations during FY 2017-2020*

- 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

Note: There were No RDRC inspections completed from FY2021-2023

*Most common observations collected from issued FDA Form 483s

IRB and RDRC Inspection Final Classifications FY 2017-2023



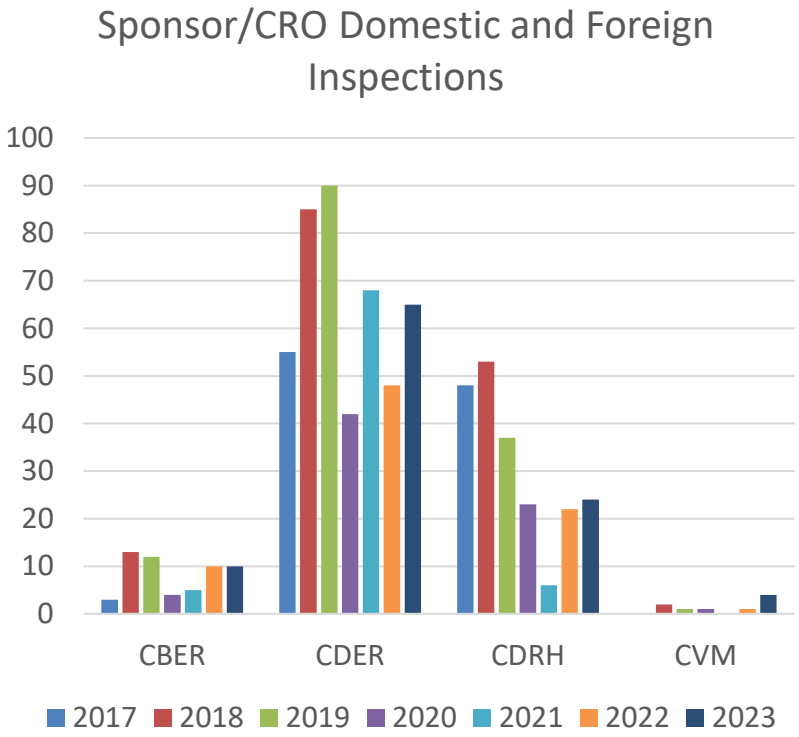
	2017	2018	2019	2020	2021	2022	2023
NAI	95	122	111	45	21	42	60
VAI	26*	39*	28*	31*	7	6	10
OAI	3	2	1	1	1	0	1

This data is inclusive of all centers' inspections.

* Includes CDER completed RDRC inspections:
FY17: 2; FY18: 4; FY19: 2; FY20: 4

Return to the inspections conducted slide

Sponsor/CRO Inspections
Final Classified FY 2017-2023*



Center	2017	2018	2019	2020	2021	2022	2023
CBER	3	13	12	4	5	10	10
CDER	55	85	90	42	68	48	65
CDRH	48	53	37	23	6	22	24
CVM	0	2	1	1	0	1	4

*RRAs not reflected in the above table. See slide 31 for more details.

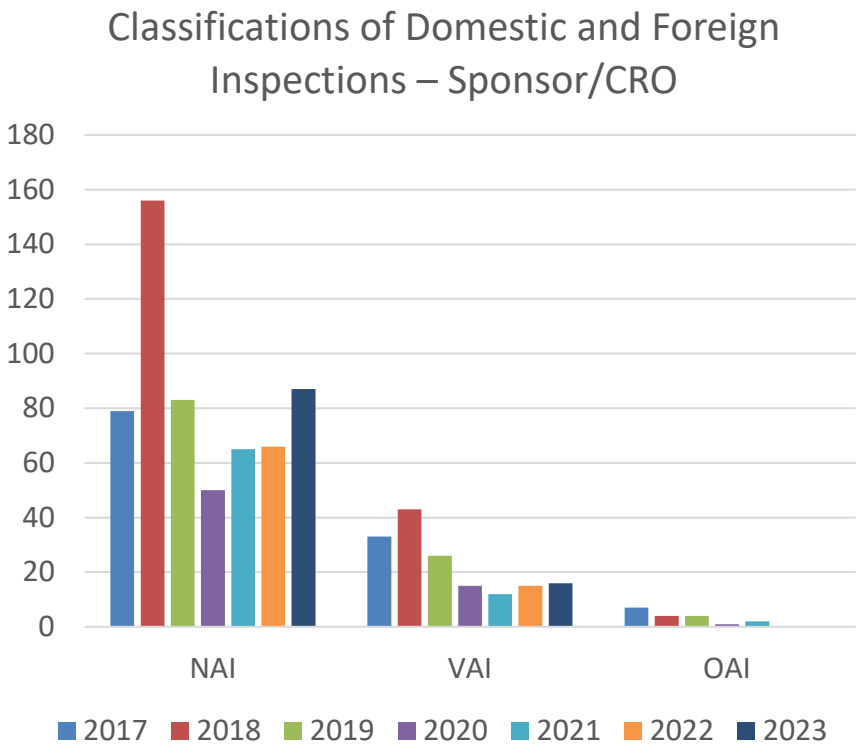
Terms

Common Sponsor/CRO Inspectional Observations*

- Failure to ensure proper monitoring of the study and ensure the study is conducted in accordance with the protocol and/or investigational plan
- Failure to meet the abbreviated requirements for investigational device exemptions (IDEs)
- 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 an Investigational New Drug (IND) application; IND safety report
- Failure to submit current list of all participating investigators to FDA at six-month interval after FDA approval of the study

*Most common observations collected from issued FDA Form 483s

Sponsor/CRO Inspection
Final Classifications FY 2017-2023

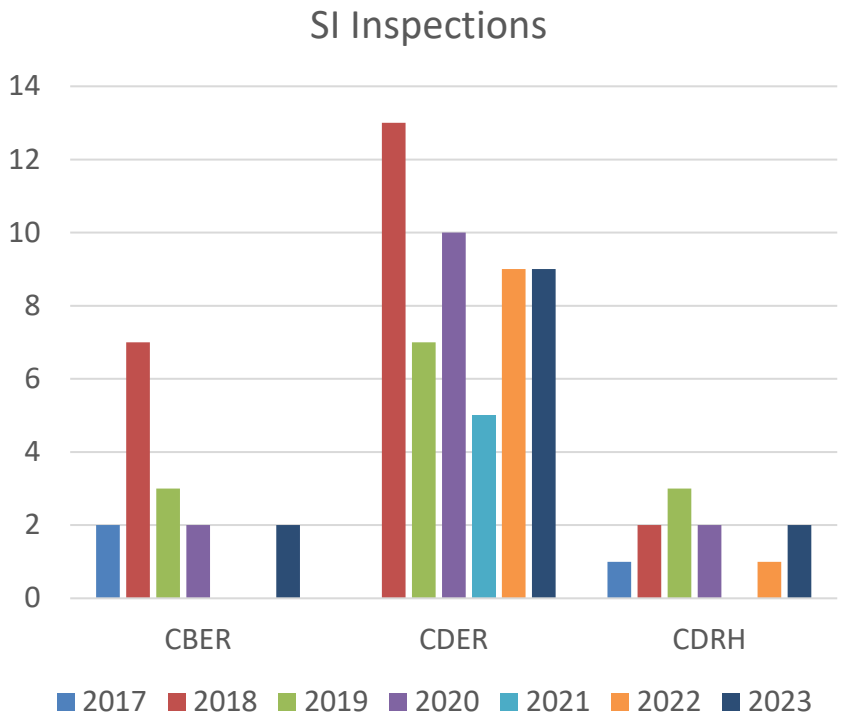


	2017	2018	2019	2020	2021	2022	2023
NAI	79	156	83	53	65	66	87
VAI	33	43	26	16	12	15	16
OAI	7	4	4	1	2	0	0

This data is inclusive of all centers' inspections.

Return to the inspections conducted slide

Sponsor-Investigator Inspections
Final Classified FY 2017-2023



Center	2017	2018	2019	2020	2021	2022	2023
CBER	2	7	3	2	0	0	2
CDER	0	2	7	10	5	9	9
CDRH	1	2	3	2	0	1	2

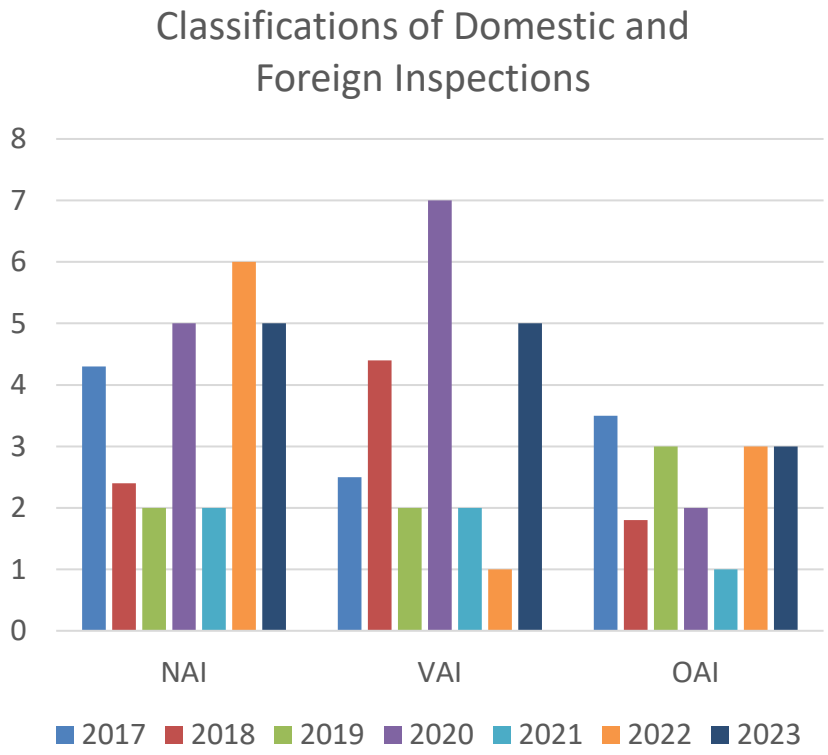
*RRAs conducted are not reflected in the above table.
See slide 31 for more details.

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

Sponsor-Investigator Inspection Final Classifications FY 2017-2023

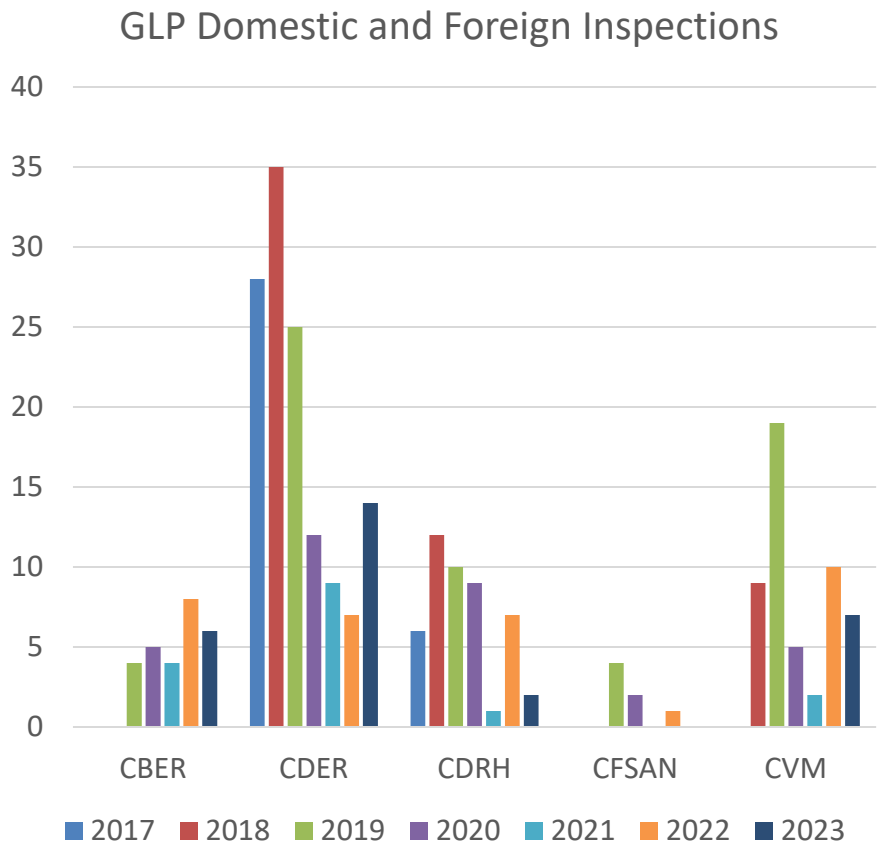


	2017	2018	2019	2020	2021	2022	2023
NAI	1	6	7	5	2	6	5
VAI	1	5	6	7	2	1	5
OAI	1	0	0	2	1	3	3

This data is inclusive of all centers' inspections.

Return to the inspections conducted slide

GLP Inspections
Final Classified FY 2017-2023



Center	2017	2018	2019	2020 *	2021 *	2022 *	2023 *
CBER	0	0	4	5	4	8	6
CDER	28	35	25	12	9	7	14
CDRH	6	12	10	9	1	7	2
CFSAN	0	0	4	2	0	1	0
CVM	0	9	19	5	2	10	7

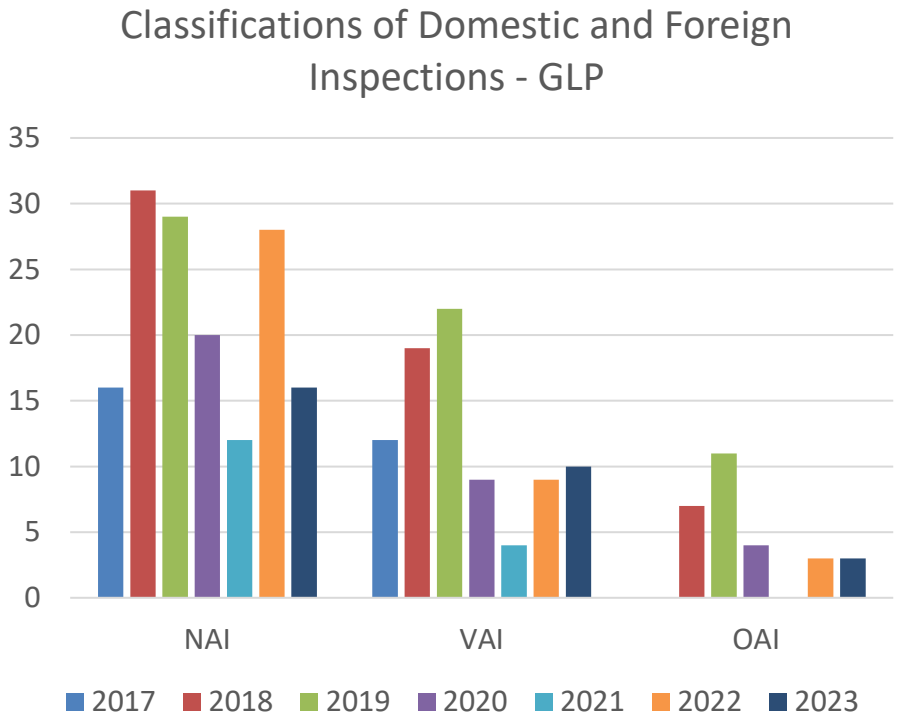
*RRAs conducted are not reflected in the above table.
See slide 31 for more details

Common GLP Inspectional Observations*

- Quality assurance unit (QAU) failed to determine if any deviations from approved protocols had been made without proper authorization and documentation
- QAU failed to monitor each study to assure management that facilities, equipment, personnel, methods, practices, records, and controls were in conformance with GLP regulations
- Final report did not include all circumstances affecting quality or integrity of the data; and the archiving of records
- Equipment calibration, equipment used for measurement or assessment was not adequately tested, calibrated and/or standardized
- Testing facility management failed to assure that all personnel clearly understood the functions they were to perform
- Missing standard operating procedures (SOPs)

 *Most common observations collected from issued FDA Form 483s

GLP Inspection Final Classifications FY 2017-2023

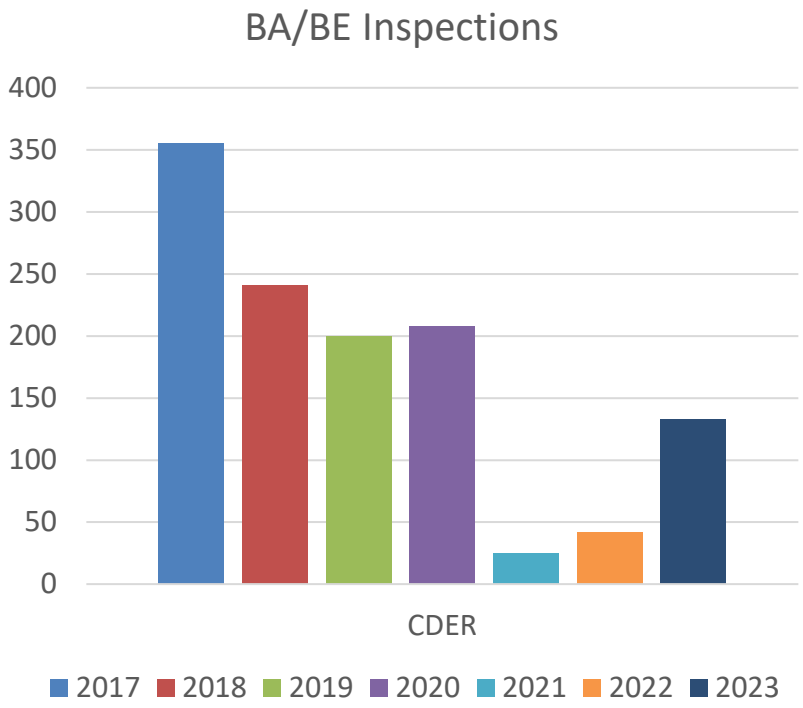


	2017	2018	2019	2020	2021	2022	2023
NAI	16	31	29	20	12	21	16
VAI	12	19	22	9	4	9	10
OAI	0	7	11	4	0	3	3

This data is inclusive of all centers' inspections.

Return to the inspections conducted slide

BA/BE Inspections
Final Classified FY 2017-2023*



Center	2017	2018	2019	2020 *	2021 *	2022 *	2023 *
CDER	355	243	200	208	25	42	133

- CDER Specific Program

*RRAs conducted are not reflected in the above table. See slide 31 for more details.

Common BA/BE Inspectional/RRA Observations*

Clinical

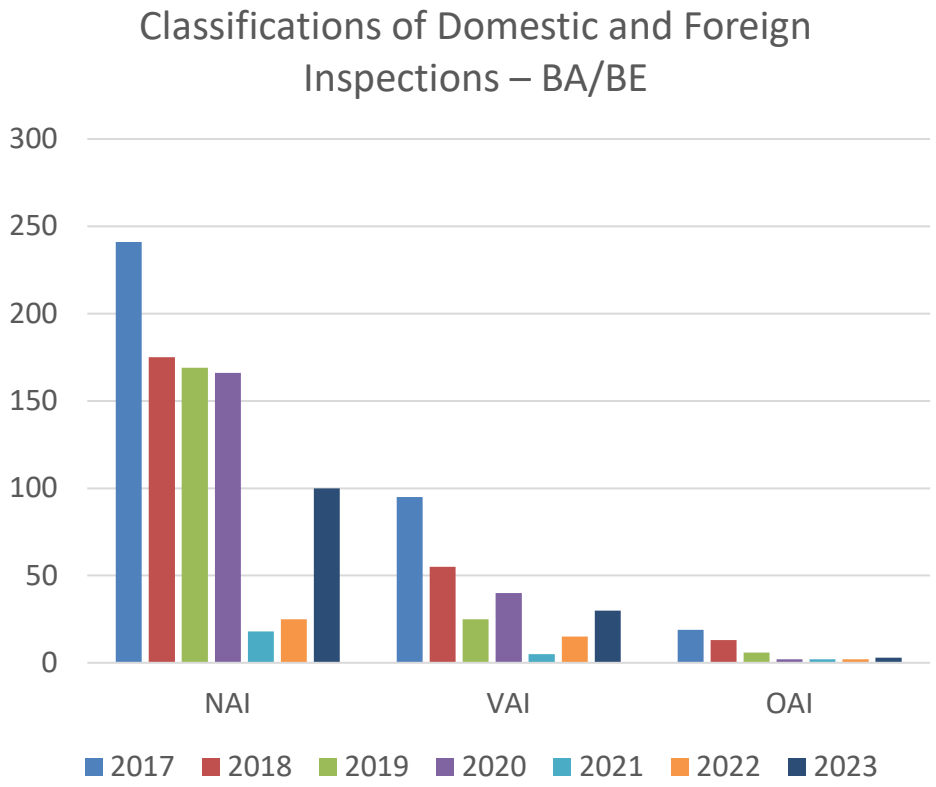
- Inadequate record keeping; inadequate drug accountability
- Did not follow the investigational plan; protocol deviations
- Inadequate subject protection; informed consent

Analytical

- Inadequate method validation
- Analytical run related unjustified data rejection
- Inadequate record keeping; inadequate drug accountability

*Most common observations collected from issued FDA Form 483s or shared with establishment post-RRA

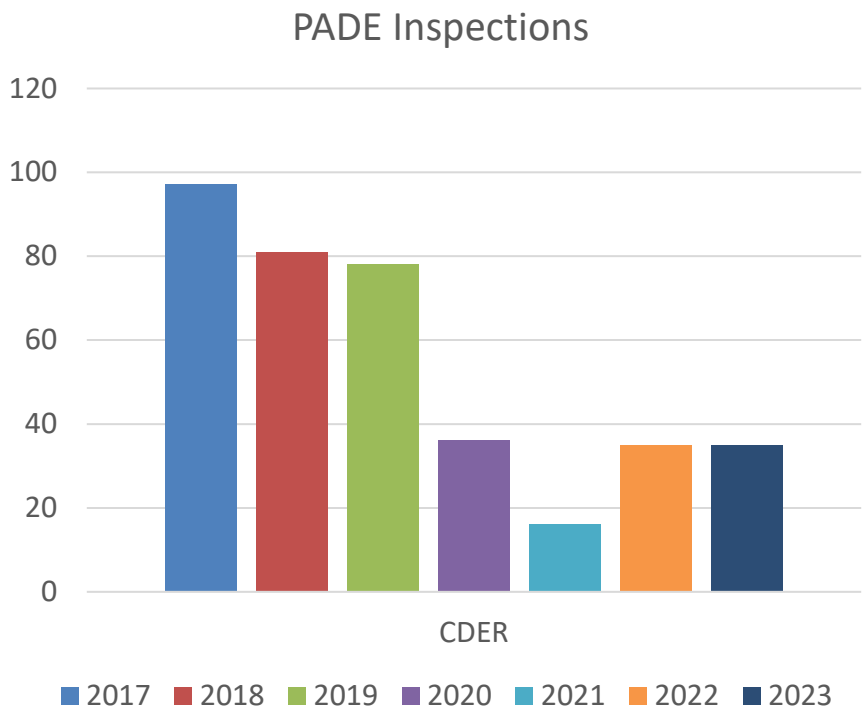
BA/BE Inspection
Final Classifications FY 2017-2023



	2017	2018	2019	2020	2021	2022	2023
NAI	241	175	169	166	18	25	100
VAI	95	55	25	40	5	15	30
OAI	19	13	6	2	2	2	3

- CDER Specific Program

PADE Inspections
Final Classified FY 2017-2023*



Center	2017	2018	2019	2020 *	2021 *	2022 *	2023 *
CDER	97	81	78	36	16	35	35

- CDER Specific Program

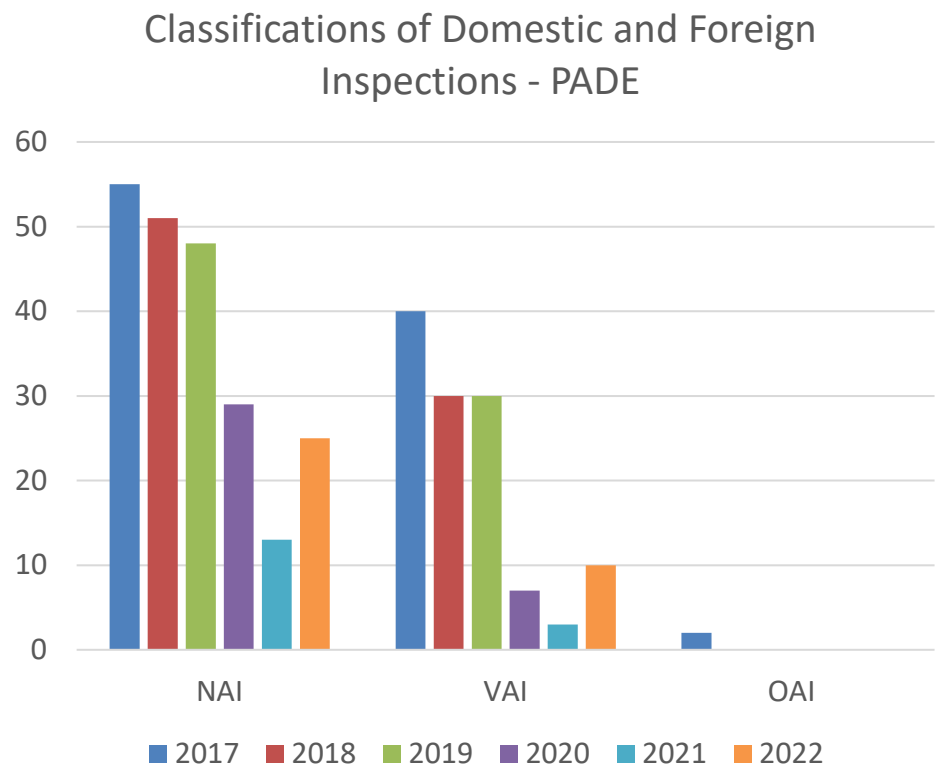
* RRAs conducted are not reflected in the above table. See slide 31 for more details.

Common PADE Inspectional Observations*

- Failure to develop written procedures for the surveillance, receipt, evaluation, and/or reporting of post-marketing adverse drug experiences
- Failure to submit annual safety reports within 60 days of the anniversary date of the approval of the application
- Failure to maintain records; incomplete initial reporter information on individual case study reports (ICSR)
- Late submission of quarterly safety reports
- Failure to investigate serious, unexpected events

*Most common observations collected from issued FDA Form 483s

PADE Inspection Final Classifications FY 2017-2023

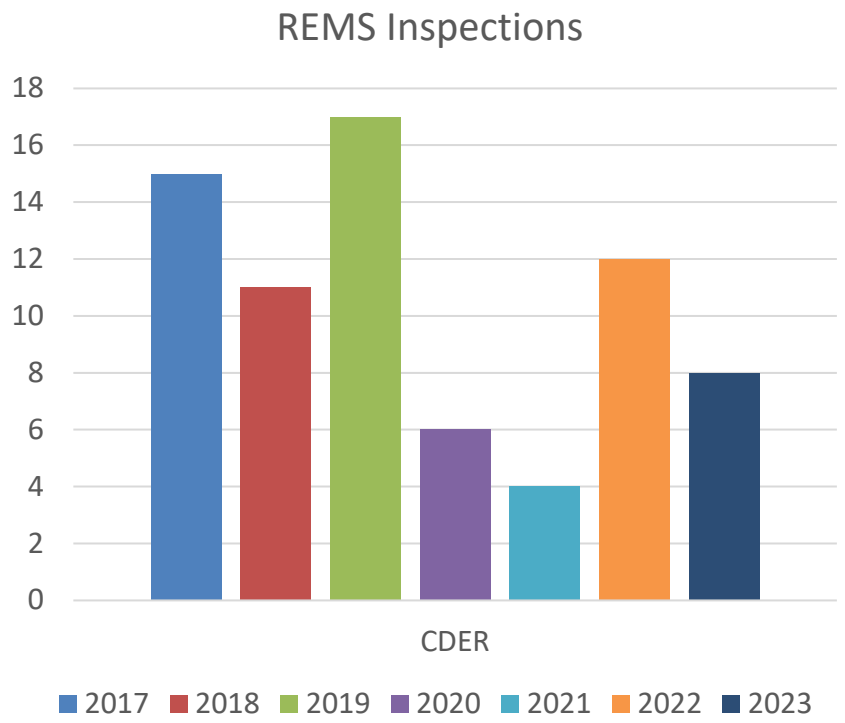


	2017	2018	2019	2020	2021	2022	2023
NAI	55	51	48	29	13	25	29
VAI	40	30	30	7	3	10	6
OAI	2	0	0	0	0	0	0

- CDER Specific Program

Terms

REMS Inspections Final Classified FY 2017-2023*



Center	2017	2018	2019	2020*	2021*	2022*	2023*
CDER	15	11	17	6	4	12	8

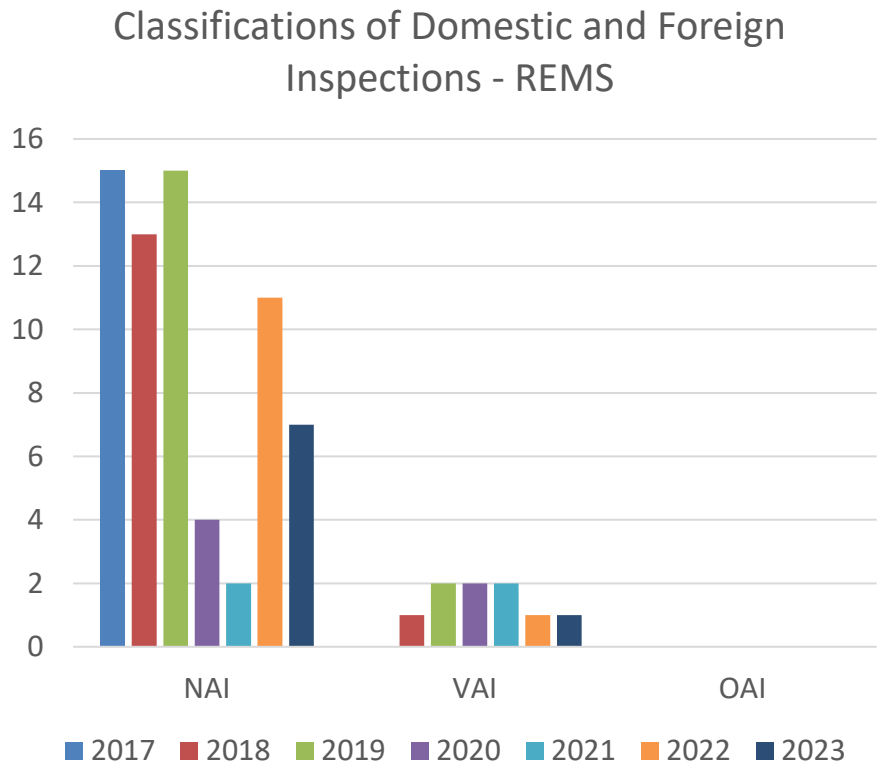
- CDER Specific Program

Common REMS Inspectional Observations*

- Failure to comply with REMS ETASU Parts A, B, C,D,F
- Failure to comply with REMS Communication Plan; failure to distribute the Communication Plan in accordance with the distribution dates in the REMS, to the target audience, or use the Communication Plan as required
- Failure to comply with REMS Implementation System; An application holder did not maintain a Support / Call Center or a REMS Program website, as required by approved REMS Implementation System

*Most common observations collected from issued FDA Form 483s

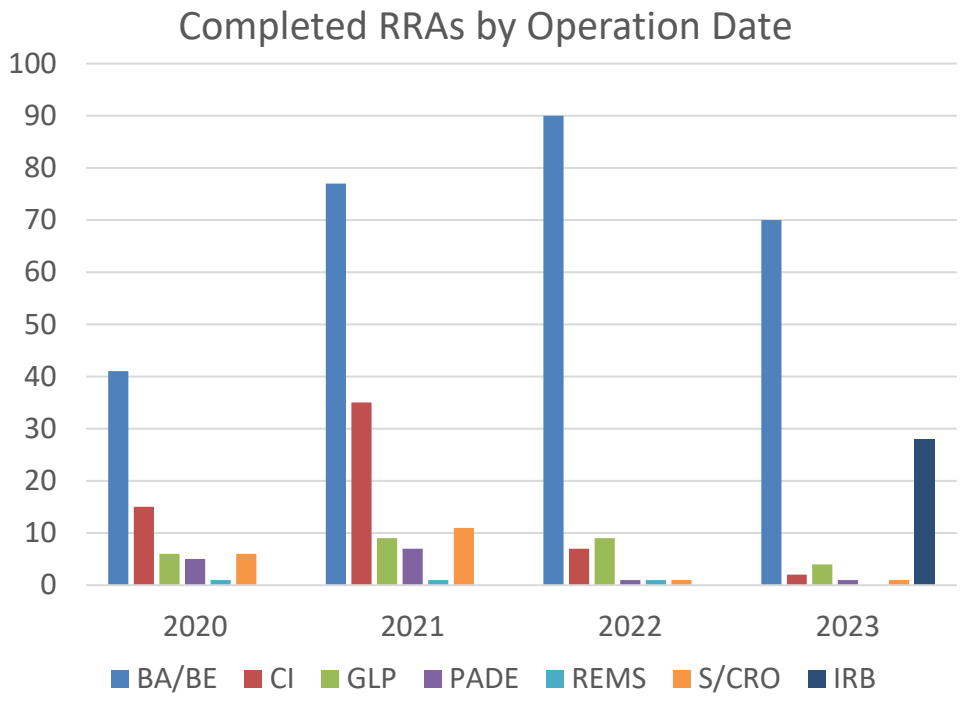
REMS Inspection Final Classifications FY 2017-2023



	2017	2018	2019	2020	2021	2022	2023
NAI	15	13	15	4	2	11	7
VAI	0	1	2	2	2	1	1
OAI	0	0	0	0	0	0	0

- CDER Specific Program

Remote Regulatory Assessments Completed FY 2020-2023



Program area	2020	2021	2022	2023
Bioavailability/ Bioequivalence	41*	77*	90*	70
Clinical Investigator	15	35	7	2
Good Laboratory Practice	6	9*	9*	4*
Postmarketing Adverse Drug Experience	5	7	1	1
Risk Evaluation and Mitigation Strategies	1	1	1	0
Sponsor/Contract Research Organization	6	11	1	1
Internal Review Board	0	0	0	28

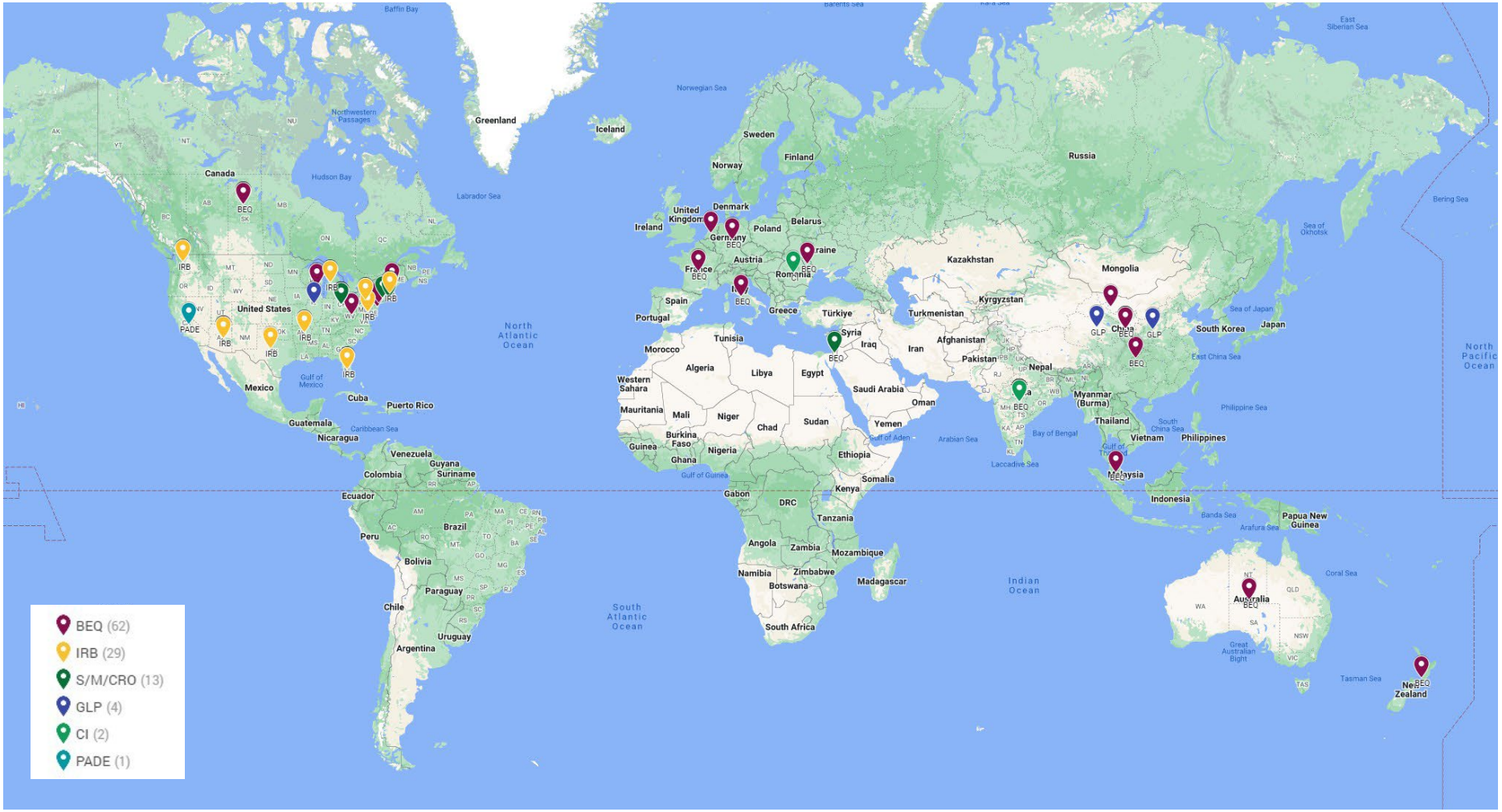
*CDER/OSIS Completed RRAs:

- FY20: 36 BA/BE RRAs (14 Clinical, 22 Analytical)
- FY21: 68 BA/BE RRAs (18 Clinical, 50 Analytical); 7 GLP RRAs
- FY22: 79 analytical BA/BE RRAs; 9 GLP RRAs
- FY23: 61 analytical BA/BE RRAs; 4 GLP RRAs

Note: *The BA/BE & GLP data for CDER/OSIS was updated on 5/29/24 to reflect the number of completed RRAs by operation date.*

Terms

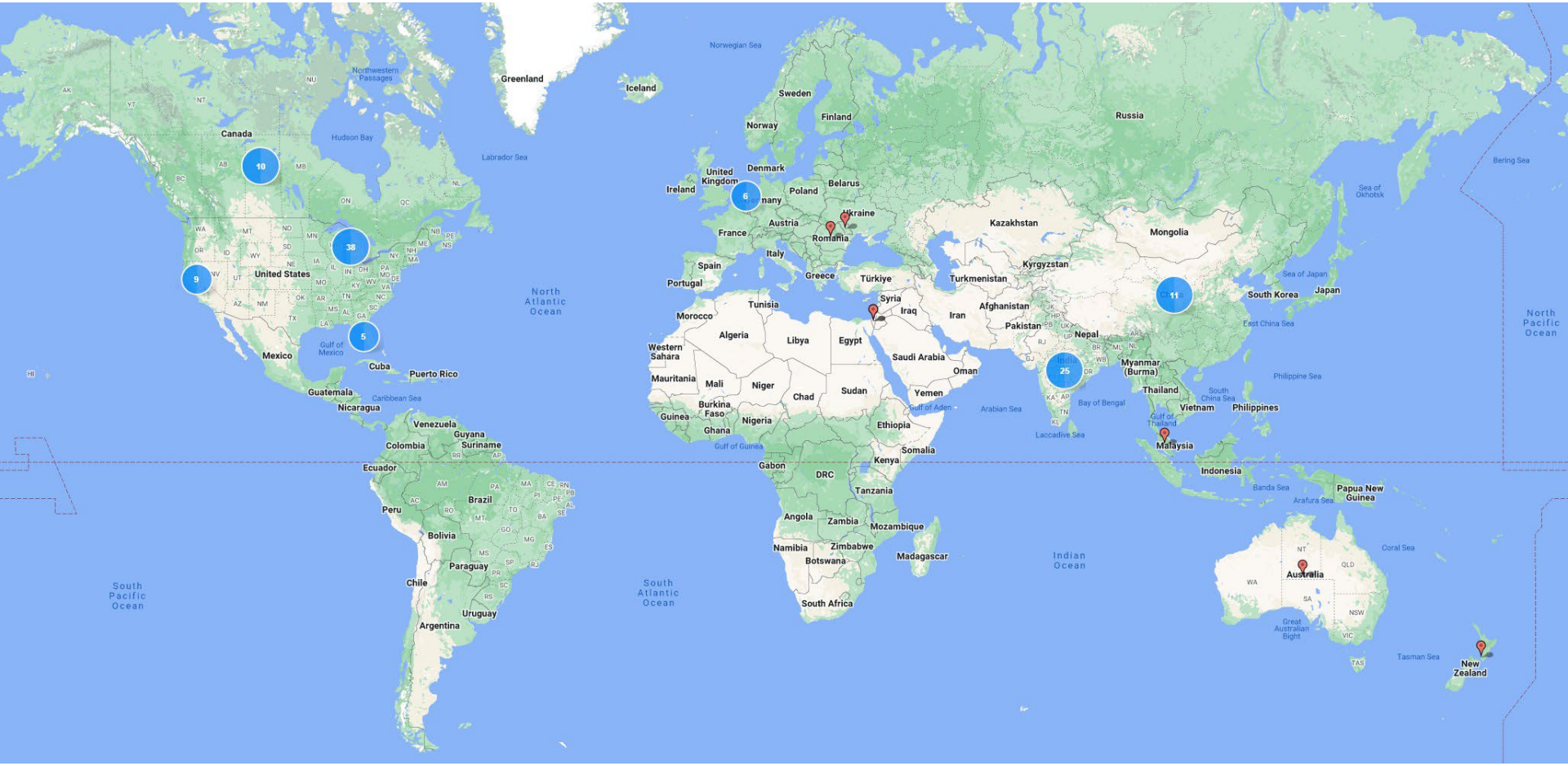
Location Points for RRAs Conducted FY23 by Program area



This GeoMap represents the location points of the firms that were evaluated by RRA.

Created using Google Maps

Location Points for RRAs Conducted in FY23



This GeoMap is static and represents the breakdown by count of the firms that were evaluated by RRA.

Created using Google Maps

References

- FDA's Bioresearch Monitoring Compliance Programs:
  - In Vivo Bioavailability-Bioequivalence Studies - Clinical, 7348.003
  - In Vivo Bioavailability-Bioequivalence Studies - Analytical, 7348.004
  - Inspections of Nonclinical Laboratories Conducting Animal Rule-Specific Studies, 7348.007
  - Good Laboratory Practice (Nonclinical Laboratories), 7348.808
  - Good Laboratory Practice Program (Nonclinical Laboratories) EPA Data Audit Inspections, 7348.808A
  - Institutional Review Board, 7348.809
  - Radioactive Drug Research Committee, 7348.809A
  - Sponsors and Contract Research Organizations, 7348.810
  - Clinical Investigators and Sponsor-Investigators, 7348.811
  - Postmarketing Adverse Drug Experience (PADE) Reporting Inspections, 7353.001
  - Risk Evaluation and Mitigation Strategies (REMS) Reporting Inspections, 7353.001c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