Bioresearch Monitoring (BIMO) Fiscal Year 2022 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) 2022.

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. On-site surveillance inspections resumed in July 2021.

- 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 slides 31- 32 for a complete breakdown.

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/conducting-remote-regulatory-assessments-questions-and-answers

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 Strategy
- S: Sponsor
- SI: Sponsor-Investigator

Inspection Classifications

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

Evaluations

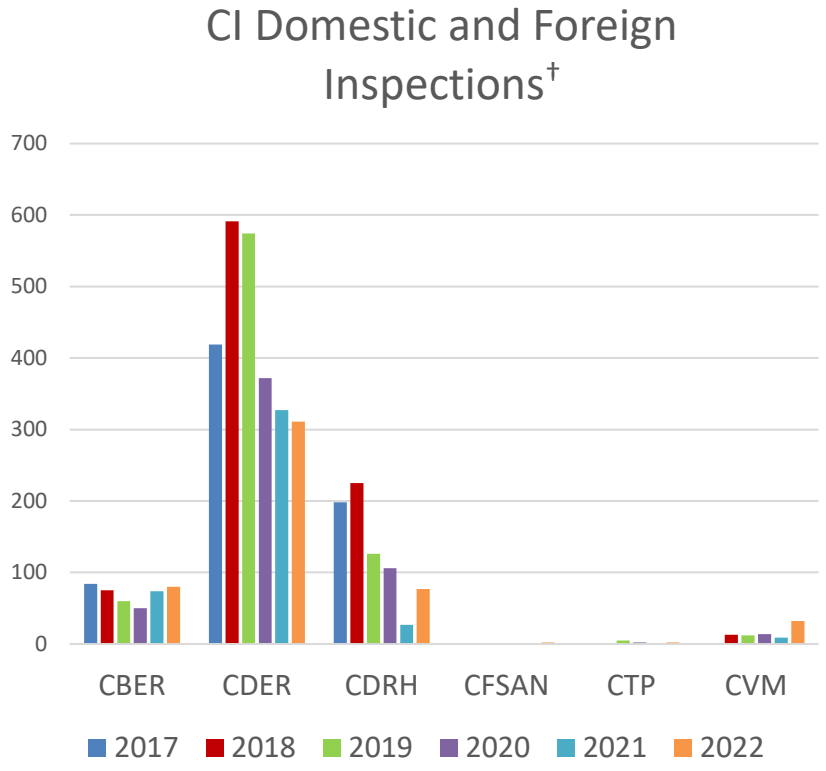
- RRA: Remote Regulatory Assessment

BIMO Inspection Final Classifications by Center – FY 2022*

Center	CI	IRB	S/M/CRO	S/I	GLP	BEQ	PADE	REMS	Total
CBER	80	10	10	0	8	0	0	0	108
CDER	311	7	48	9	7	42	35	12	471
CDRH	77	31	22	1	7	0	0	0	138
CFSAN	2	1	0	0	1	0	0	0	4
CTP	2	0	0	0	0	0	0	0	2
CVM	32	0	1	0	10	0	0	0	43
Total	504	49	81	10	33	42	35	12	766

www.fda.gov *Includes both Domestic and Foreign inspections

Clinical Investigator Inspections Conducted FY 2017- 2022*



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

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

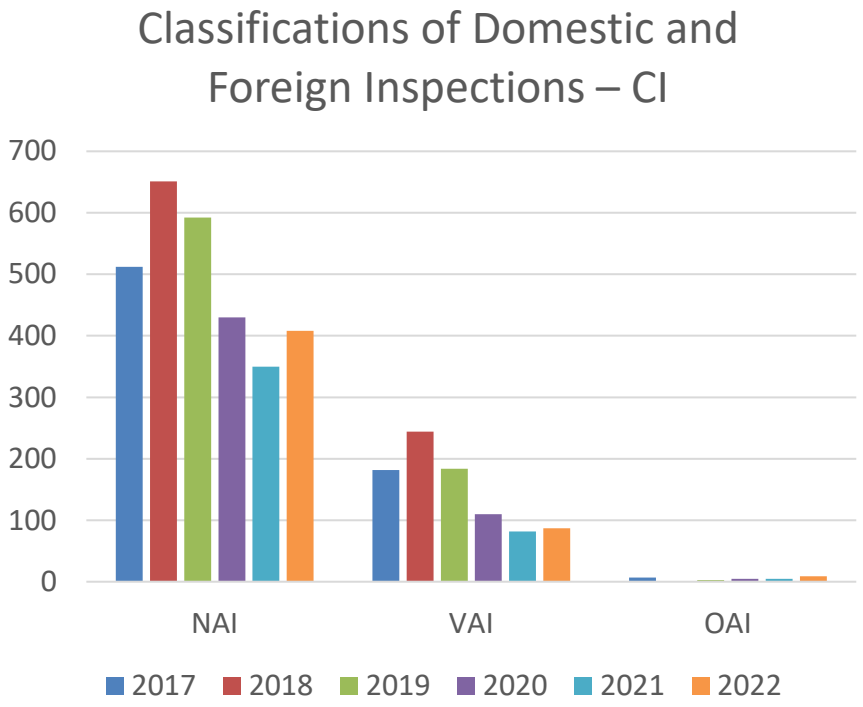
†Based on final classification date

Common Clinical Investigator Inspectional Observations*

- Failure to comply with Form FDA 1572 requirements, protocol compliance
- 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
- Safety reporting; failure to report and/or record adverse events
- Inadequate subject protection; informed consent issues

 *Most common observations collected from issued FDA Form 483s

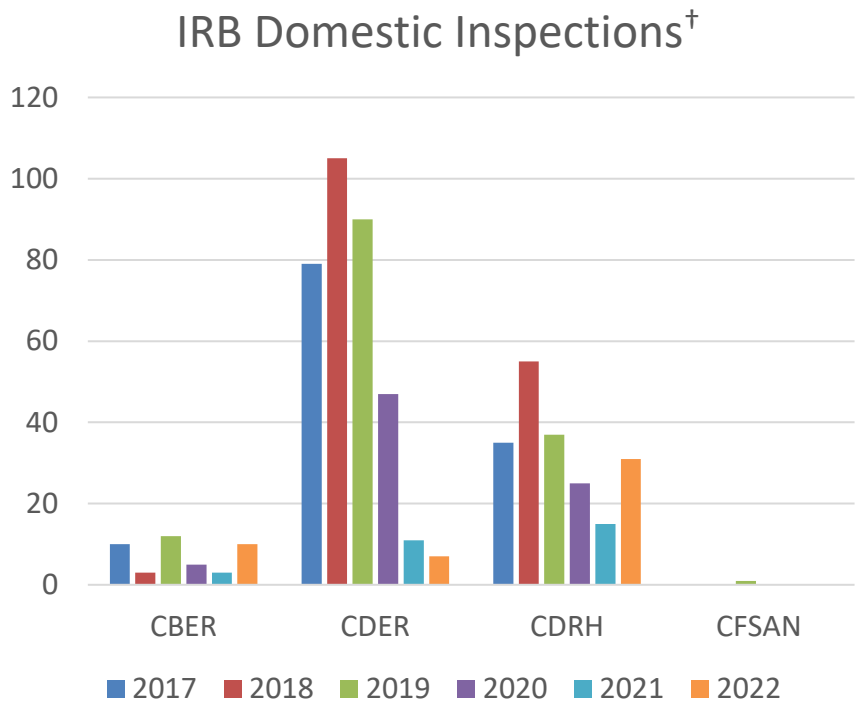
Clinical Investigator Inspections Final Classified FY 2017-2022



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

Return to the inspections conducted slide

IRB and RDRC Inspections Conducted FY 2017- 2022*



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

* Includes CDER completed RDRC inspections (none conducted FY21 and FY22):
FY17: 2; FY18: 4; FY19: 2; FY20: 4

Terms †*Based on final classification date*

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

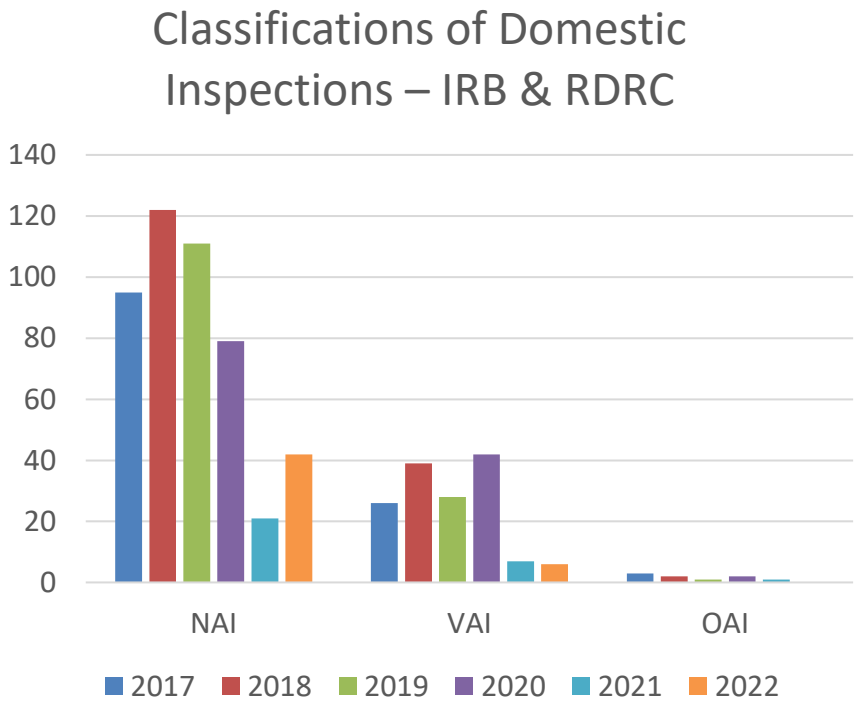
 *Most common observations collected from issued FDA Form 483s

Radioactive Drug Research Committee Inspectional Observations during FY2017-FY2020*

- 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

* There were No RDRC inspections completed for FY2021 & FY2022

IRB and RDRC Inspections Final Classified FY 2017-2022

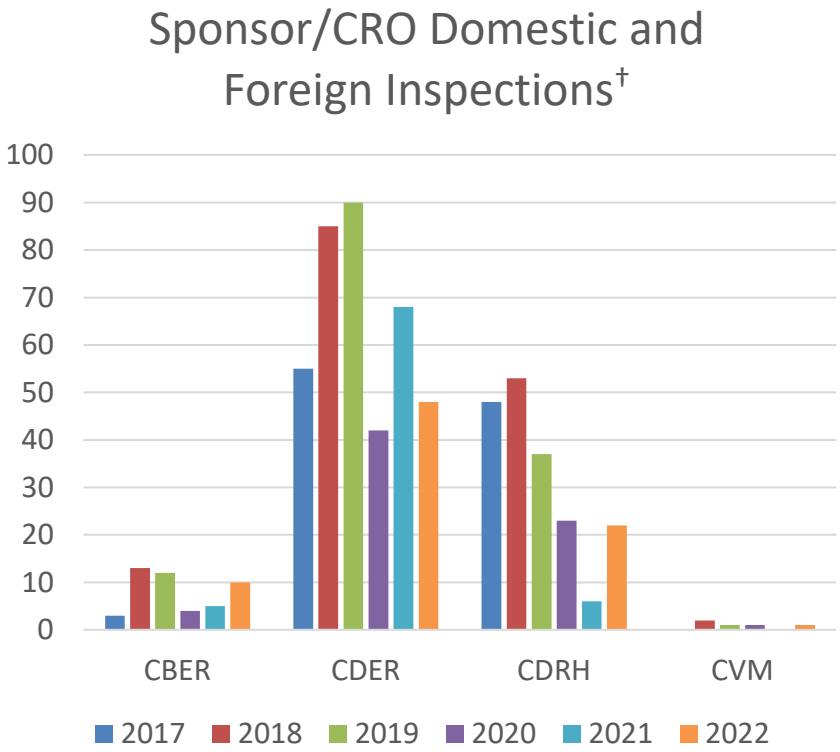


	2017	2018	2019	2020	2021	2022
NAI	95	122	111	45	21	42
VAI	26*	39*	28*	31*	7	6
OAI	3	2	1	1	1	0

* Includes CDER completed RDRC inspections (none conducted FY21 and FY22):
FY17: 2; FY18: 4; FY19: 2; FY20: 4

Return to the inspections conducted slide

Sponsor/CRO Inspections Conducted FY 2017-2022*



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

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

Terms

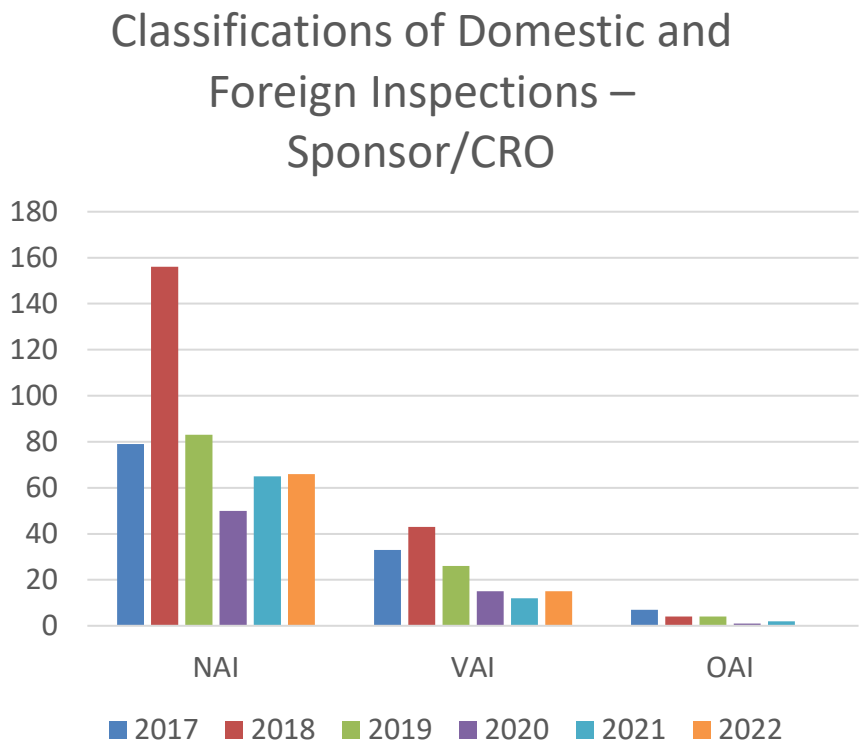
†Based on final classification date

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

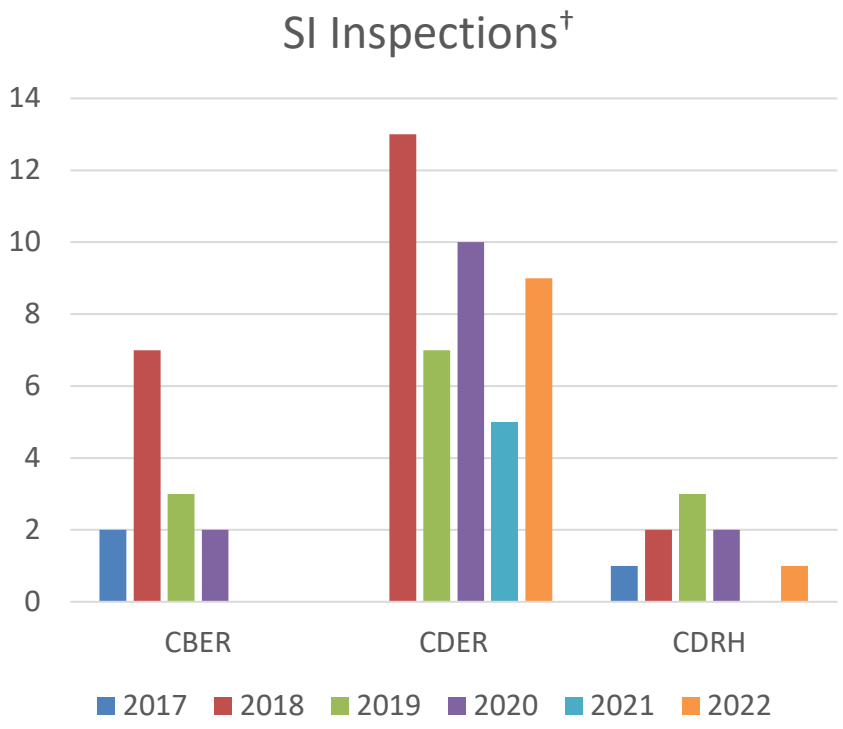
Sponsor/CRO Inspections
Final Classified FY 2017-2022



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

Return to the inspections conducted slide

Sponsor-Investigator Inspections Conducted FY 2017-2022



Center	2017	2018	2019	2020*	2021*	2022
CBER	2	7	3	2	0	0
CDER	0	13	7	10	5	9
CDRH	1	2	3	2	0	1

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

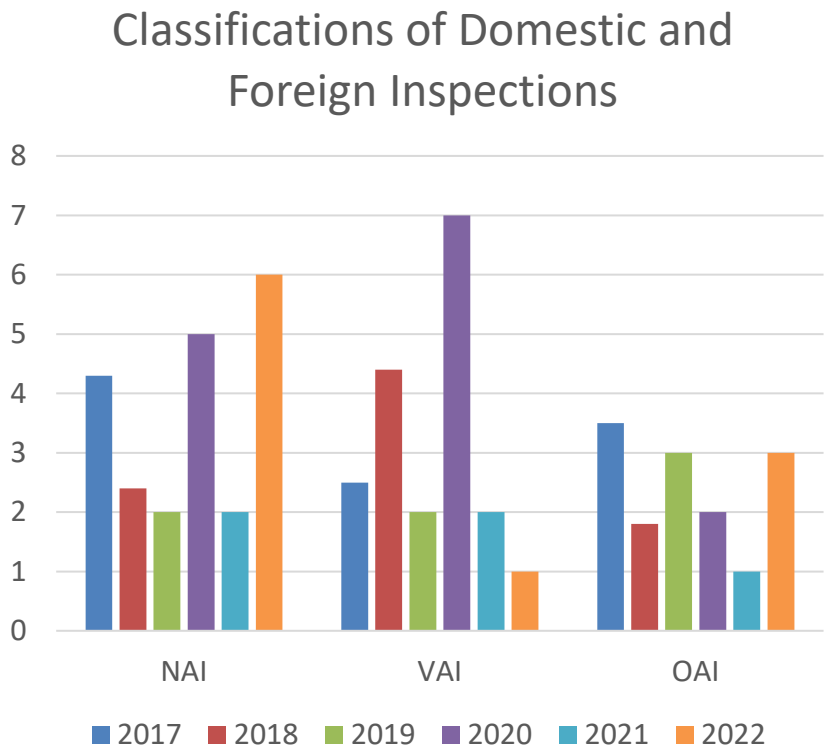
†Based on final classification date

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

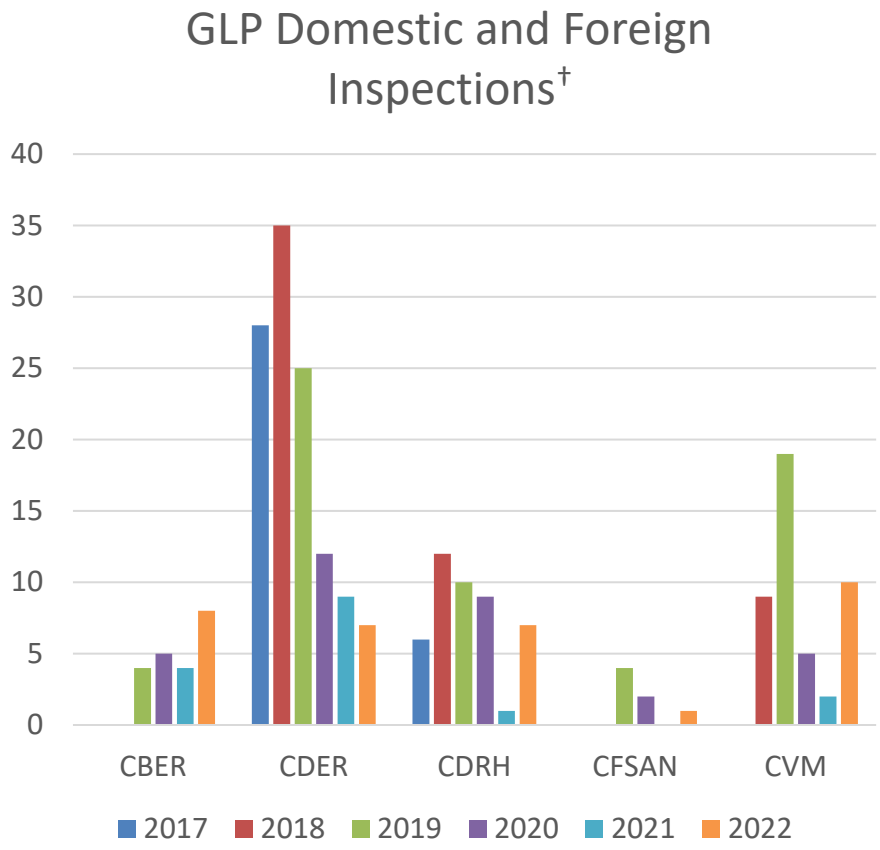
Sponsor-Investigator Inspections Final Classified FY 2017-2022



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

Return to the inspections conducted slide

Good Laboratory Practice Inspections Conducted FY 2017-2022



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

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

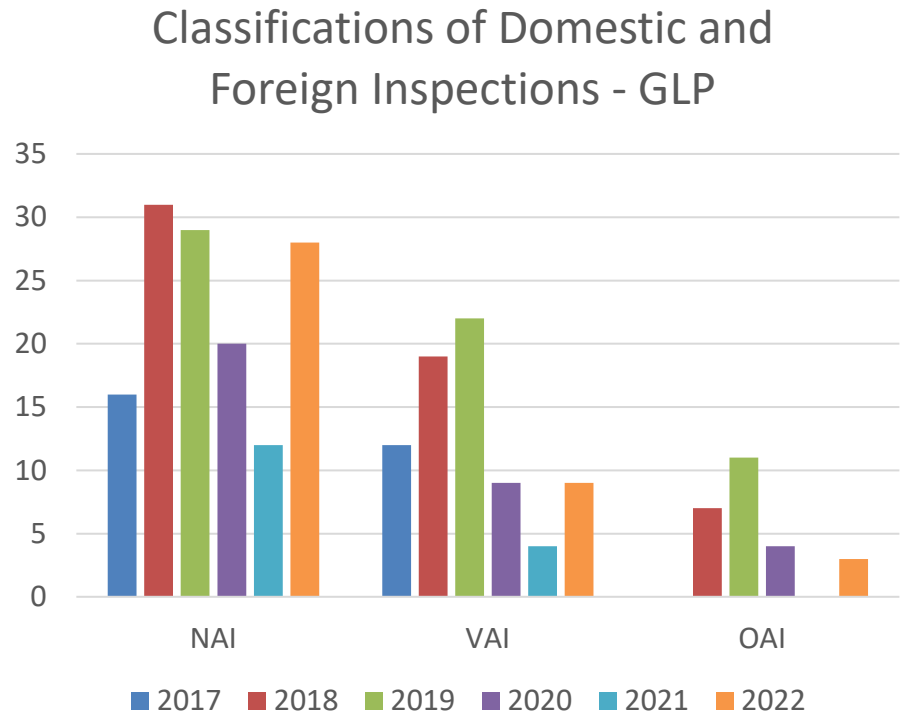
†Based on final classification date

Common Good Laboratory Practice Inspectional Observations*

- 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
- 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
- Missing standard operating procedures (SOPs)
- Final report did not include all circumstances affecting quality or integrity of the data

 *Most common observations collected from issued FDA Form 483s

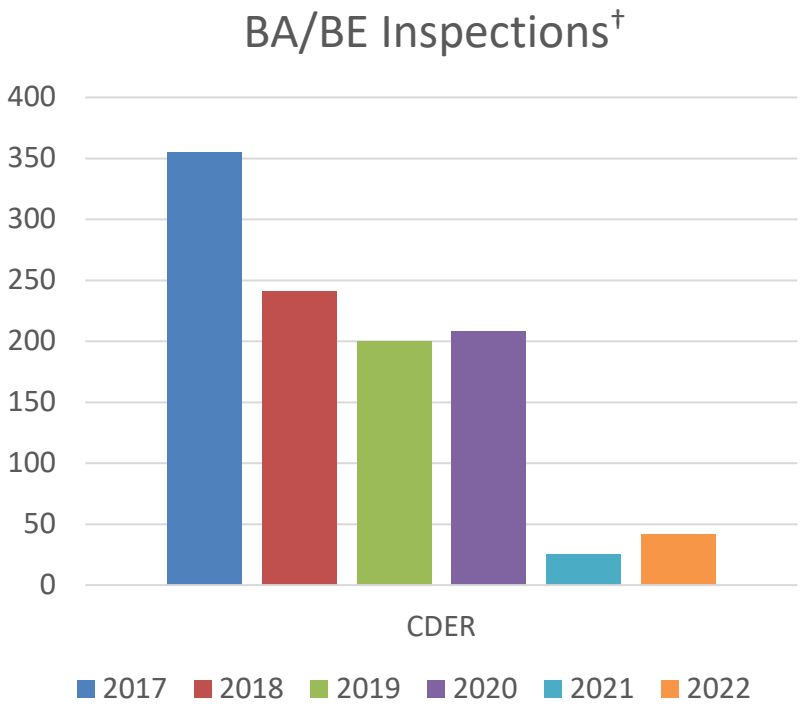
Good Laboratory Practice Inspections Final Classified FY 2017-2022



	2017	2018	2019	2020	2021	2022
NAI	16	31	29	20	12	28
VAI	12	19	22	9	4	9
OAI	0	7	11	4	0	3

Return to the inspections conducted slide

Bioavailability/Bioequivalence Inspections Conducted FY 2017-2022*



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

- 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.

†Based on final classification date

Common Bioavailability/Bioequivalence Inspectional/RRA Observations*

Clinical

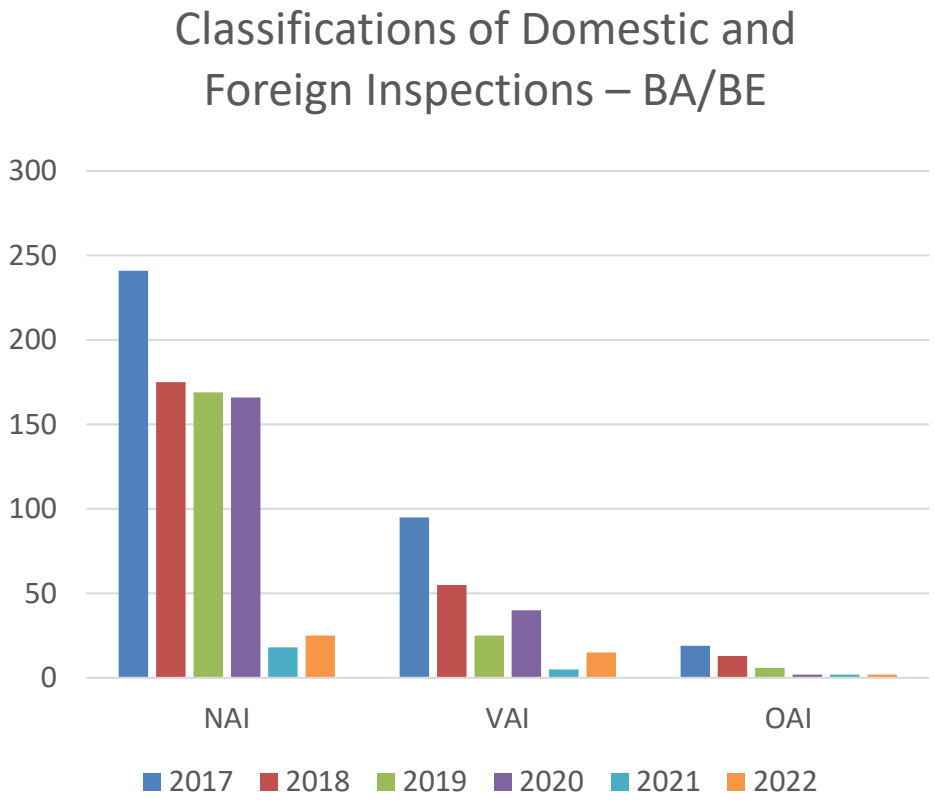
- Inadequate record keeping; inadequate drug accountability
- Did not follow the investigational plan; protocol deviations
- Inadequate subject protection; informed consent

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

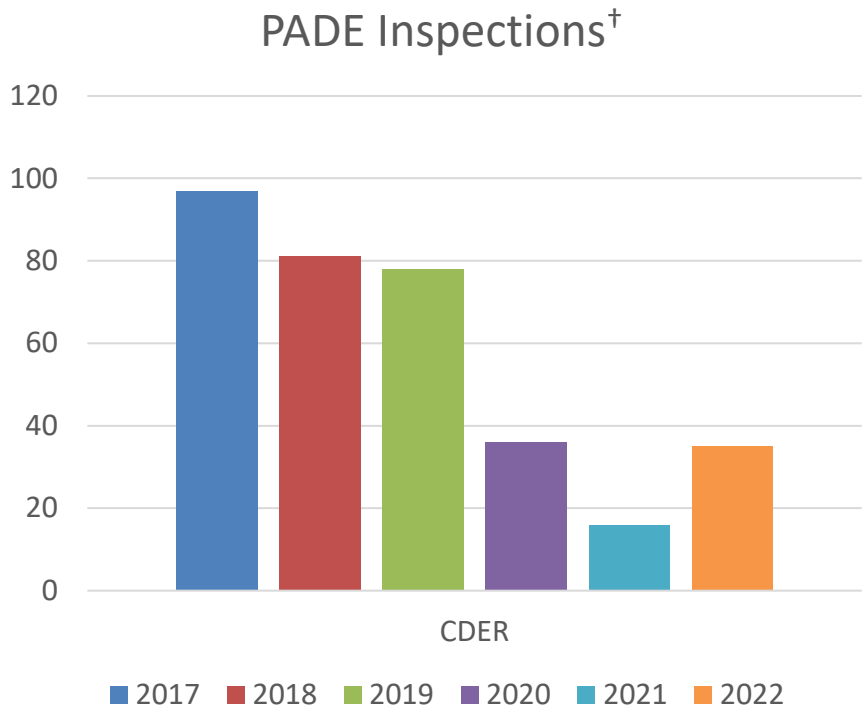
Bioavailability/Bioequivalence Inspections Final Classified FY 2017-2022



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

- CDER Specific Program

Postmarketing Adverse Drug Experience Inspections Conducted FY 2017-2022*



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

- CDER Specific Program

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

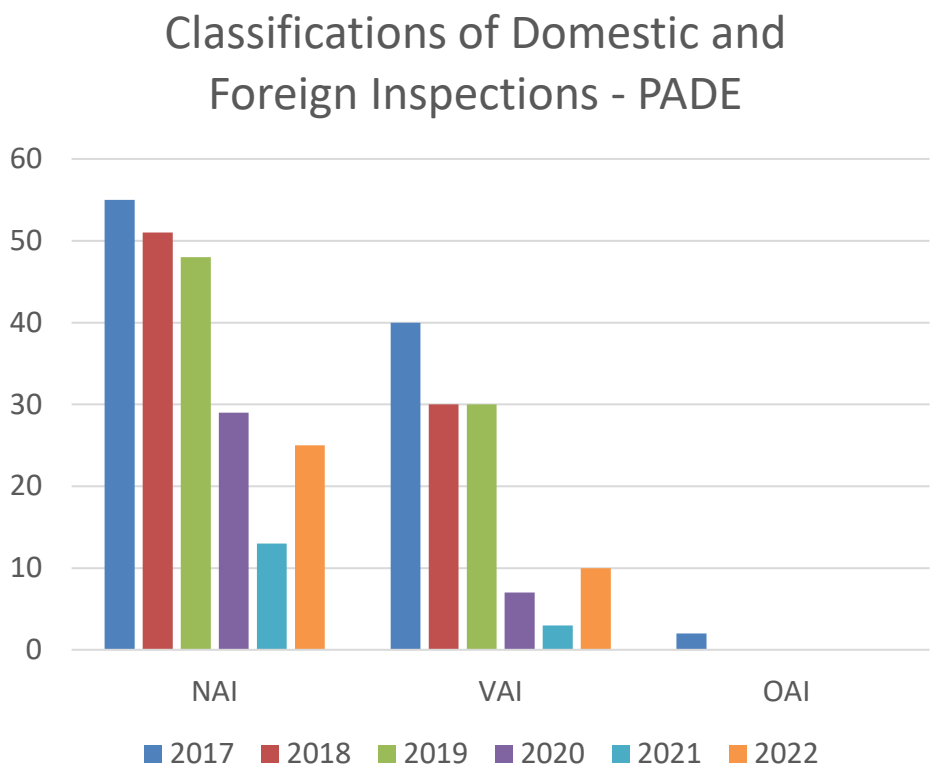
†Based on final classification date

Common Postmarketing Adverse Drug Experience 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
- Late submission of quarterly safety reports
- Failure to investigate serious, unexpected events
- Failure to maintain records; incomplete initial reporter information on individual case study reports (ICSR)

 *Most common observations collected from issued FDA Form 483s

PADE Inspections Final Classified FY 2017-2022

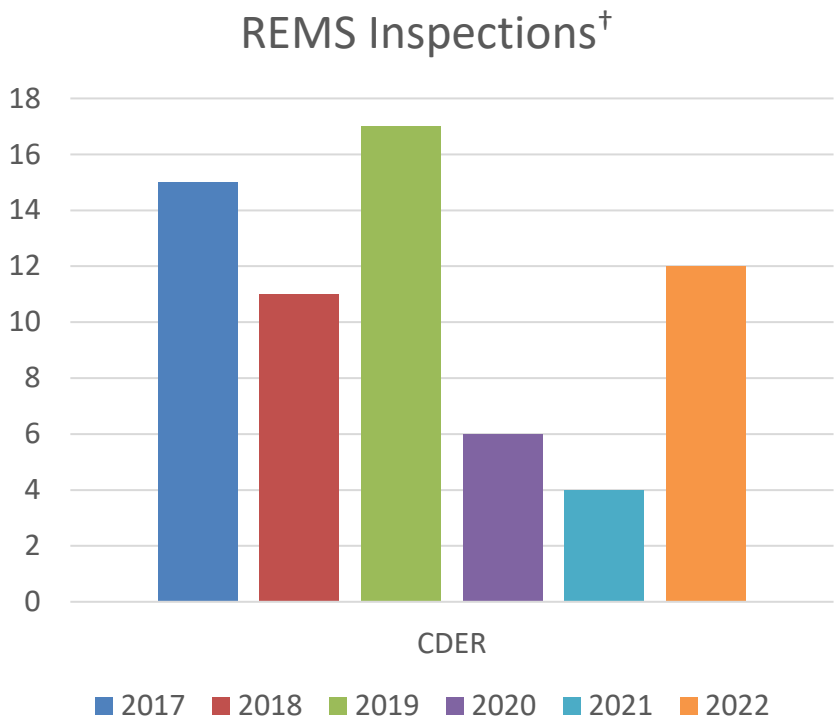


	2017	2018	2019	2020	2021	2022
NAI	55	51	48	29	13	25
VAI	40	30	30	7	3	10
OAI	2	0	0	0	0	0

- CDER Specific Program

Terms

Risk Evaluation and Mitigation Strategies Inspections Conducted FY 2017-2022*



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

- CDER Specific Program

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

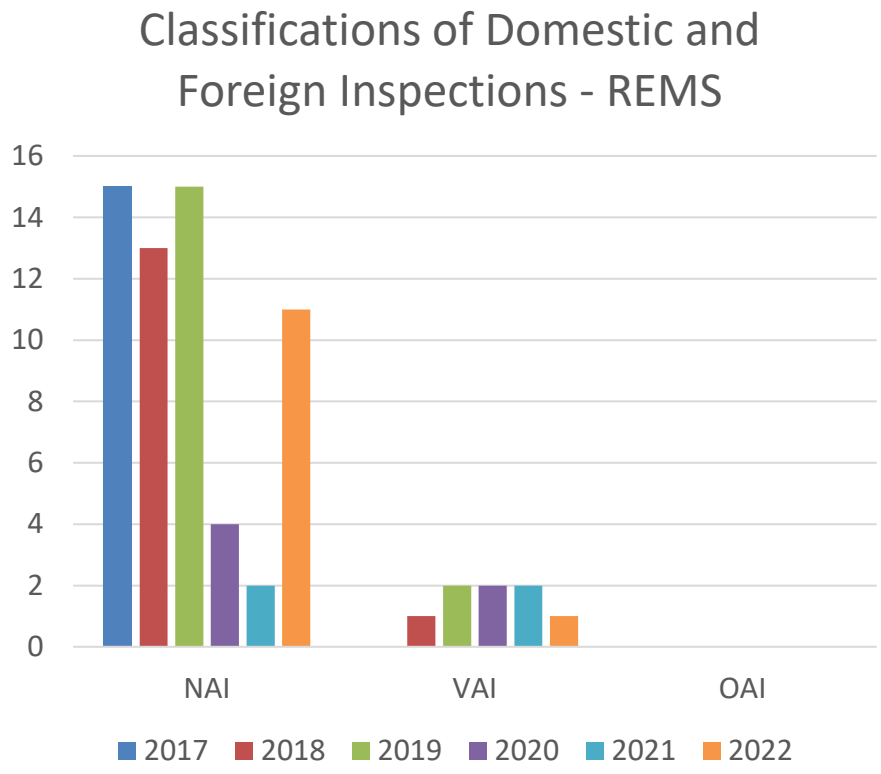
†*Based on final classification date*

Common Risk Evaluation and Mitigation Strategies Inspectional Observations*

- 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
- Failure to dispense the Medication Guide, as required by approved REMS Medication Guide

*Most common observations collected from issued FDA Form 483s

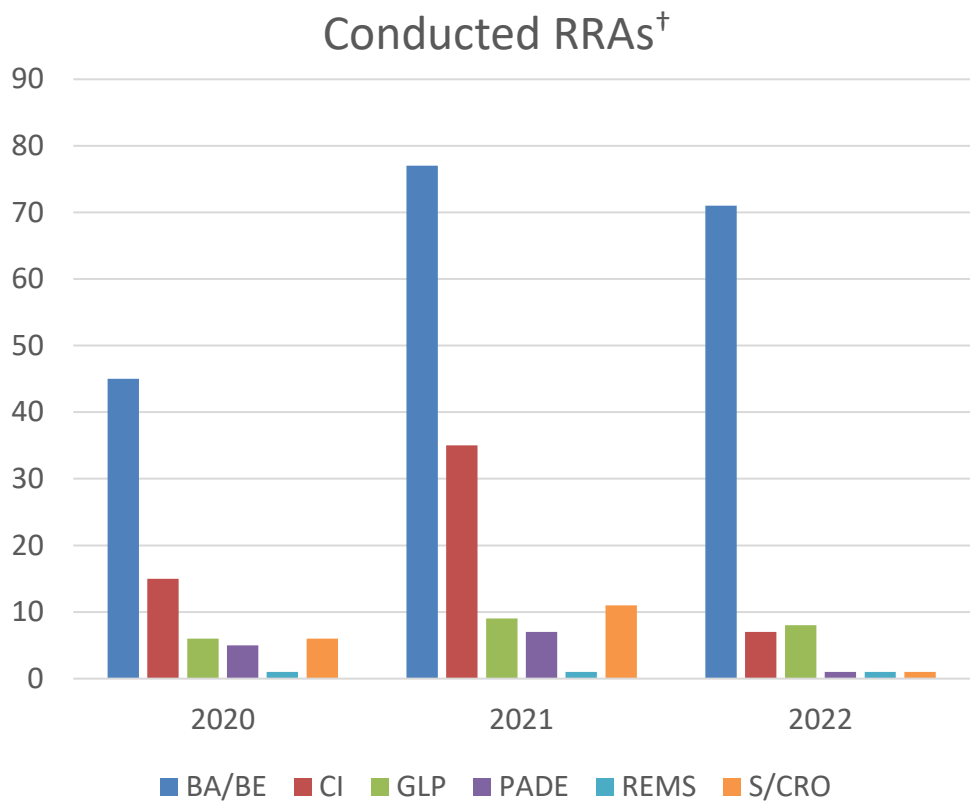
REMS Inspections Final Classified
FY 2017-2022



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

- CDER Specific Program

Remote Regulatory Assessments Conducted FY 2020-2022



Program area	2020	2021	2022
Bioavailability/ Bioequivalence	45*	77*	71*
Clinical Investigator	15	35	7
Good Laboratory Practice	6	9*	8*
Postmarketing Adverse Drug Experience	5	7	1
Risk Evaluation and Mitigation Strategies	1	1	1
Sponsor/Contract Research Organization	6	11	1
totals	78	140	89

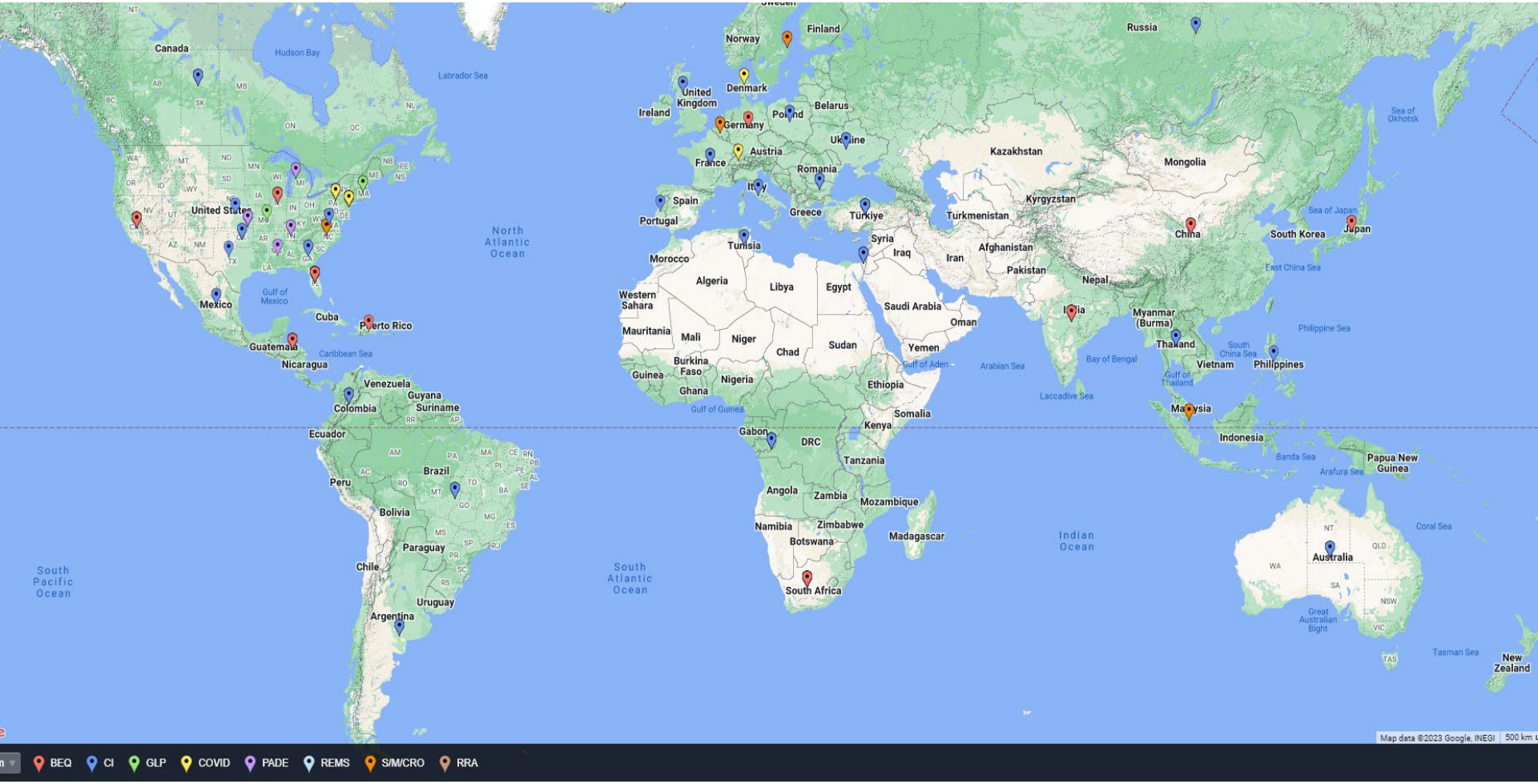
*CDER/OSIS Completed RRAs:

- FY20: 40 BA/BE RRAs (18 Clinical, 22 Analytical)
- FY21: 68 BA/BE RRAs (18 Clinical, 50 Analytical); 7 GLP RRAs
- FY22: 60 analytical BA/BE RRAs; 8 GLP RRAs

Terms

†Based on completion date

Location Points for RRAs Conducted FY20-FY22 by Program area



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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