Office of Scientific Investigations & Office of Study Integrity and Surveillance

BIMO Metrics

Fiscal Year 2020

(Oct 1, 2019 – Sep 30, 2020)

[Data Updated: Feb 9, 2021]

Metrics Overview

- These slides provide annual inspection metrics for the compliance programs overseen by the Office of Scientific Investigations (OSI) and the Office of Study Integrity and Surveillance (OSIS) in FDA's Center for Drug Evaluation and Research (CDER). The vast majority of Inspection Activities are conducted by FDA's Office of Regulatory Affairs (ORA).
- As FDA's approval decisions are based on a review of the data submitted by an applicant, it is essential to ensure the integrity of the data submitted and to verify that the rights, safety and welfare of those who participated in the studies were protected and that applicants continue to meet their obligations (e.g., for safety reporting) after approval. On-site inspection is one of many tools the FDA has for ensuring the integrity of data, the health and welfare of research participants, and the protection of public health.

CDER Bioresearch Monitoring Metrics Overview

- Data source:
  - Data obtained from FDA's Complis (Complis Management System) database and other sources as noted.

- Data conventions
  - Metrics are based on key events during the inspection process, including issuing an inspection assignment, starting an inspection, or issuing post-inspectional correspondence to the inspected party.

  - Differences in inspection counts when comparing data across varying sources (e.g. The Office of Regulatory Affairs' eNspect & FACTS databases) may be the result of different tallying methods of inspection-related data.

- Changes from prior versions
  - Footnotes in individual slides indicate where significant changes from previous versions have occurred. These changes are due to refinements in data collection and associated processes.

For further information, please call 301-796-3150.

COVID-19 Pandemic

- Due to the COVID-19 pandemic, routine surveillance inspections in support of the BIMO program were postponed beginning in March 2020. Pre-approval and for-cause assignments deemed mission-critical are being considered for inspection on a case-by-case basis.

- ORA is now using a COVID-19 Advisory Rating system to determine when other Inspection Activity may be conducted (i.e., surveillance and other non-mission critical Inspection Activity) in a given geographic region.

- Where possible, other pathways are being used to inform decisions regarding pending applications including requesting existing inspection reports from other trusted foreign regulator partners and requesting information from applicants and other inspected entities directly.

https://www.fda.gov/media/141312/download

COVID-19 Alternative Approaches

- To continue supporting our mission, BIMO introduced Remote Regulatory Assessments (RRA), which are voluntary remote evaluations of data and processes conducted via video and teleconference. RRAs allow ORA/BIMO staff to continue to review study data and information and provide an evaluation to center staff to aid in application review.

- Remote Record Reviews (RRR) are an alternative to inspection involving a voluntary interaction with a site of interest. Site records are evaluated by Center staff, which are followed by a series of remote video and teleconference meetings to discuss questions, concerns and findings.

- RRAs and RRRs are not equivalent to on-site inspection.

- Data for RRAs and RRRs are not reflected in the final classification charts for each program area as they did not result in a final classification.

Metrics Terms

Organizations and Programs

- BA/BE: Bioavailability/Bioequivalence
- BE or BEQ: Bioequivalence
- BIMO: Bioresearch Monitoring
- CBER: Center for Biologics Evaluation and Research
- CDER: Center for Drug Evaluation and Research
- CDRH: Center for Devices and Radiological Health
- CI: Clinical Investigator
- CRO: Contract Research Organization
- GCP: Good Clinical Practice
- GLP: Good Laboratory Practice
- IRB: Institutional Review Board
- PADE: Postmarketing Adverse Drug Experience
- PMR: Postmarketing Requirements
- RDRC: Radioactive Drug Research Committee
- REMS: Risk Evaluation and Mitigation Strategy
- Sponsor: Sponsor or Sponsor-Investigator

Classifications

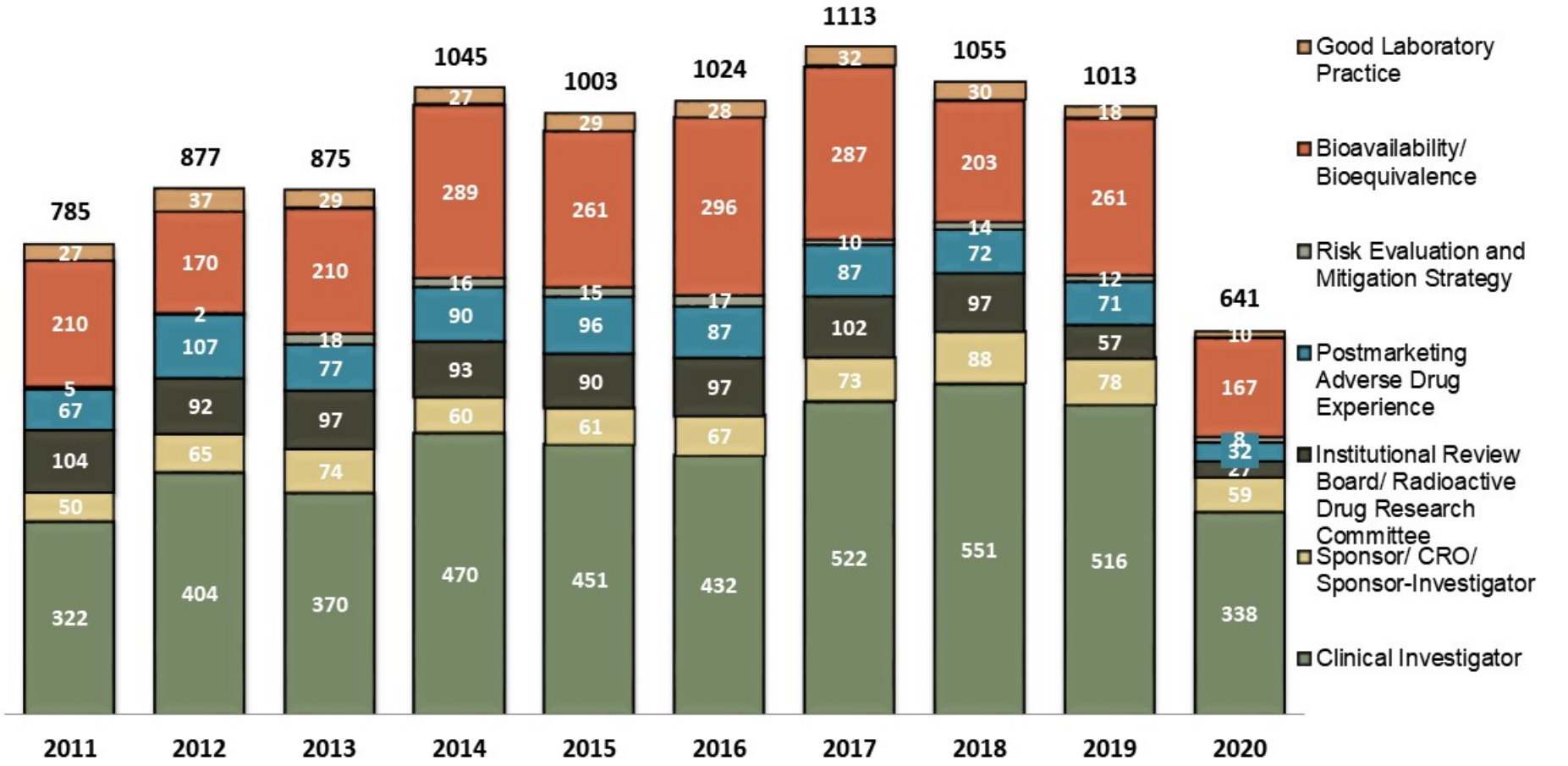
- CA-Restricted: Consent Agreement (Restricted Agreement)
- CA-Full DQ: Consent Agreement (Full Disqualification)
- DQ: Disqualification by Hearing or Commissioner
- NAI: No Action Indicated
- NIDPOE: Notice of Initiation of Disqualification Proceedings and Opportunity to Explain
- NOOH: Notice of Opportunity for Hearing
- OAI: Official Action Indicated
- VAI: Voluntary Action Indicated

Alternative Approaches

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

OSI/OSIS Inspection Activities*

(CDER, FY 2011 - FY 2020)

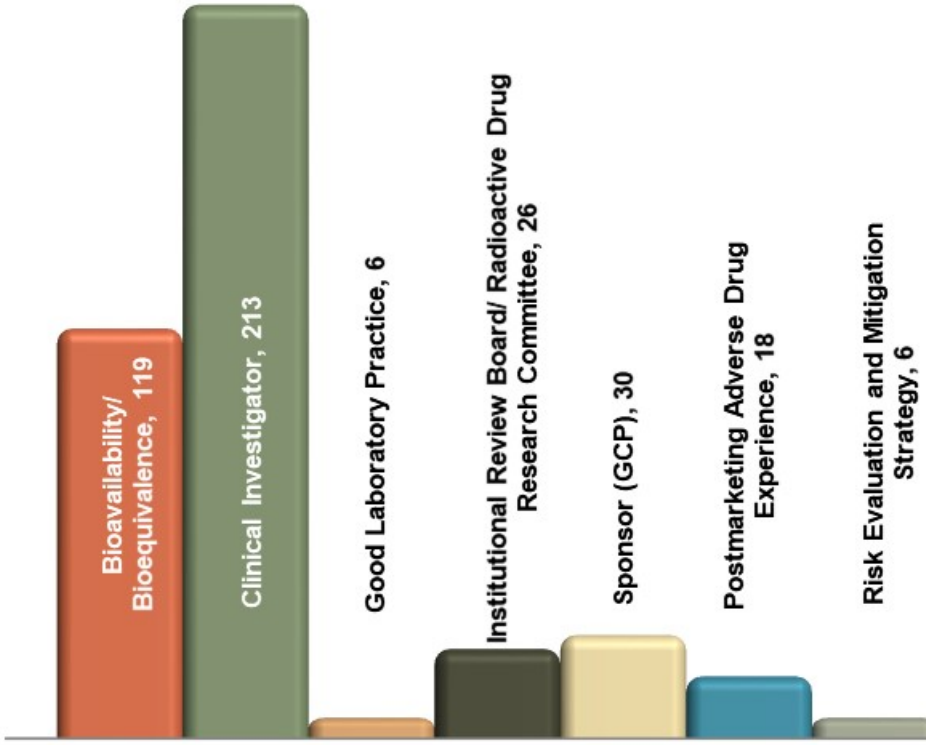


* Based on inspection activity start date – [Complis database as of Feb 9, 2021].

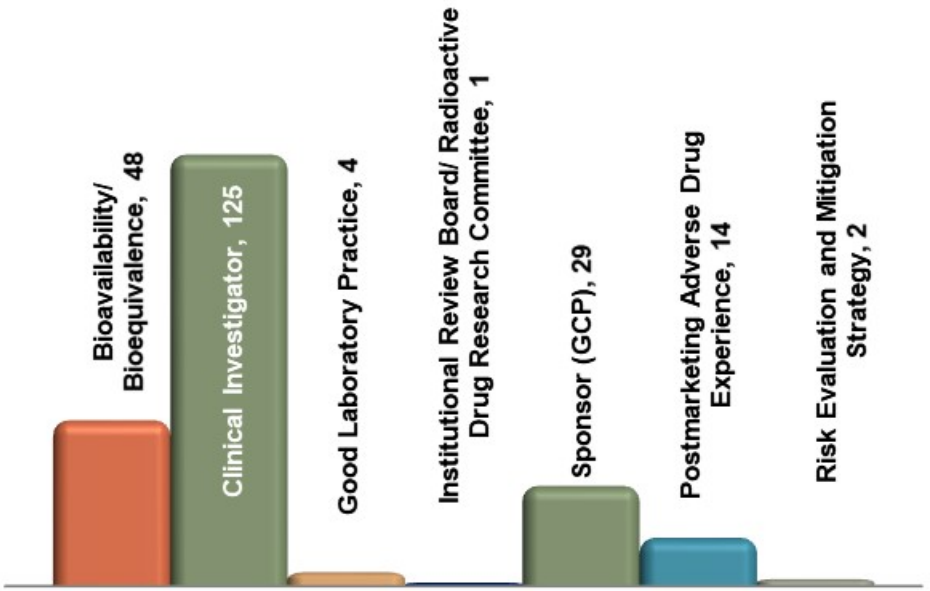
- inspection activities include use of alternative approaches (e.g., RRAs and RRR).
- An inspection activity may involve multiple applications and/or studies.

BIMO Inspection Activities: Impact of Pandemic*

(CDER, FY 2020)



Pre-Pandemic (Oct 1, 2019 - Mar 12, 2020)



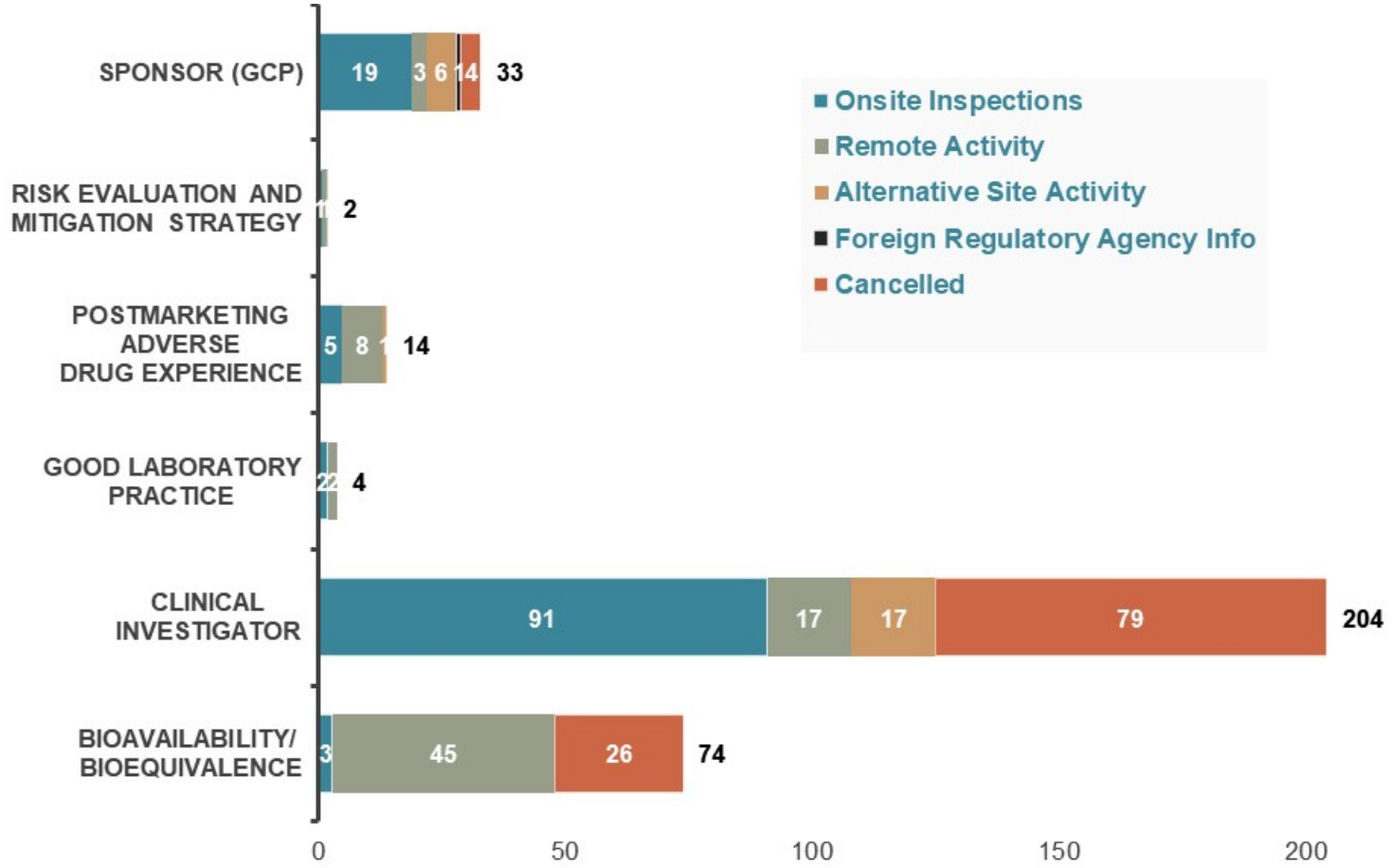
Post-Pandemic (Mar 13, 2020 - Sep 30, 2020)

*Based on inspection start date – [Complis database as of Feb 9, 2021].

- Travel restrictions began on March 13, 2020 in response to presidential declaration of national emergency.
- inspection activities include use of alternative approaches (e.g., RRAs and RRR).

Inspection Activity during COVID-19 Pandemic*

(CDER, FY 2020)

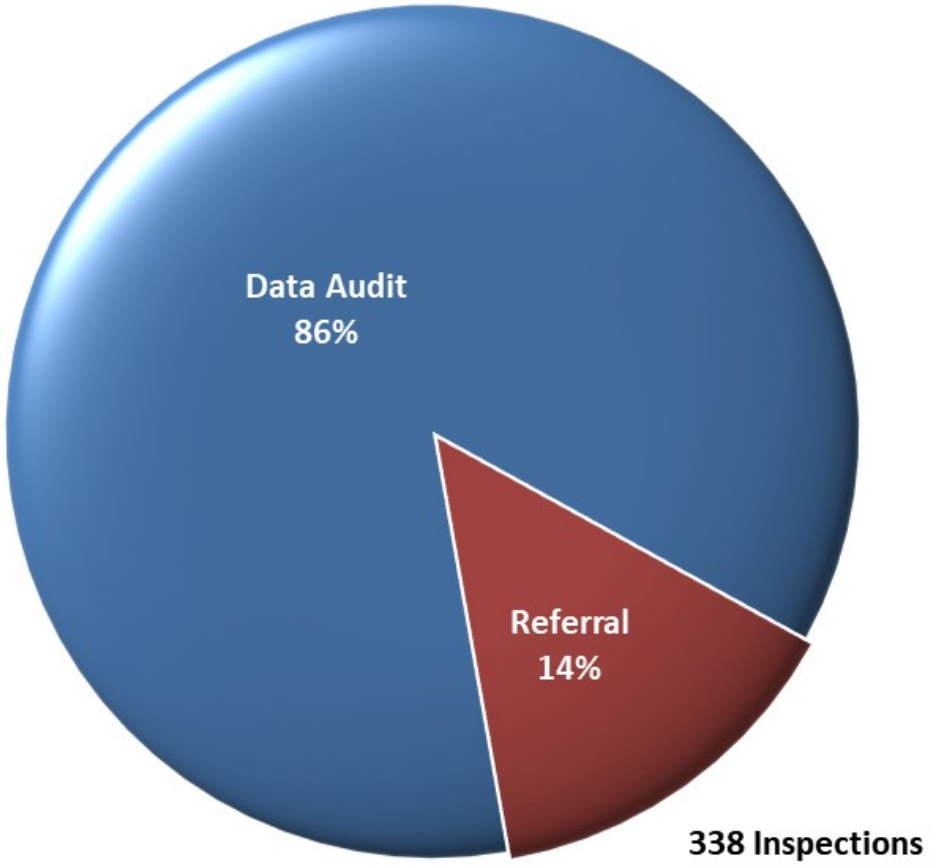


*Based on inspection start date – [Complis database as of Feb 9, 2021]..

- Foreign Regulatory Agency Info includes review using information sharing with Foreign Regulatory Counterparts.
- Remote Activity includes Remote Regulatory Assessments (RRA), Remote Record Reviews (RRR), Technical Assistance Memo (TAM).
- Alternative Site Activities include Inspection Activity and investigations at an alternative location to the site of interest.

Clinical Investigator: Data Audit versus Referral

(CDER, FY 2020)

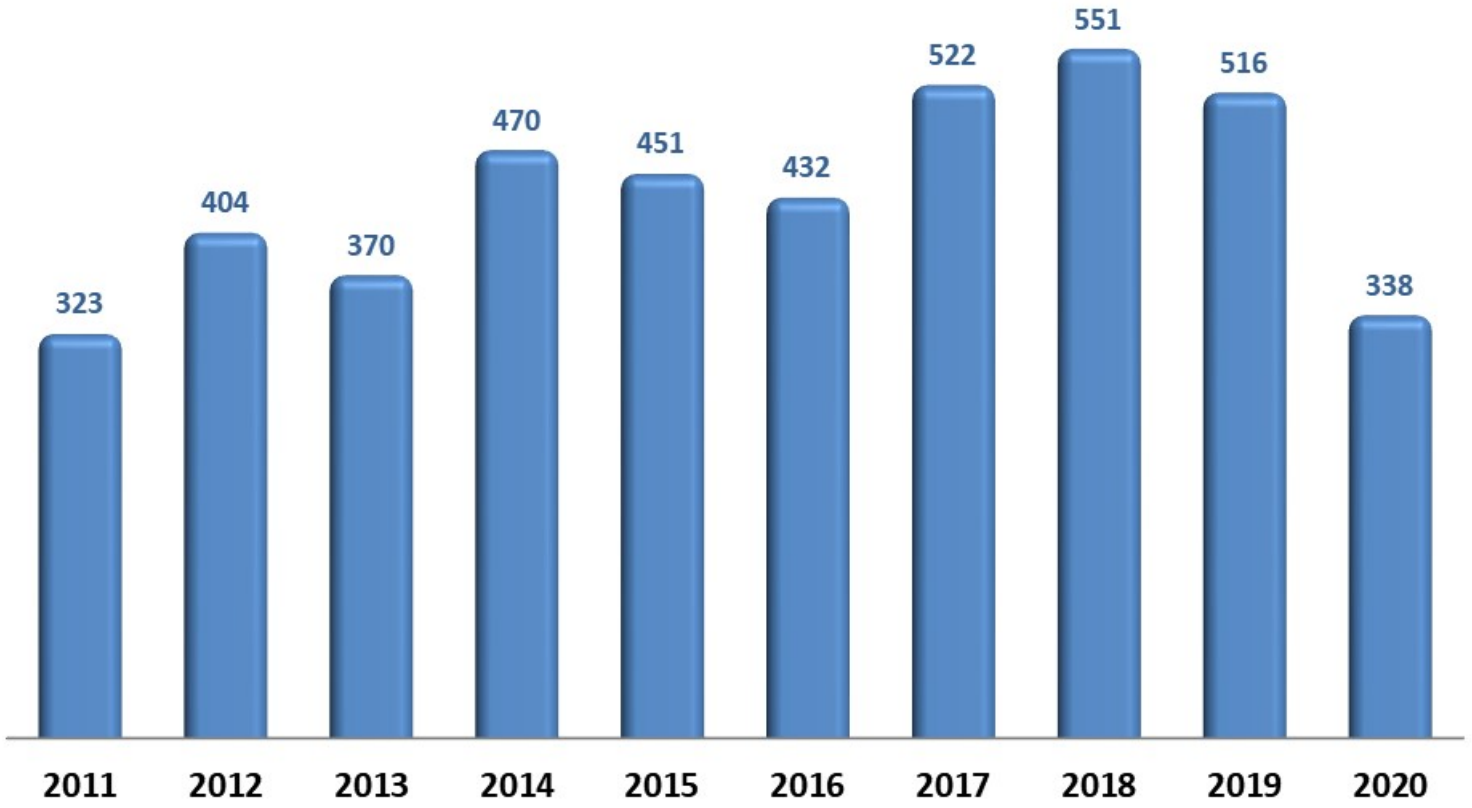


*Based on inspection start date – [Complis database as of Feb 9, 2021].

- Data Audits include Inspection Activity conducted in support of a marketing application.
- Referrals include Complaints, Required Reports, IRB/Sponsor Notifications, and other referrals-internal and external.

Clinical Investigator Inspection Activity*

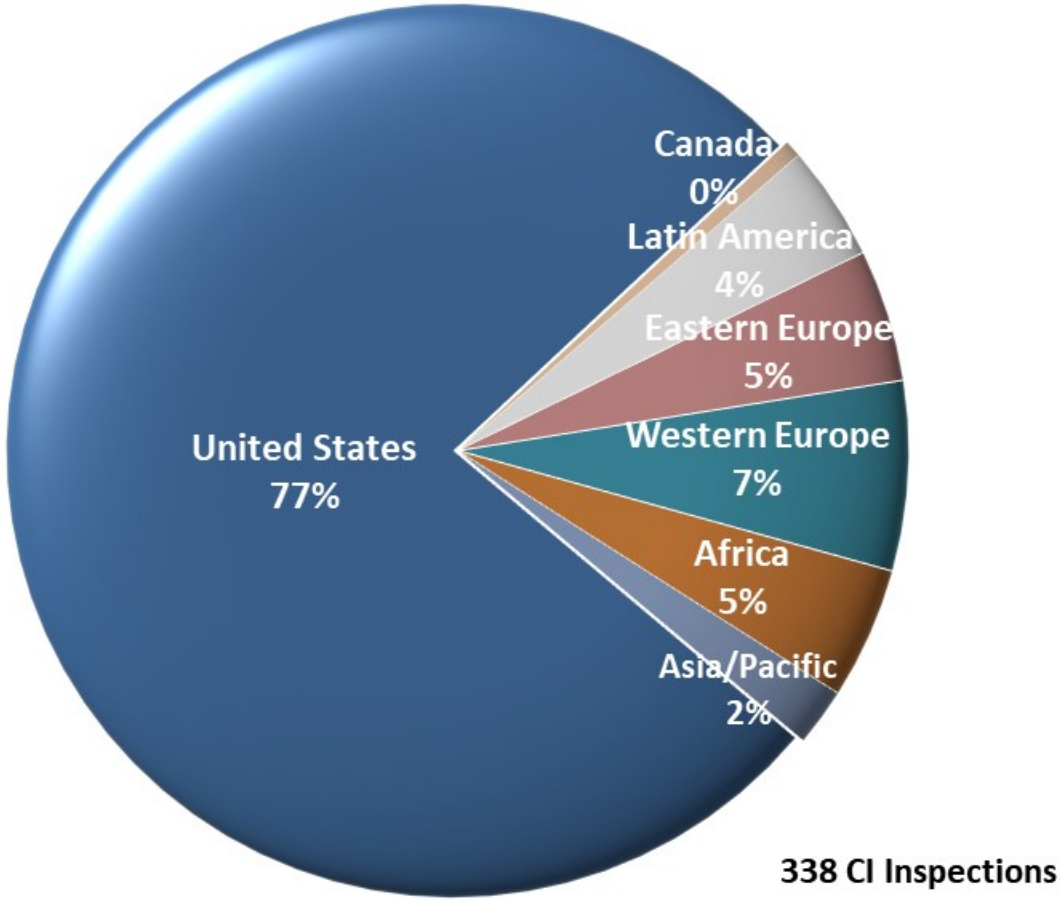
(CDER, FY 2011 – FY 2020)



* Based on inspection start date – [Complis database as of Feb 9, 2021].

Clinical Investigator Inspection Activity by Location*

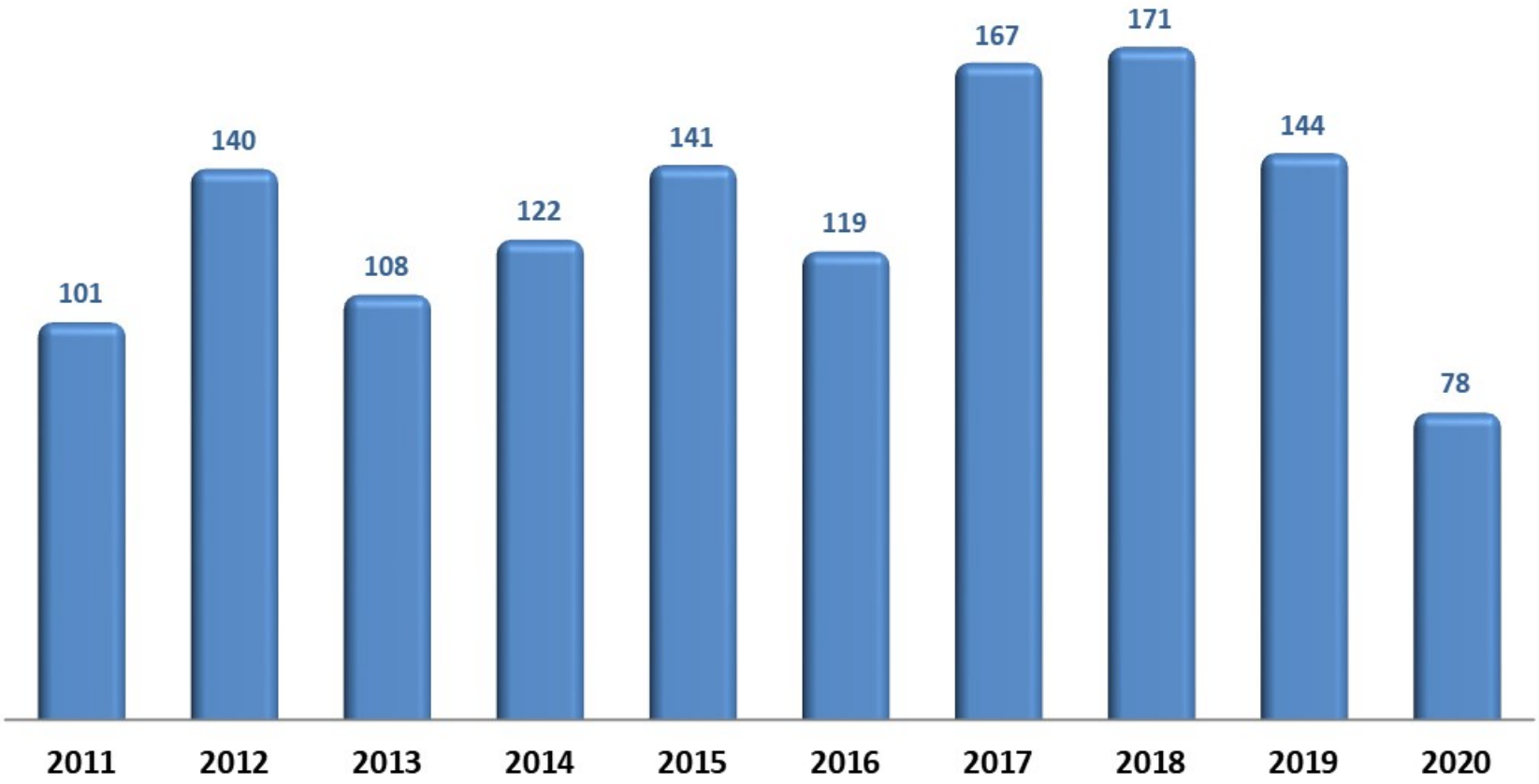
(CDER, FY 2020)



*Based on inspection start date – [Complis database as of Feb 9, 2021].

International Clinical Investigator Inspection Activity*

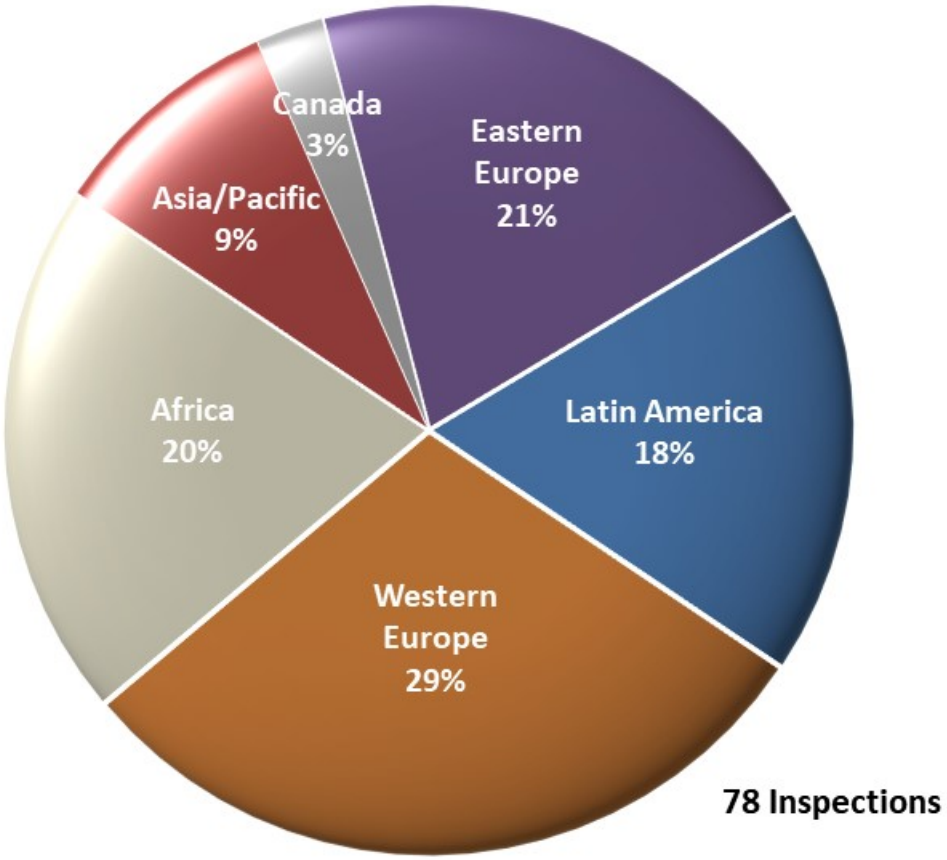
(CDER, FY 2011 - FY 2020)



*Based on inspection start date – [Complis database as of Feb 9, 2021].

International Clinical Investigator Inspection Activity by Location*

(CDER, FY 2020)

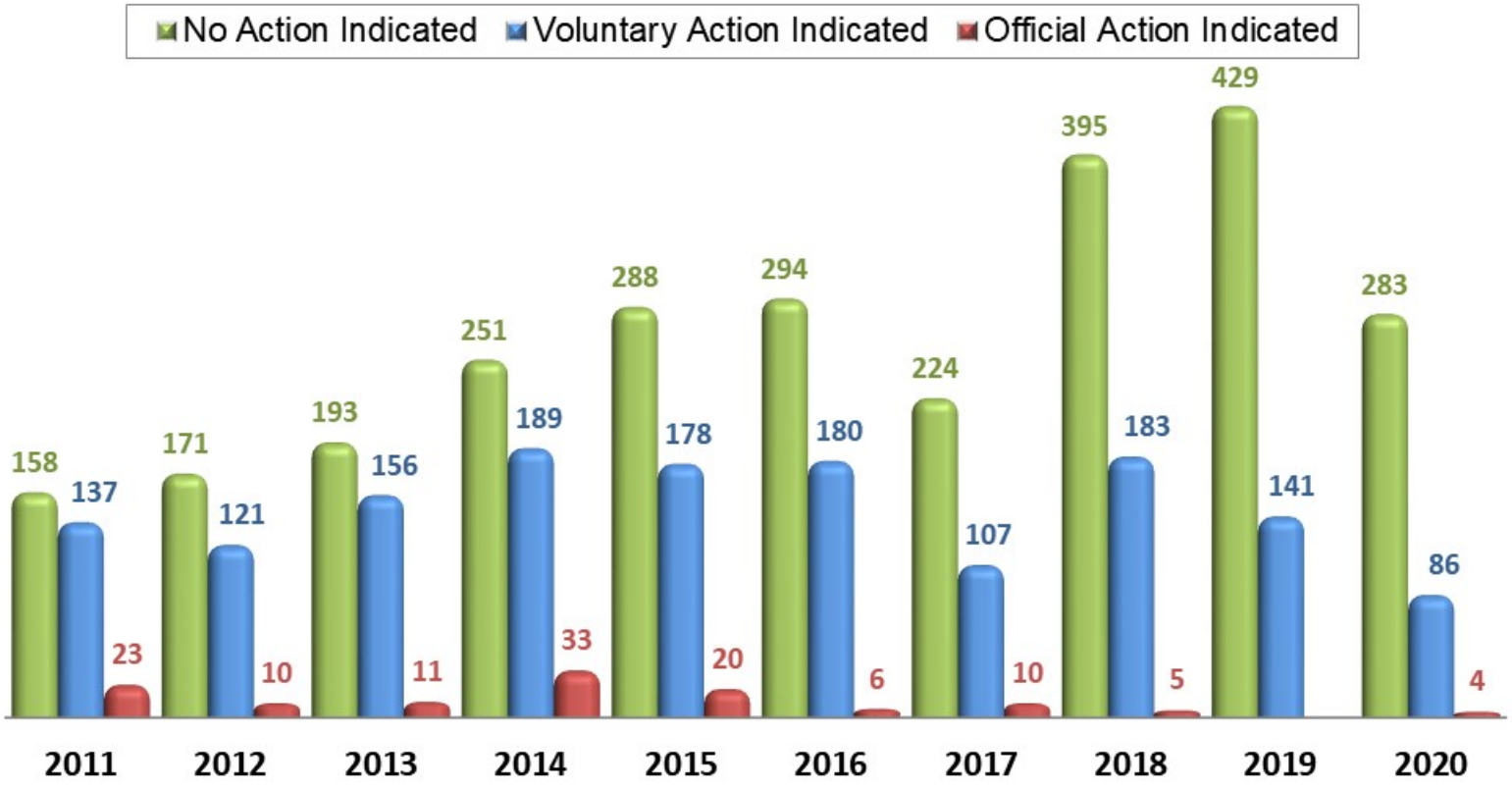


*Based on inspection start date – [Complis database as of Feb 9, 2021].

Clinical Investigator Inspection Activity Final Classification*

Domestic & Foreign

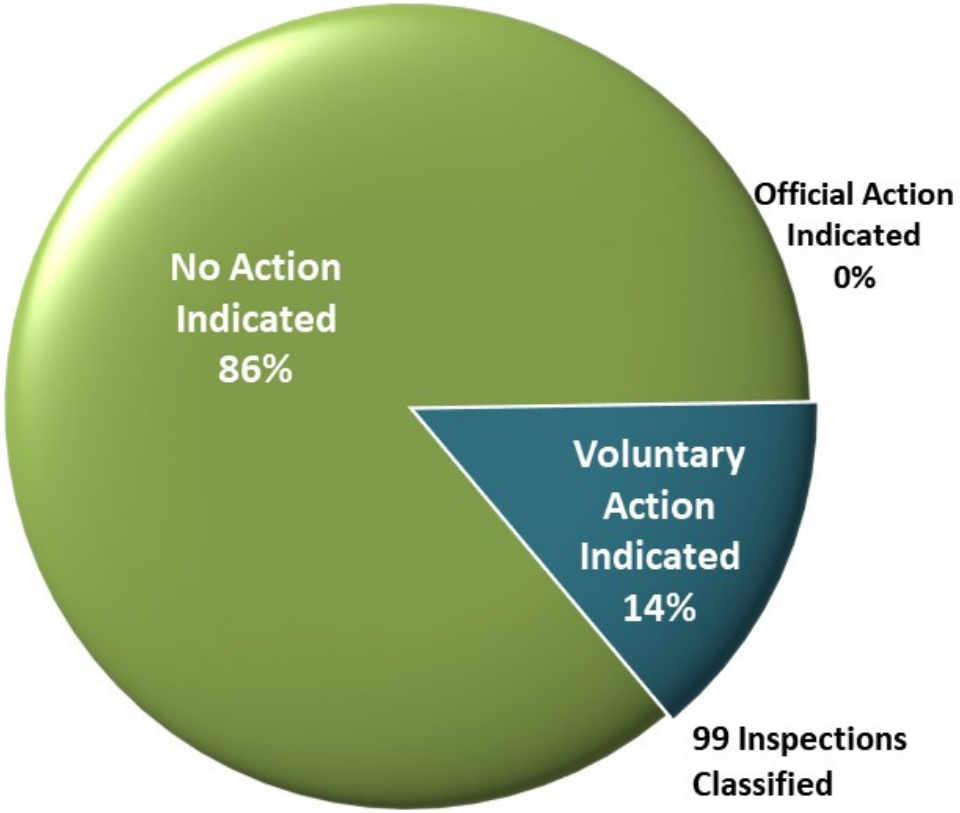
(CDER, FY 2011 - 2020)



*Based on Letter Date and Final Classification [Complis database as of Feb 9, 2021].

International Clinical Investigator Inspection Activity Final Classification*

(CDER, FY 2020)

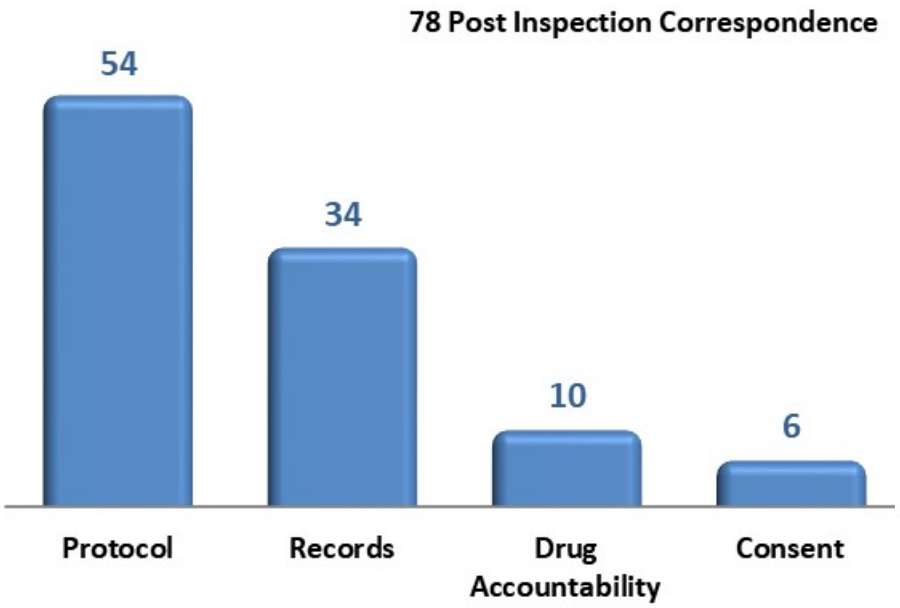


*Based on Letter Date; Includes OAI Untitled Letters, [Complis database as of Feb 9, 2021].

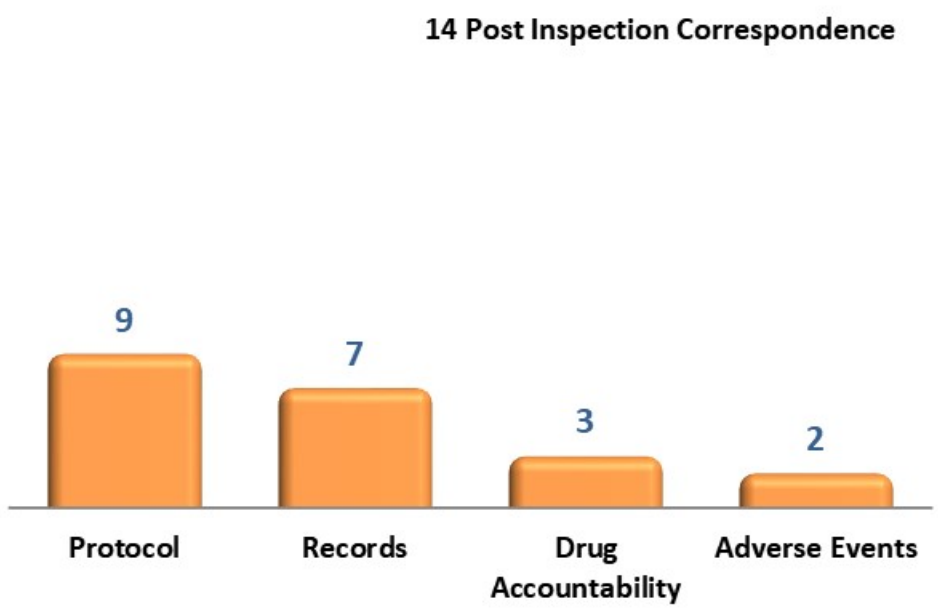
- Note: this does not denote number of Inspection Activity completed, but rather number of inspection reports evaluated and closed.

Clinical Investigator Related Deficiencies*
Post-Inspection Correspondence Issued**
(CDER, FY 2020)

Domestic CI Deficiencies



Foreign CI Deficiencies



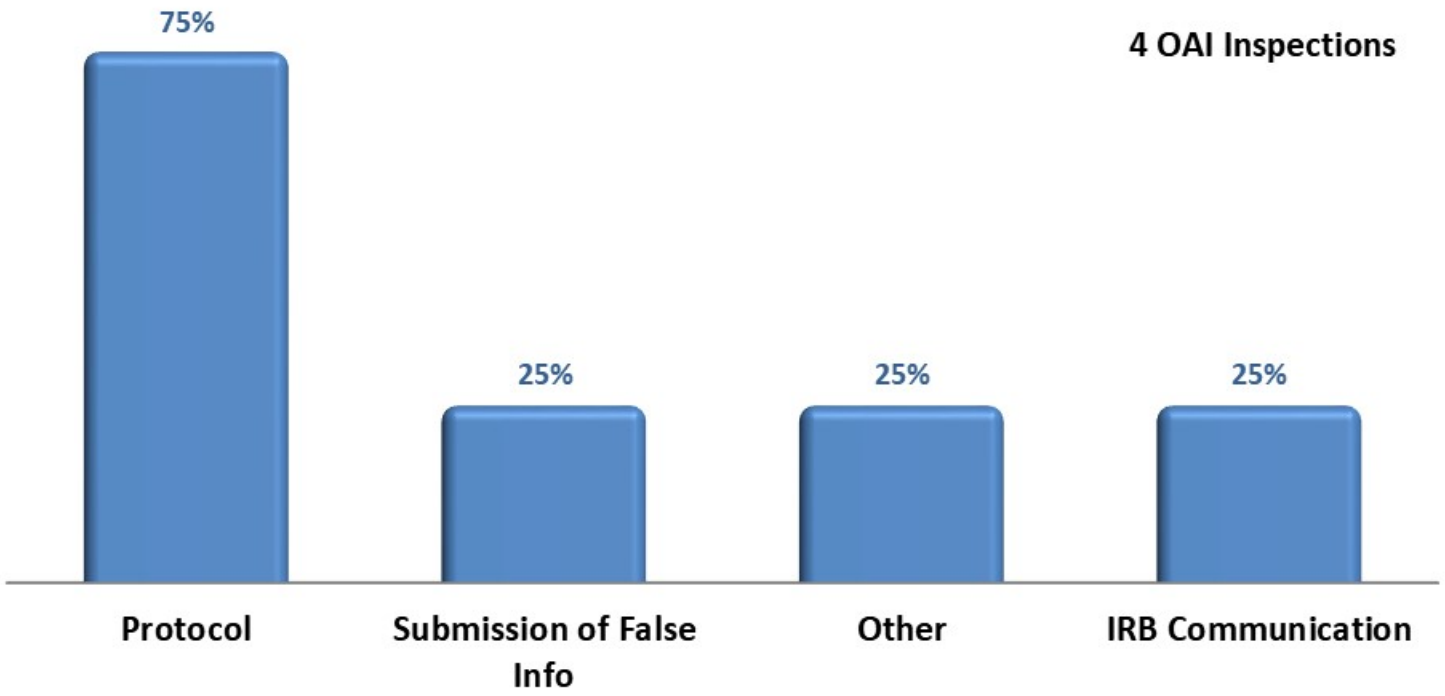
*Based on LogOut Date and Classification. [Complis database as of Feb 9, 2021].
** Inspection Activity with Voluntary Action Indicated (VAI) and Official Action Indicated (OAI) Classifications.

- Note: this does not denote number of Inspection Activity completed, but rather number of inspection reports evaluated and closed. *Inspection Activity may have multiple deficiencies.*

Frequency of Clinical Investigator Related Deficiencies

Official Action Indicated (OAI) Final classification*

(CDER, FY 2020)

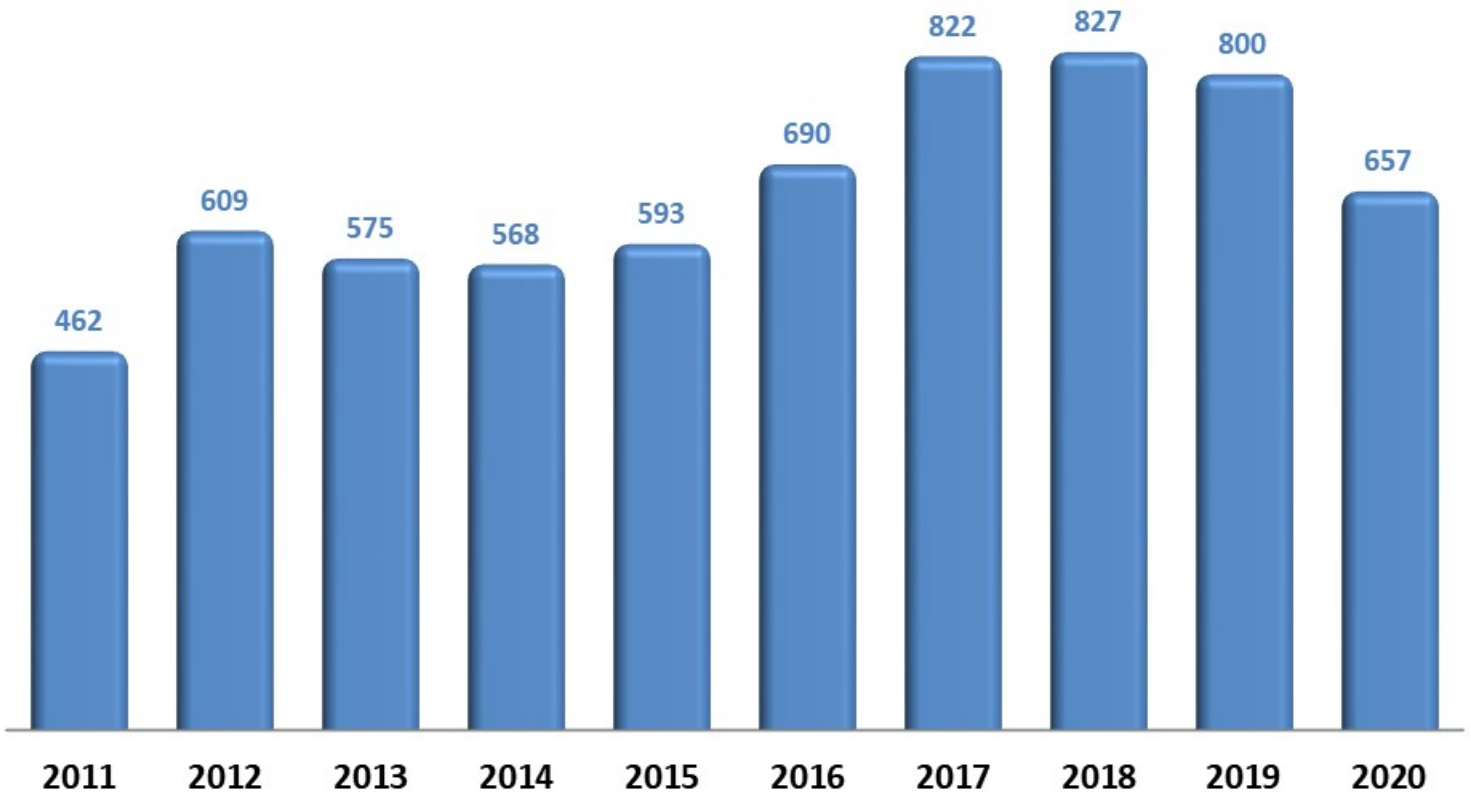


*Based on letter issue date. [Complis database as of Feb 9, 2021].

- Note: this represents the number of inspection reports evaluated and closed which differs from the number of Inspection Activity performed. *Inspection Activity may have multiple deficiencies.*

Referrals Received by OSI*

(CDER, FY 2011 - FY 2020)

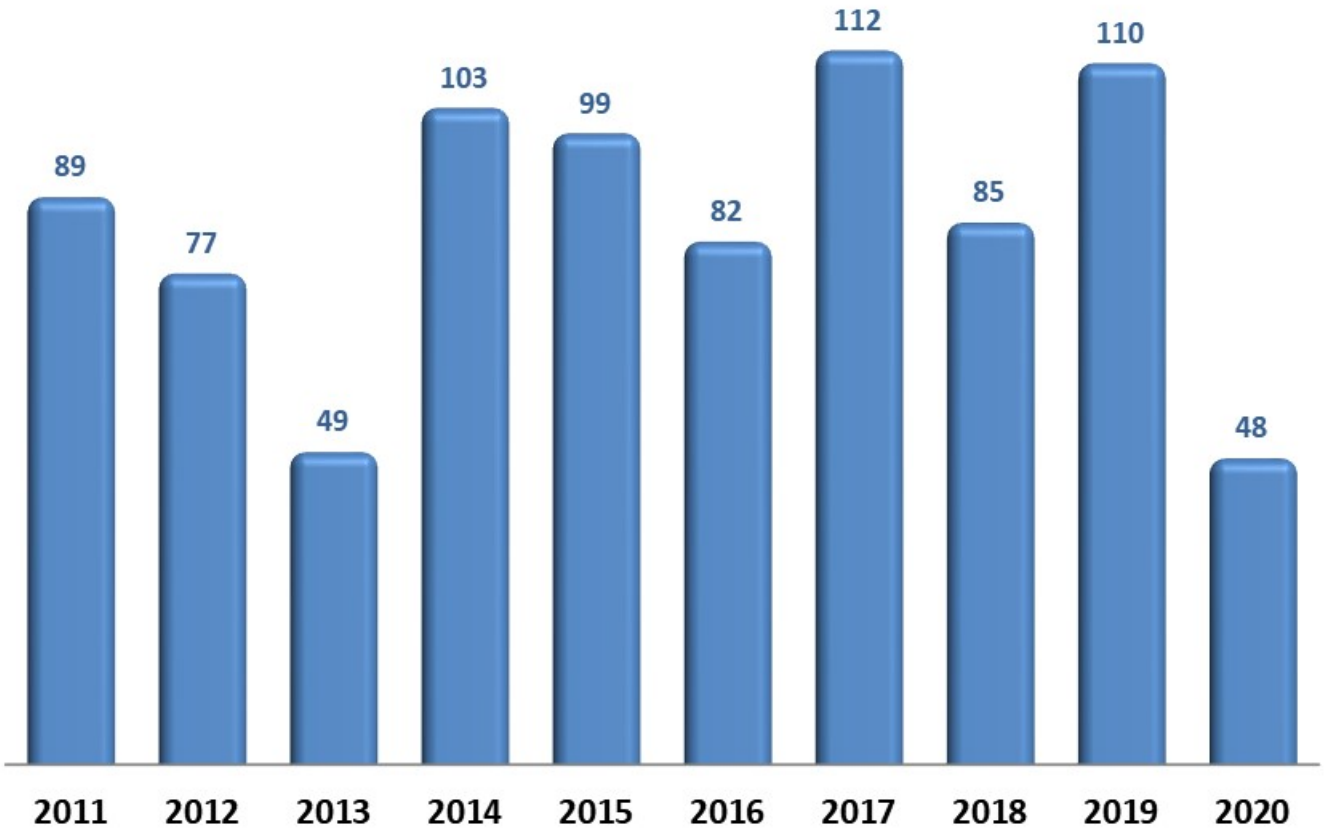


*Based on referral received date.[Complis database as of Feb 9, 2021].

- Referrals include Complaints, Required Reports, IRB/Sponsor Notifications, and other referrals-internal and external.

Referral-Related Clinical Investigator Inspection Activity*

(CDER, FY 2011 - FY 2020)

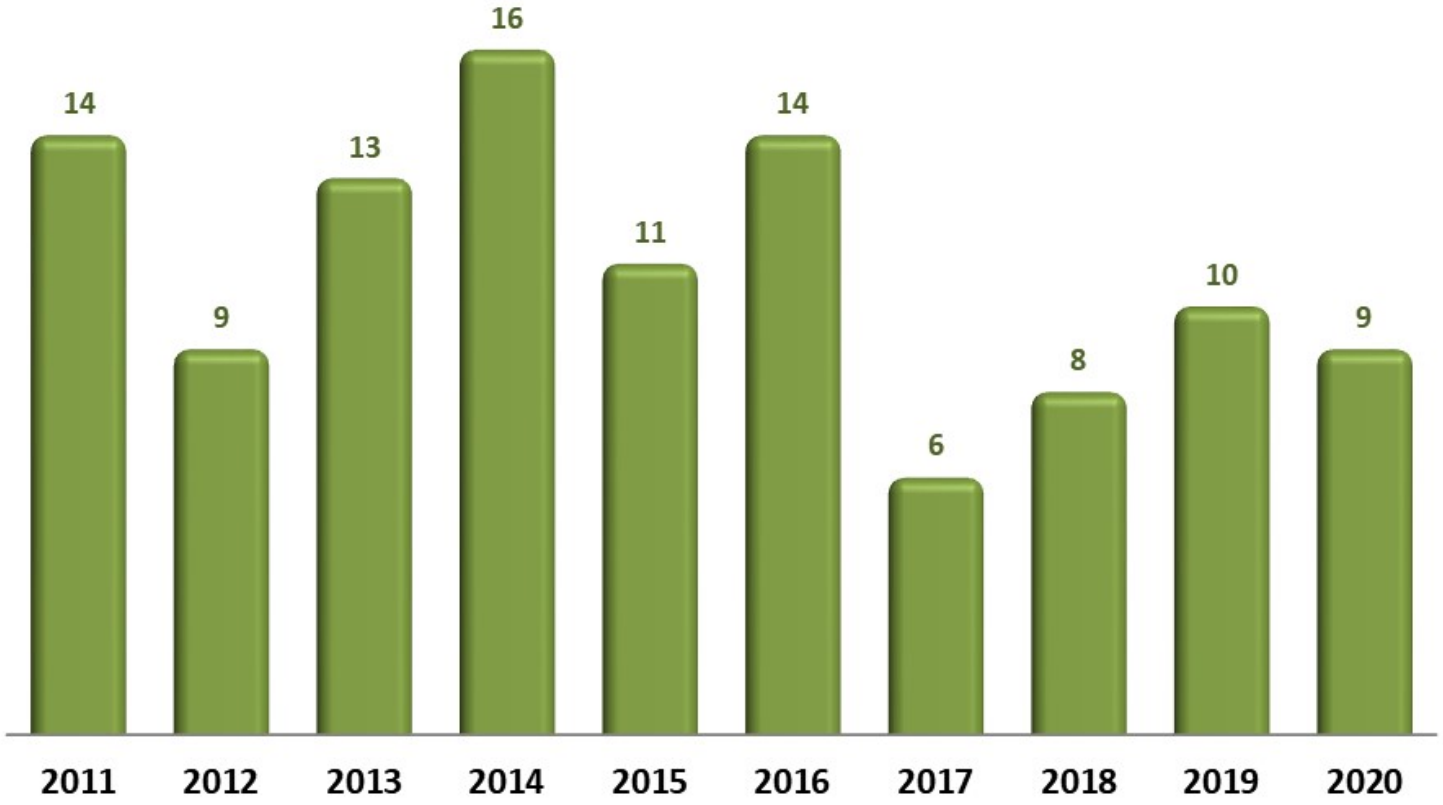


*Based on referral received date.[Complis database as of Feb 9, 2021].

- Based on inspection start date. Referrals include Complaints, Required Reports, IRB/Sponsor Notifications, and other referrals-internal and external.

Referral-Related Sponsor Inspection Activity*

(CDER, FY 2011 - FY 2020)

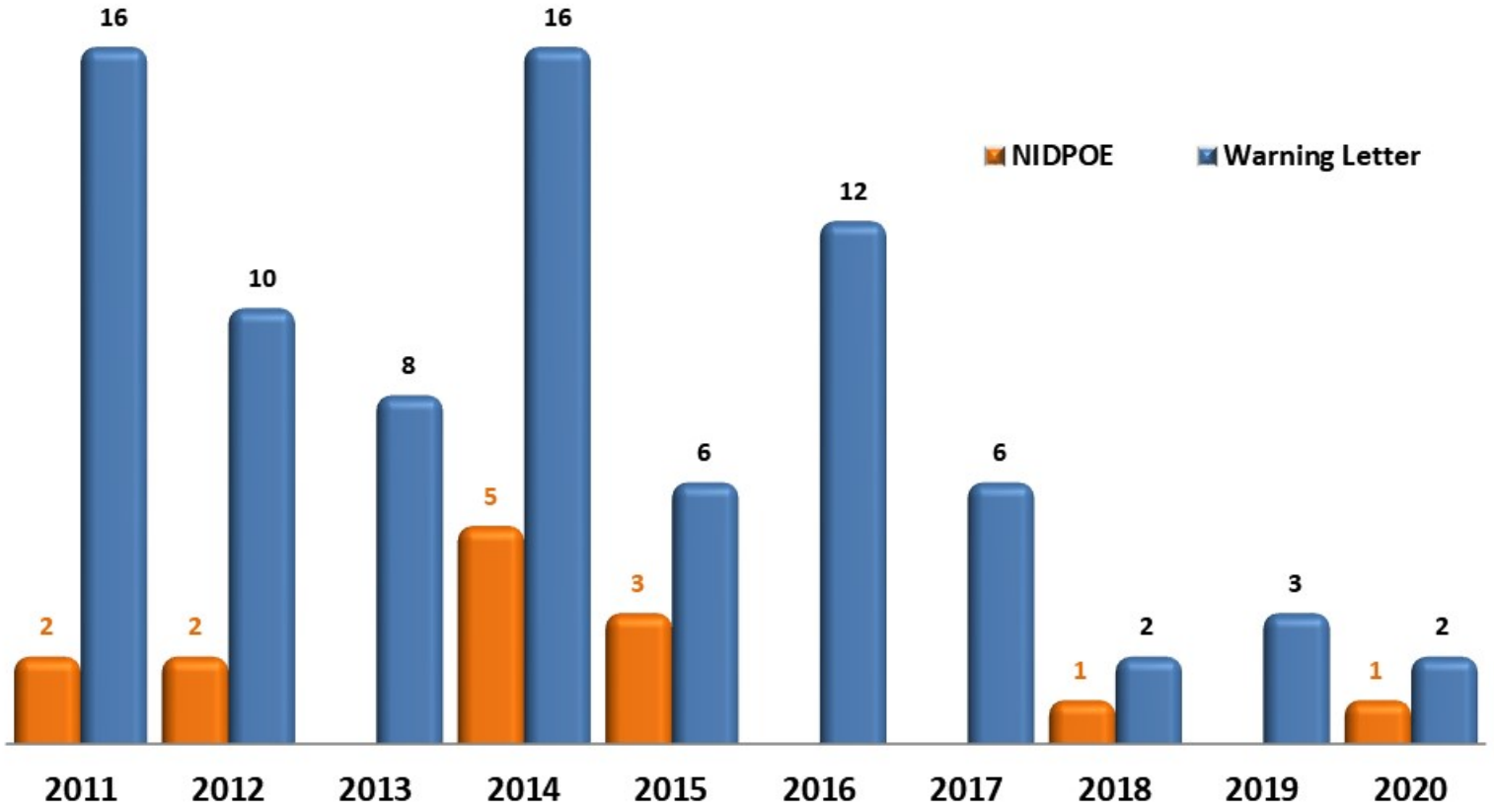


*Based on referral received date.[Complis database as of Feb 9, 2021].

- Based on inspection start date; Referrals include Complaints, Required Reports, IRB/Sponsor Notifications, and other referrals-internal and external.
- Sponsor metrics include both Sponsor and Sponsor-Investigator.

BIMO Warning/NIDPOE Letters*

(CDER, FY 2011 - FY 2020)

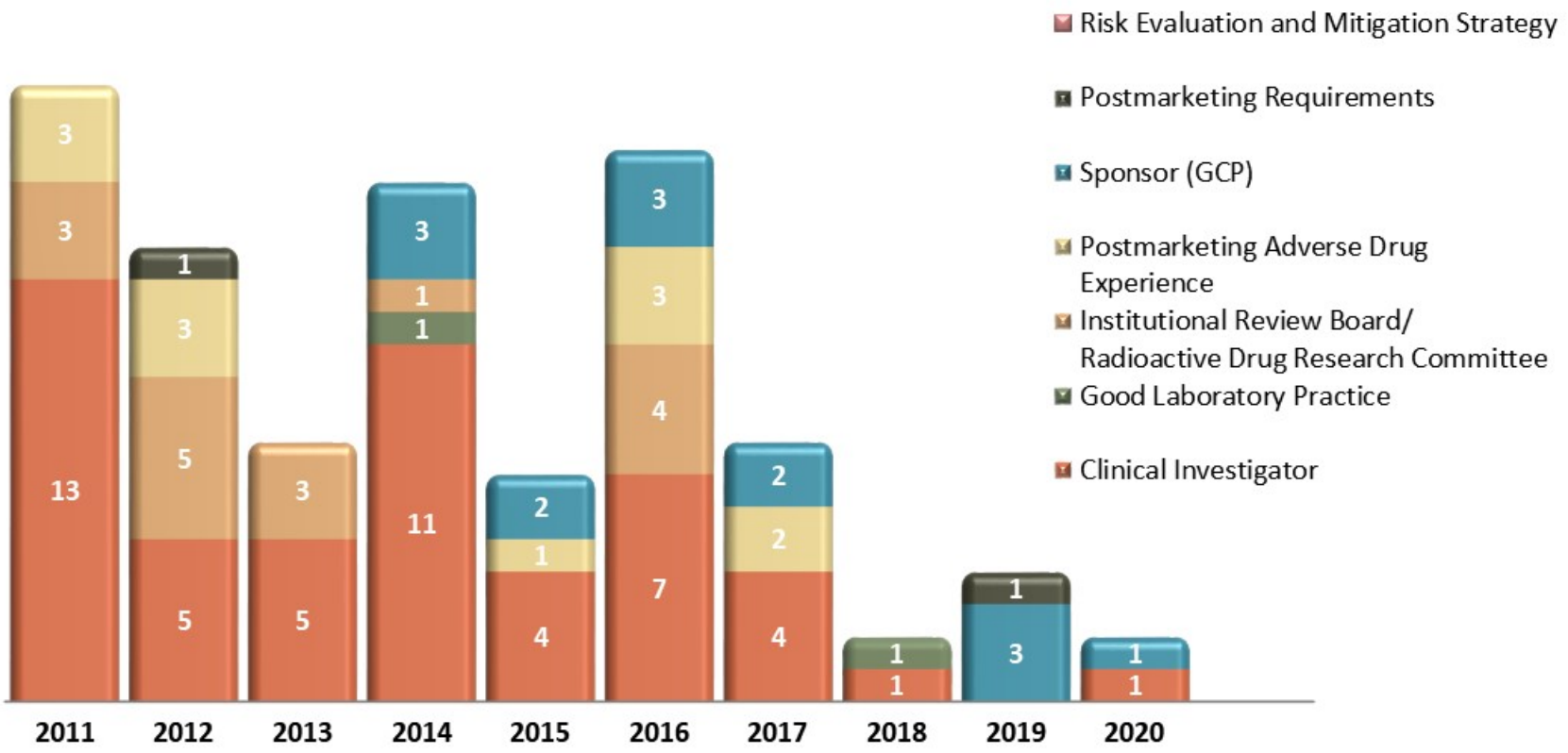


*Based on letter issue date [Complis database as of Feb 9, 2021]

- Inspection Activity may have occurred in prior fiscal year.
- BIMO = Bioresearch Monitoring (Clinical Investigators, Sponsor/CRO/Sponsor-Investigator (GCP), IRB, BEQ, GLP, PADE, REMS).
- NIDPOE = Notice of Initiation of Disqualification Proceedings and Opportunity to Explain.

Warning Letters*

(CDER, FY 2011 - FY 2020)

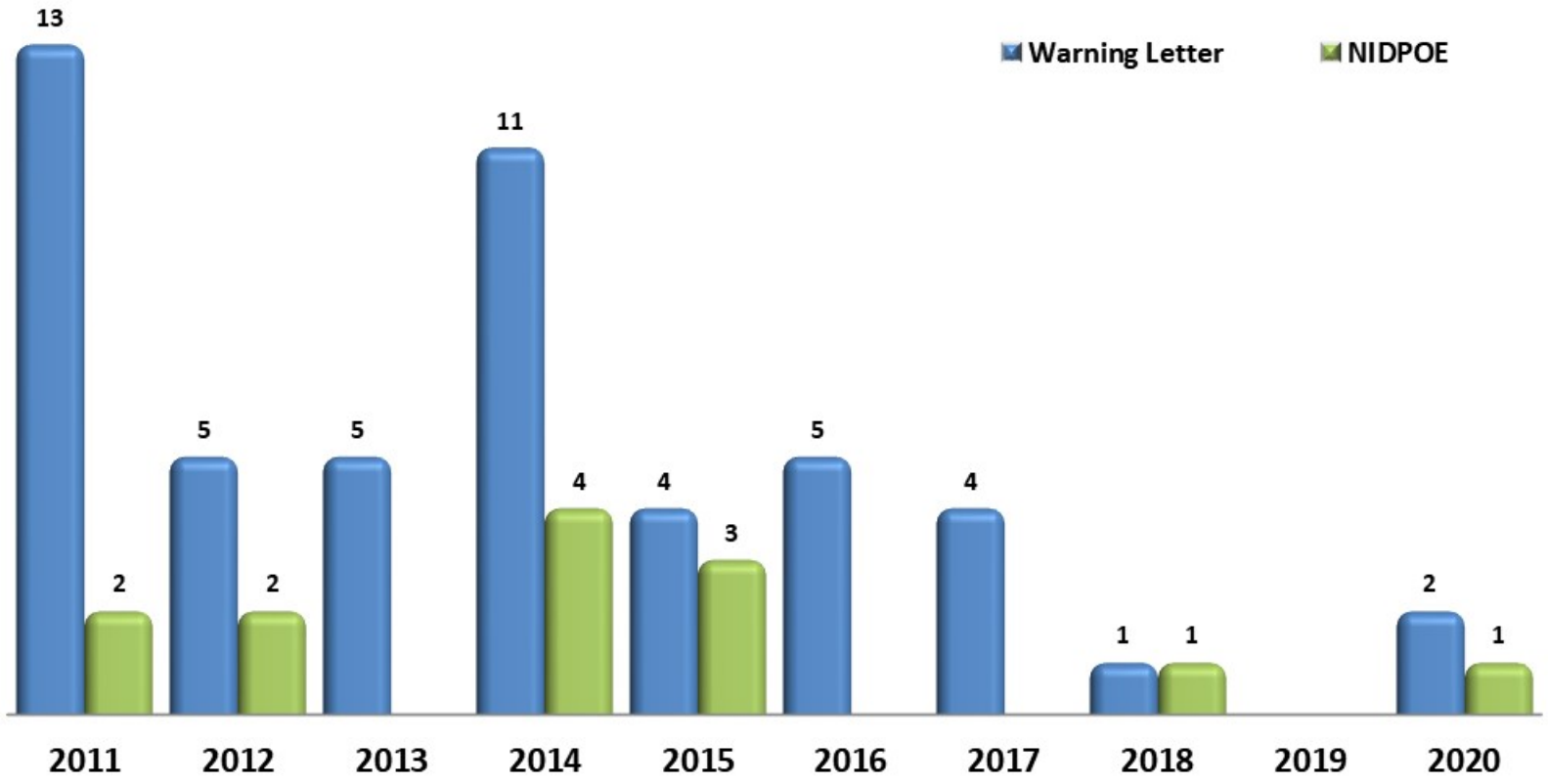


*Based on letter issue date [Complis database as of Feb 9, 2021].

- PMR includes: Accelerated Approval PMR (21 CFR part 314, subpart H); Pediatric Research and Equity Act PMR; Animal Efficacy PMR (21 CFR part 314, subpart I), and FDA Amendments Act PMRs (section 505(o)(3) of the Federal Food Drug & Cosmetic Act).
- Sponsor metrics include both Sponsor and Sponsor-Investigator.

Clinical Investigator Warning/NIDPOE Letters*

(CDER, FY 2011 - FY 2020)



*Based on letter issue date [Complis database as of Feb 9, 2021].

- NIDPOE = Notice of Initiation of Disqualification Proceedings and Opportunity to Explain.

Clinical Investigator Regulatory Actions*

(CDER, FY 2011 - FY 2020)

Action	FY11	FY12	FY13	FY14	FY15	FY16	FY17	FY18	FY19	FY20
WL**	13	5	5	11	4	7	4	1	0	2
NIDPOE	2	2	0	5	3	0	0	1	0	1
NOOH	2	1	0	0	1	0	0	0	0	0
CA-Restricted	0	0	0	0	0	0	0	0	0	0
CA-Full DQ	2	0	0	2	2	0	0	1	0	0
DQ-Hearing/Commissioner	1	1	0	1	0	0	0	0	0	1

WL = Warning Letter
NIDPOE = Notice of Initiation of Disqualification Proceedings and Opportunity to Explain
NOOH = Notice of Opportunity for Hearing
CA-Restricted = Consent Agreements (Restricted Agreements)
CA-Full DQ = Consent Agreements (Full Disqualification)
DQ = Disqualification by Hearing or Commissioner

*Based on letter issue date [Complis database as of Feb 9, 2021].
**Warning Letters are informal and advisory in nature, not regulatory actions (FDA Regulatory Procedures Manual Chapter 4, Section 1-1).

Warning Letters by Program Area*

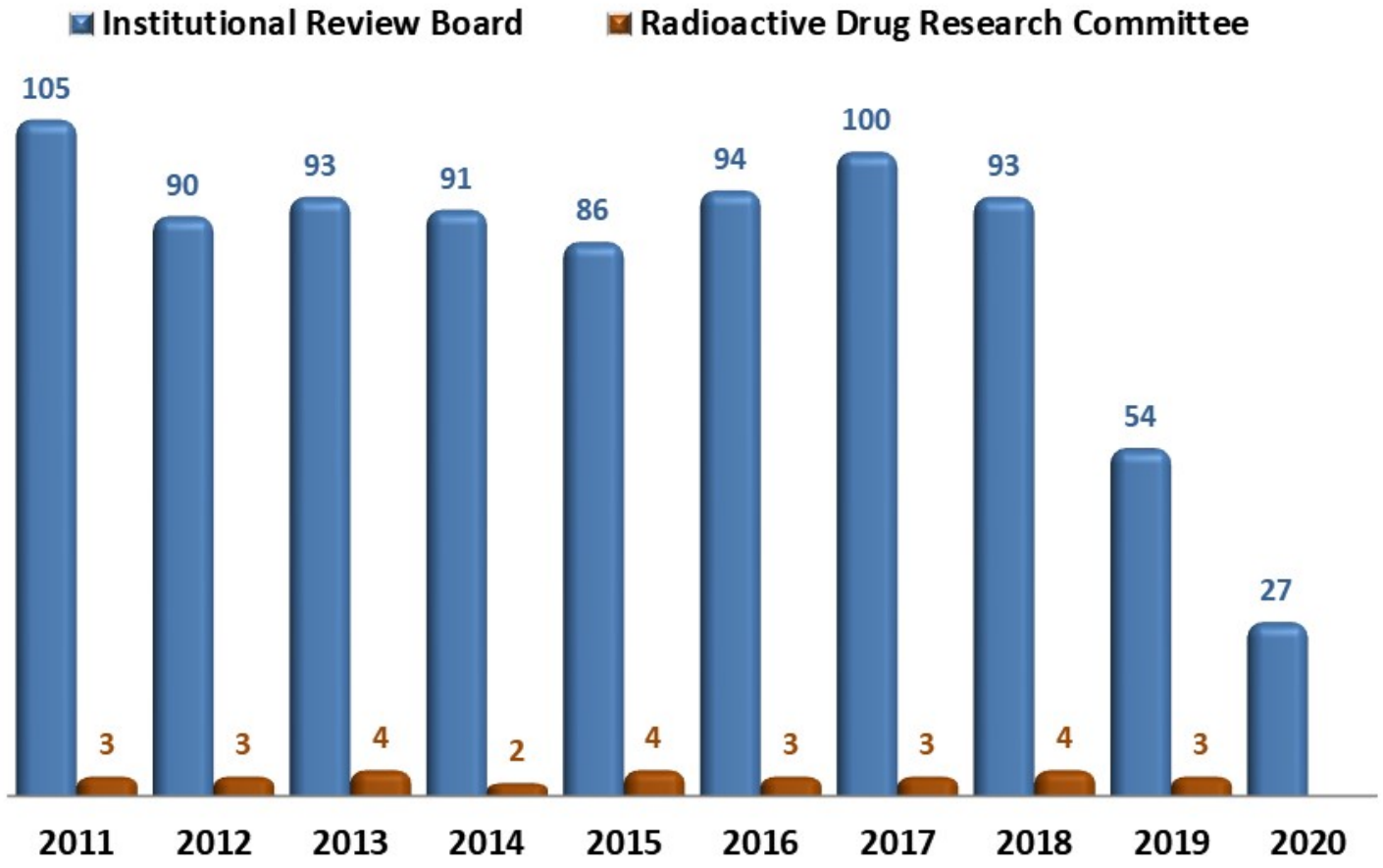
(CDER, FY 2011 - FY 2020)

Program Area	FY11	FY12	FY13	FY14	FY15	FY16	FY17	FY18	FY19	FY20
Bioavailability/ Bioequivalence**	1**	0	0	0	0	1**	0	0	0	0
Good Laboratory Practice	0	0	0	1	0	0	0	1	0	0
Clinical Investigator	13	5	5	11	4	5	4	1	0	1
Sponsor-Investigator (GCP)	0	0	0	0	0	2	1	0	3	1
Sponsor (GCP)	0	0	0	3	2	2	2	0	0	0
Contract Research Organization (GCP)	0	0	0	0	0	0	0	0	0	0
Institutional Review Board	2	5	3	1	0	4	0	0	0	0
Radioactive Drug Research Committee	1	0	0	0	0	0	0	0	0	0
Postmarketing Adverse Drug Event	3	3	0	0	1	3	2	0	0	0
Risk Evaluation and Mitigation Strategy	0	0	0	0	0	0	0	0	0	0
Postmarketing Requirements^	N/A	1	0	0	0	0	0	0	1	0

*Based on letter issue date [Complis database as of Feb 9, 2021].
**Posted Bioavailability/ Bioequivalence OAI untitled letters.
^ PMR includes: Accelerated Approval PMR (21 CFR part 314, subpart H); Pediatric Research and Equity Act PMR; Animal Efficacy PMR (21 CFR part 314, subpart I), and FDAAA PMRs (section 505(o)(3) of the FD&C Act).

Institutional Review Board/ Radioactive Drug Research Committee Inspection Activity*

(CDER, FY 2011 - FY 2020)

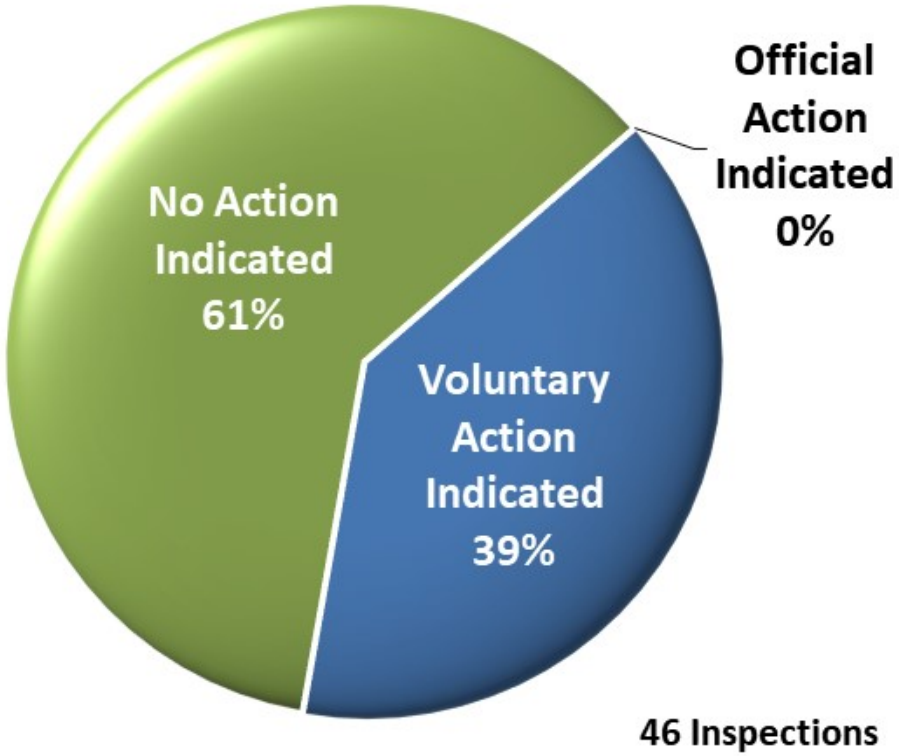


*Based on inspection start date [Complis database as of Feb 9, 2021].

- Includes only CDER numbers – previously reported metrics may have used combined data across CDER, CBER and CDRH.

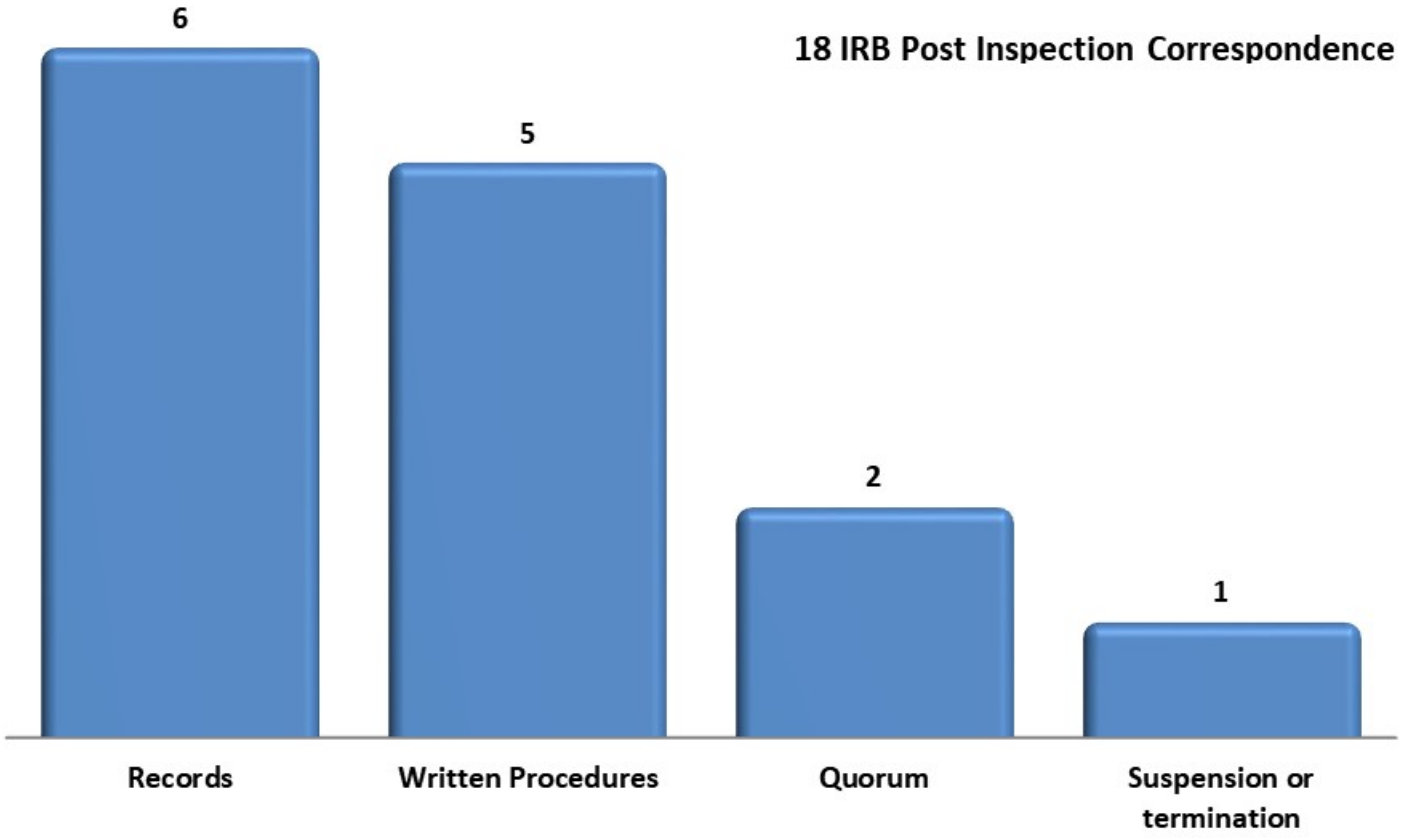
Institutional Review Board/ Radioactive Drug Research Committee Inspection Final Classifications*

(CDER, FY 2020)



*Based on letter issue date, [Complis database as of Feb 9, 2021].

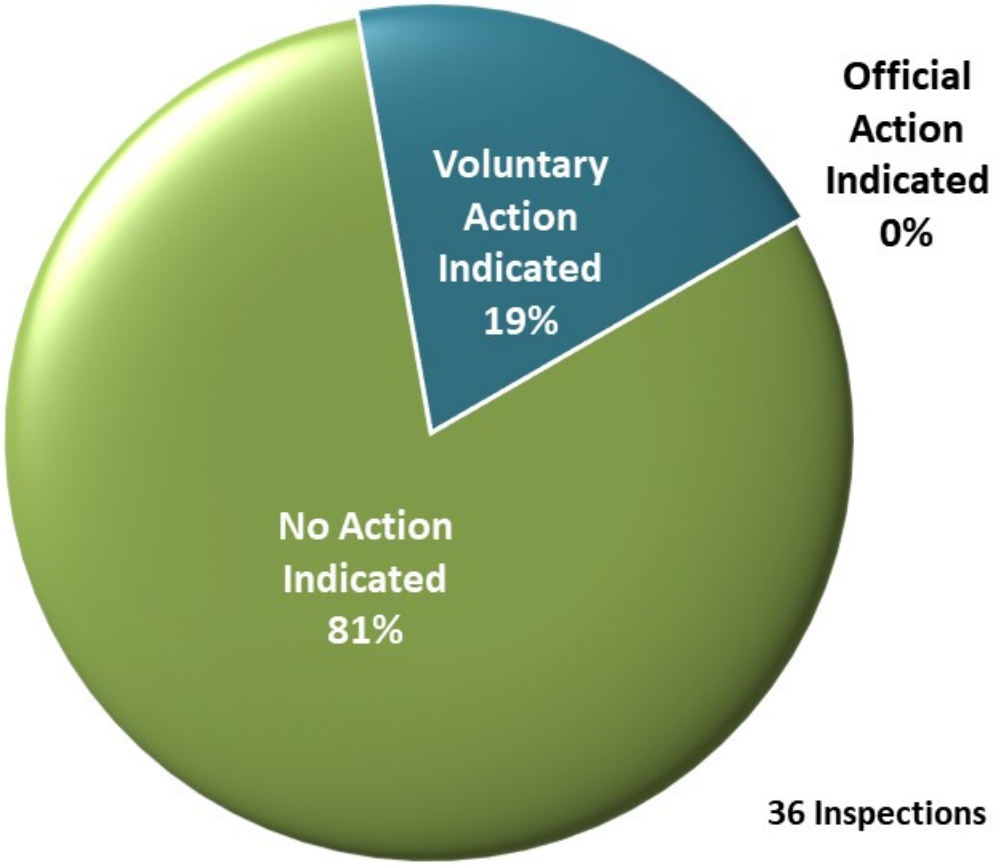
Frequency of IRB-Related Deficiencies*
Post-Inspection Correspondence Issued**
(CDER, FY 2020)



*Based on letter issue date, [Complis database as of Feb 9, 2021].
** Inspection Activity with Voluntary Action Indicated (VAI) and Official Action Indicated (OAI) Classifications.
- Note: this represents the number of inspection reports evaluated and closed which differs from the number of Inspection Activity performed.

Postmarketing Adverse Drug Experience Inspection Activity*

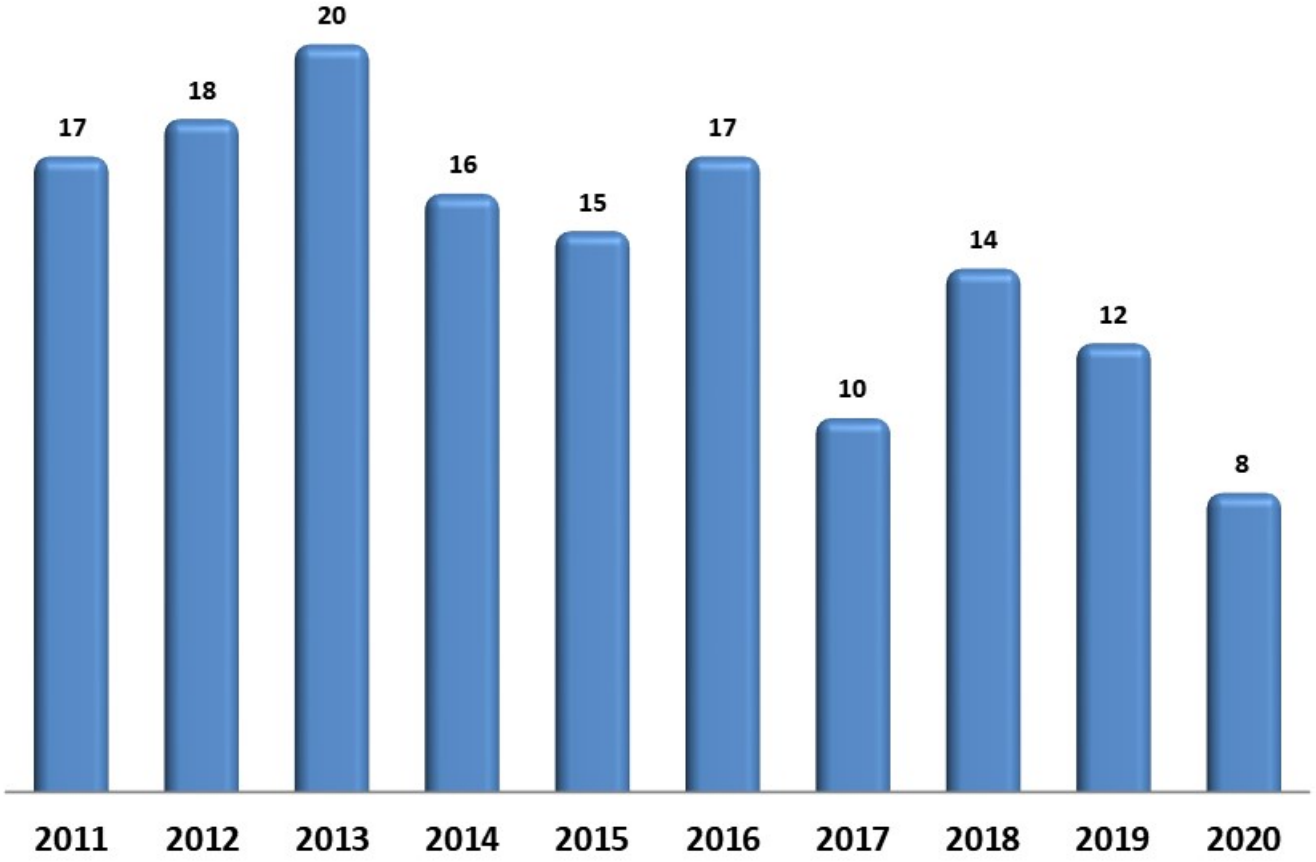
(CDER, FY 2020)



*Based on Close/Log Out Date. [Complis database as of Feb 9, 2021].

Risk Evaluation and Mitigation Strategies Inspection Activity*

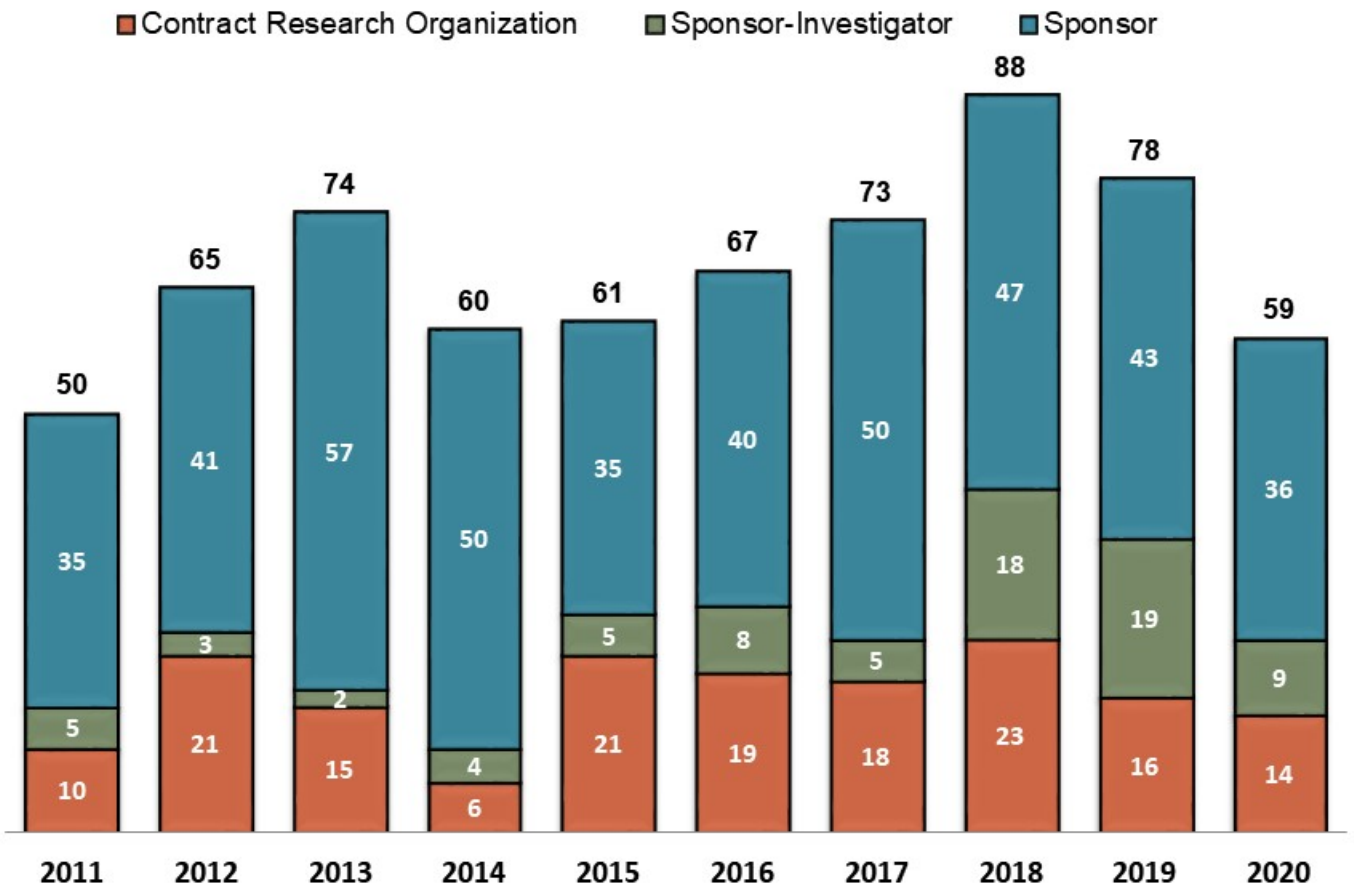
(CDER, FY 2011 - 2020)



*Based on date inspection started [Complis database as of Feb 9, 2021].

GCP-Related Sponsor/ Contract Research Organizational Inspection Activity*

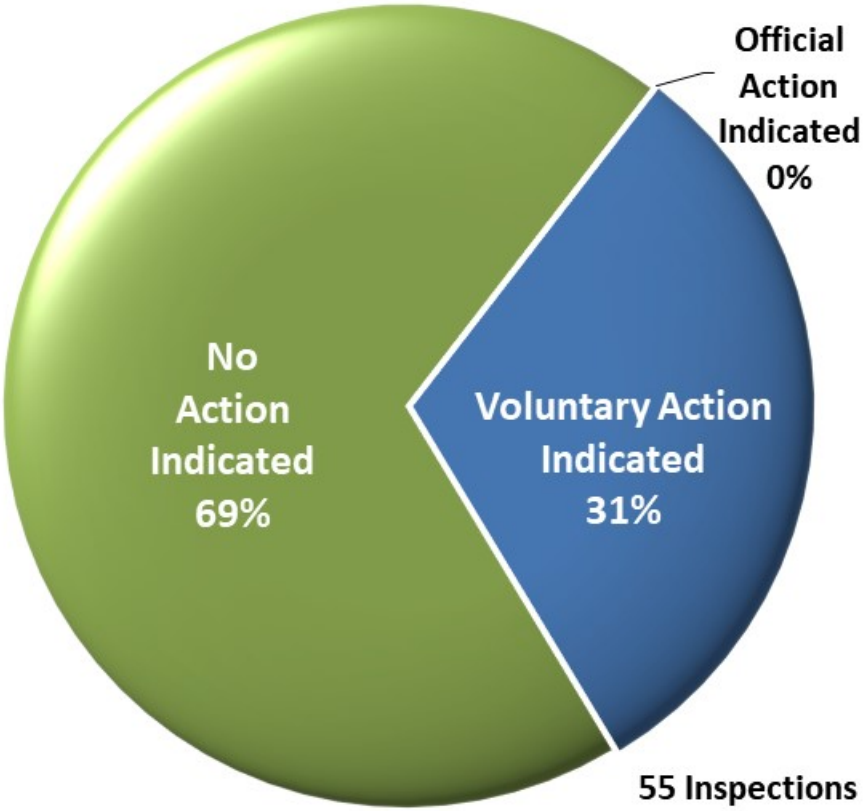
(CDER, FY 2020)



*Based on inspection start date [Complis database as of Feb 9, 2021].

GCP-Related Sponsor/ Contract Research Organization Inspection Activity Final Classification*

(CDER, FY 2020)

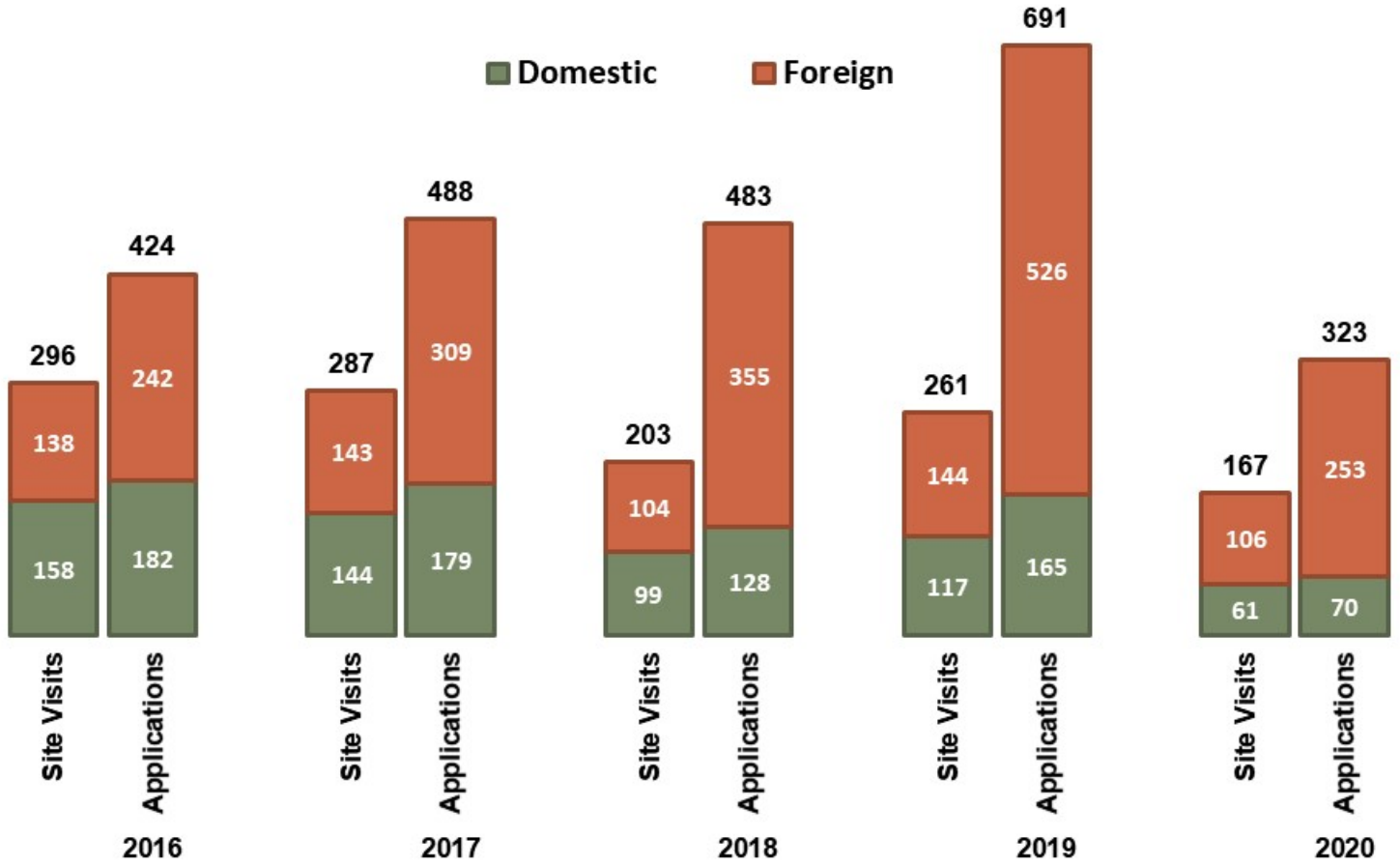


*Based on letter issue date [Complis database as of Feb 9, 2021].

- Includes Sponsor-Investigator Inspection Activity.

Bioavailability/Bioequivalence Site Visits and Applications Inspected*

(CDER, FY 2014 - FY 2020)

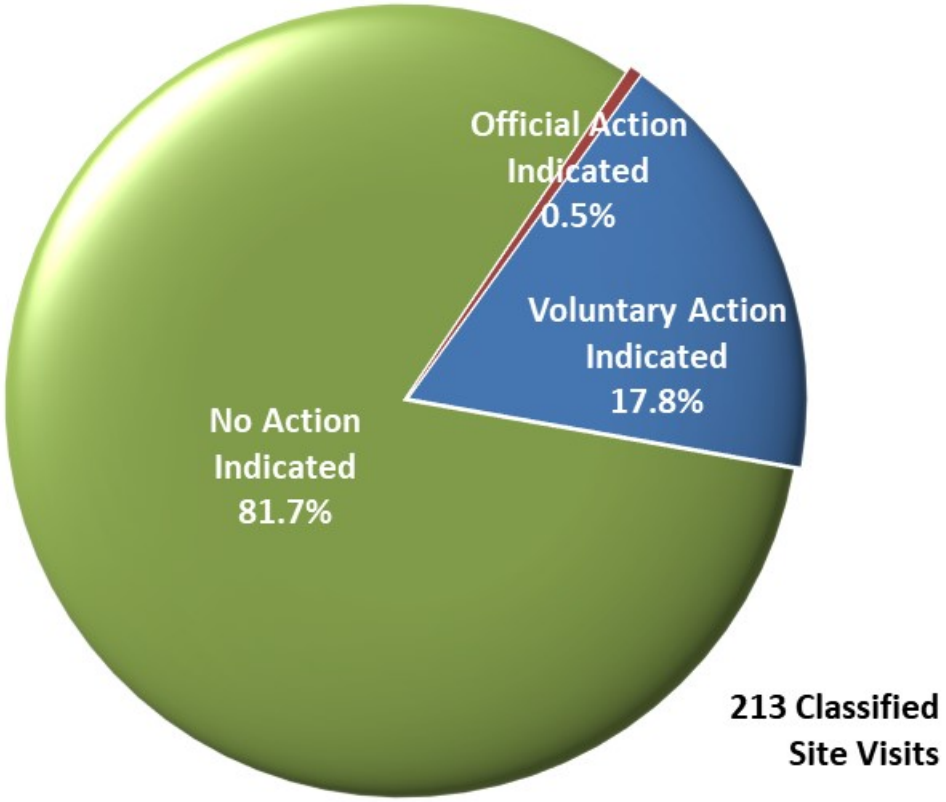


*Based on inspection Start Date [Complis database as of Feb 9, 2021].

- Bioequivalence inspection programs and Good Laboratory Practice operated by OSIS as of January 2015.
- Site visit number includes use of alternative approaches (e.g., RRAs and RRR) and includes only CDER numbers.

Bioavailability/Bioequivalence Site Visit Final Classifications*

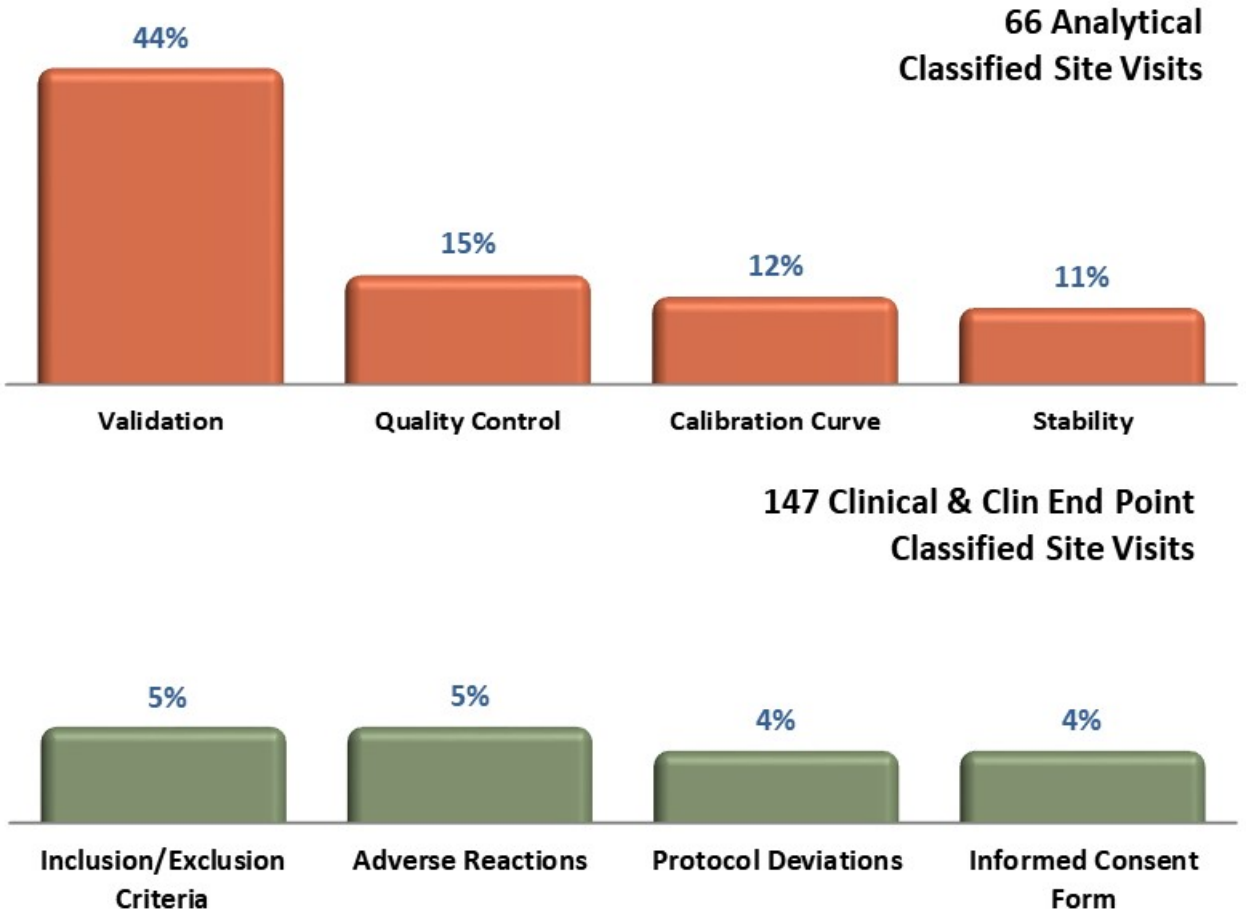
(CDER, FY 2020)



*Based on Logout date and Final Classification, [Complis database as of Feb 9, 2021].

Frequency of BA/BE-Related Deficiencies*

(CDER, FY 2020)

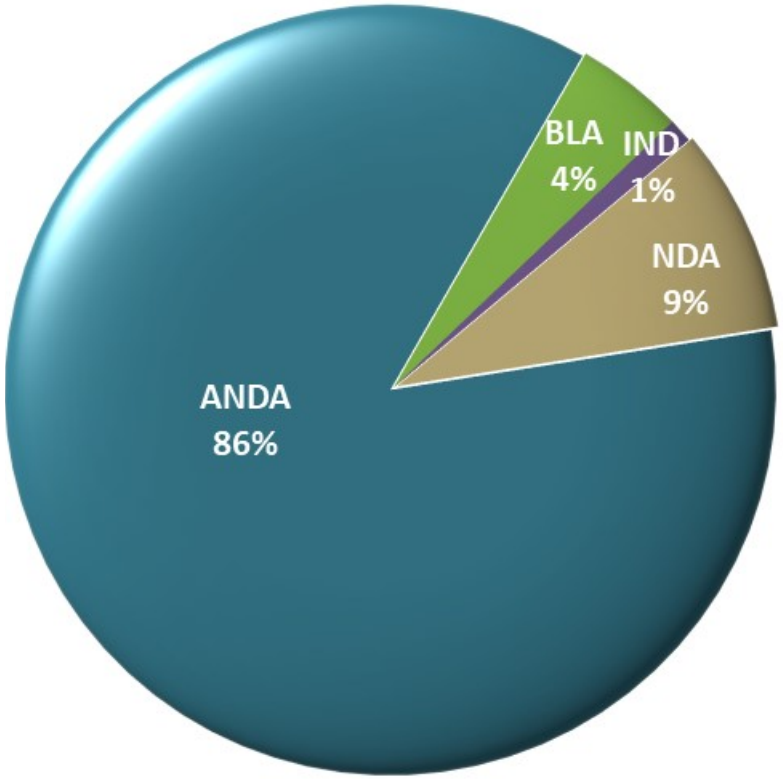


*Based on Logout date and Final Classification, [Complis database as of Feb 9, 2021].

- Note that this does not denote number of Inspection Activity completed, but rather number of inspection reports evaluated and closed in the fiscal year. *Site Visits may have multiple deficiencies.*

Bioavailability/Bioequivalence Analytical Site Visit Final Classifications and Application Types*

(CDER, FY 2020)



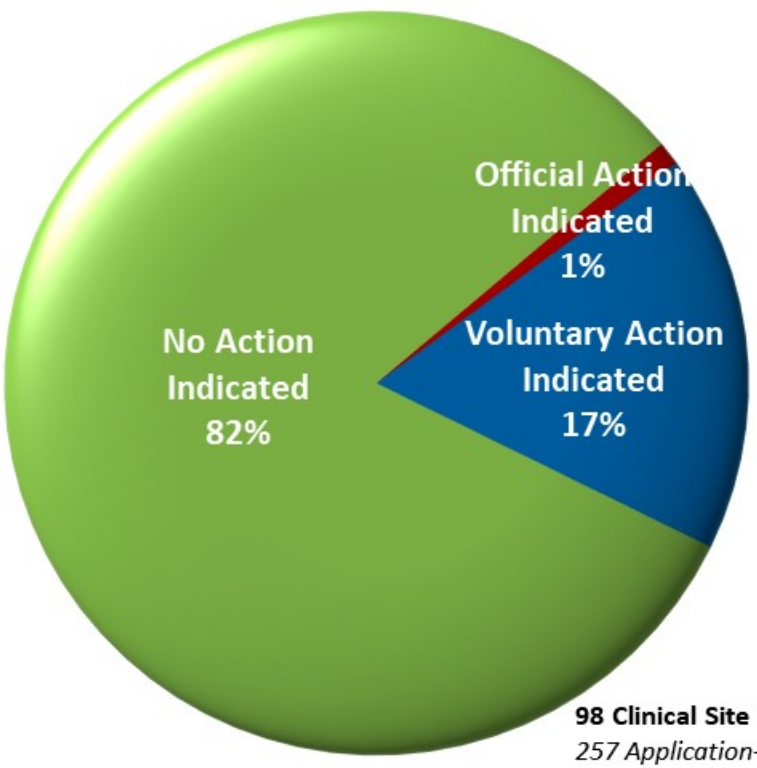
66 Analytical Site Visits

197 Application-Inspections covering 185 unique applications

*Based on Logout date and Final Classification, [Complis database as of Feb 9, 2021].

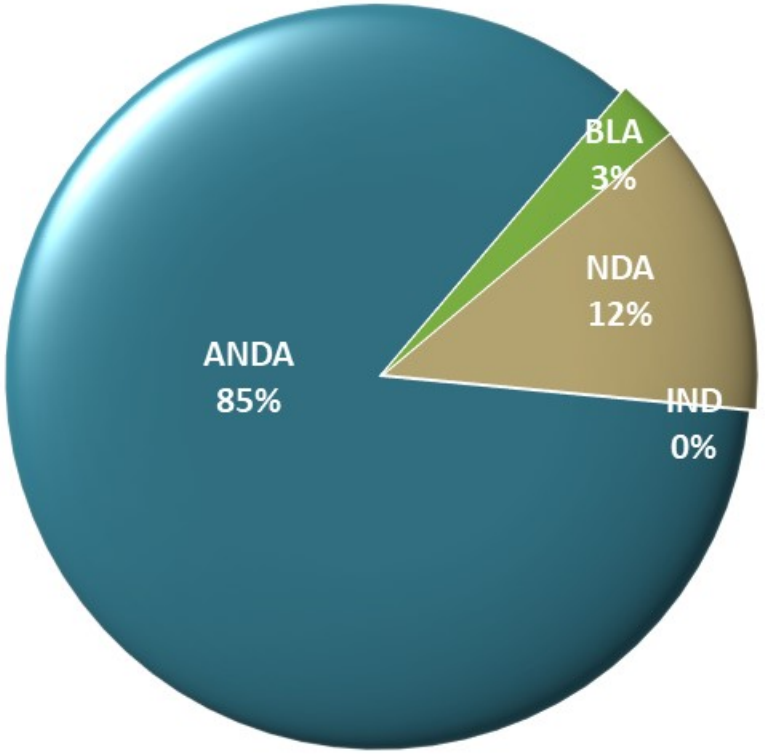
Bioavailability/Bioequivalence Clinical Site Visit Final Classifications and Application Types*

(CDER, FY 2020)



98 Clinical Site Visits

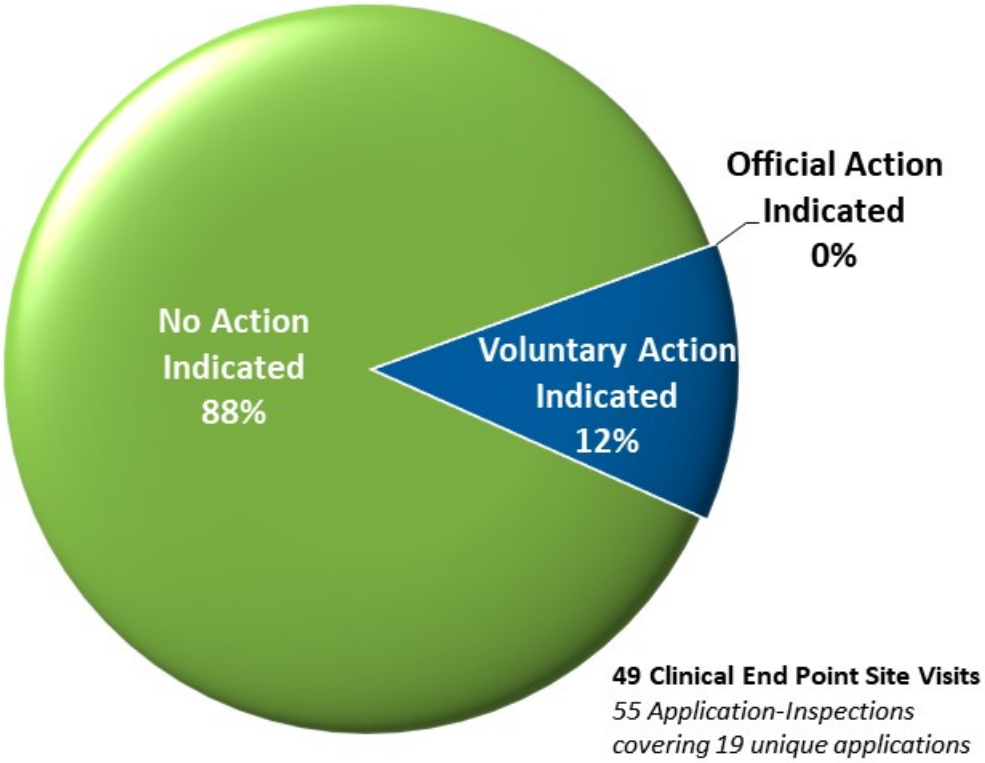
257 Application-Inspectio
covering 218 unique applications



*Based on Logout date and Final Classification, [Complis database as of Feb 9, 2021].

Bioavailability/Bioequivalence Clinical End Point Site Visit Final Classifications*

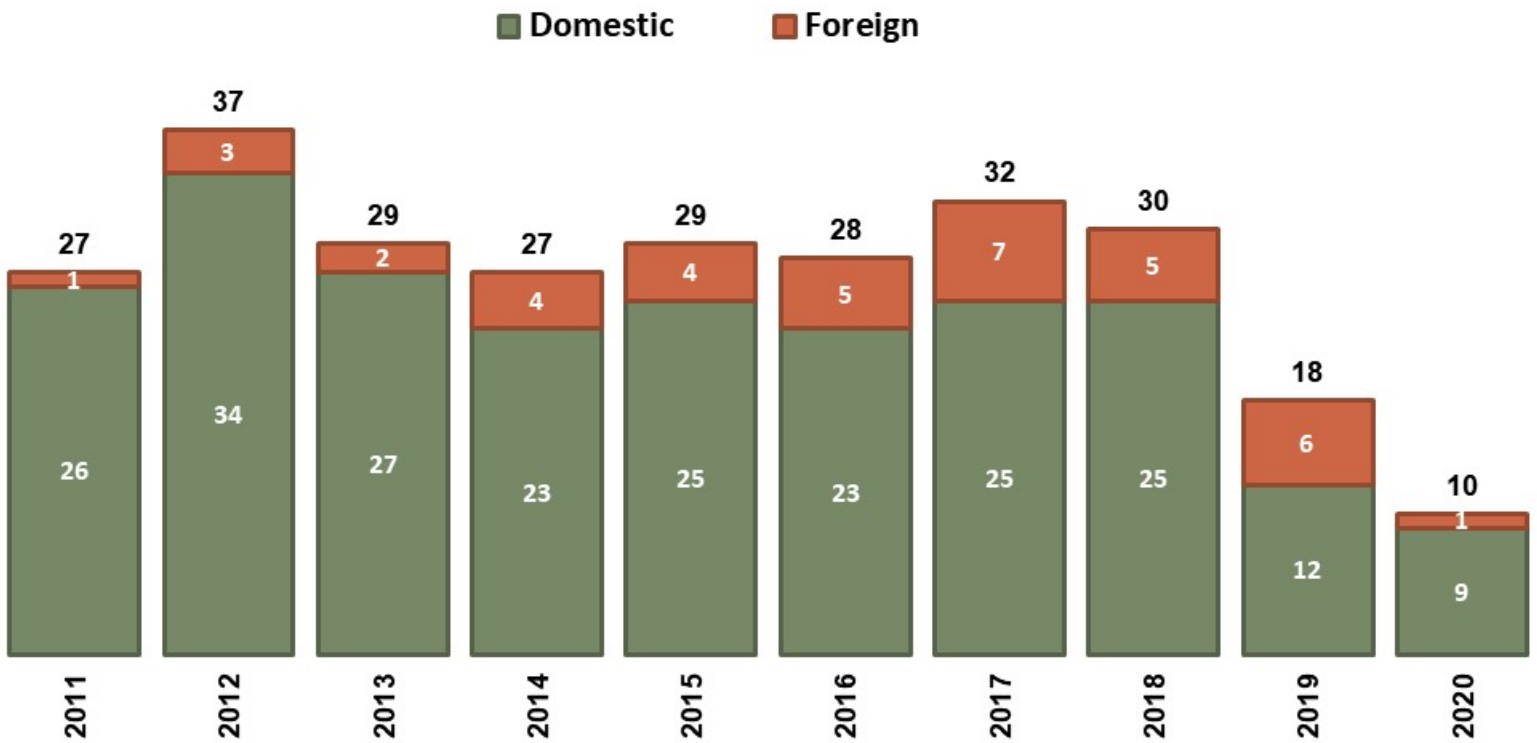
(CDER, FY 2020)



*ANDA Applications based on Logout date and Final Classification, [Complis database as of Feb 9, 2021].

Good Laboratory Practices Inspection Activity*

(CDER, FY 2011 - 2020)

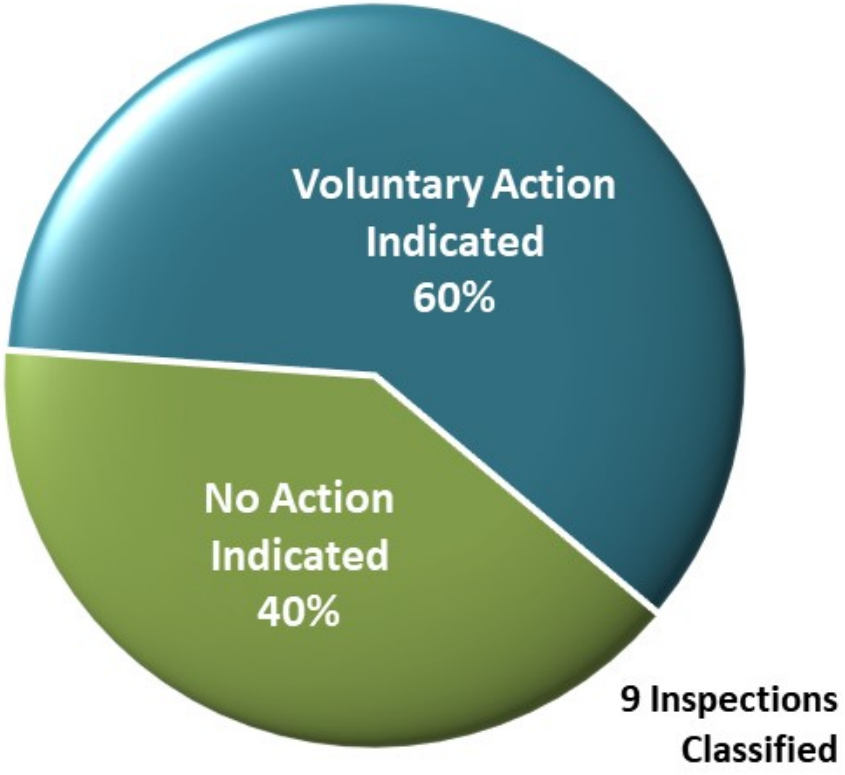


*Based on date inspection started. [Complis database as of Feb 9, 2021].

- Bioequivalence inspection programs and Good Laboratory Practice operated by OSIS as of January 2015.
- Inspection Activity in FY20 includes use of alternative approaches (e.g., RRAs and RRR).

GLP Inspection Final Classifications*

(CDER, FY 2020)



*Based on Log Out date, [Complis database as of Feb 9, 2021].