Office of Scientific Investigations &
Office of Study Integrity and Surveillance

BIMO Metrics

[Updated: May 30, 2019]
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 these inspections 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, health 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 Bioreserach Monitoring Metrics Overview

• Data source:
  – Data obtained from FDA’s Complis database and other sources as noted.

• Data conventions
  – Metrics are based on key events during the inspection process, including starting an inspection, issuing an inspection assignment, 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’ (ORA) 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.
Metrics Terms

- BA/BE - Bioavailability/Bioequivalence
- BE or BEQ – Bioequivalence
- BIMO – Bioresearch Monitoring
- CI or Clin– 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
- CDER – Center for Drug Evaluation and Research
- CBER – Center for Biologics Evaluation and Research
- CDRH – Center for Devices and Radiological Health
*Based on inspection start date – [Complis database as of January 7, 2019]

• Sponsor (GCP) includes Sponsor/CRO/Sponsor-Investigator

• BA/BE Application-Inspections accomplished with 205 FY18 Site Visits (see page 33).

• Good Laboratory Practice and Bioequivalence inspection programs operated by OSIS as of January 2015.

Application-Inspections Overseen by OSI/OSIS*

(CDER, FY 2009 - FY 2018)
Domestic vs. Foreign Application-Inspections Overseen by OSI/OSIS*
(CDER, FY 2014 - FY 2018)

*Based on inspection start date – [Complis database as of January 7, 2019]
- Sponsor (GCP) includes Sponsor/CRO/Sponsor-Investigator
- Good Laboratory Practice and Bioequivalence inspection programs operated by OSIS as of January 2015
Bioresearch Monitoring Program Inspections*
(CDER, FY 2018)

- Clinical Investigator: 44%
- Bioavailability/Bioequivalence: 39%
- Good Laboratory Practice: 2%
- Institutional Review Board/Radioactive Drug Research Committee: 8%
- Sponsor (GCP): 7%

1242 BIMO Application-Inspections

*Based on inspection start date – [Complis database as of January 7, 2019]
Clinical Investigator Inspections Classified*
(All Centers, FY 2018)

* Center numbers based on number of classified inspections reported to BIMO Operations Steering Committee for FY18.
• CDER: Center for Drug Evaluation and Research. CBER: Center for Biologics Evaluation and Research. CDRH: Center for Devices and Radiological Health. CVM: Center for Veterinary Medicine.
Clinical Investigator: Data Audit versus Referral*
(CDER, FY 2018)

- DataAudit 84%
- Referral 16%

547 Inspections

* Based on inspection start date – [Complis database as of January 7, 2019]
* Referrals include Complaints, Required Reports, IRB/Sponsor Notifications, and other referrals-internal and external for All OSI Branches
Clinical Investigator Inspections*
(CDER, FY 2009 – FY 2018)

* Based on inspection start date – [Complis database as of January 7, 2019]
Clinical Investigator Inspections by Location*
(CDER, FY 2018)

*Based on inspection start date – [Complis database as of January 7, 2019]
International Clinical Investigator Inspections*
(CDER, FY 2007 - FY 2018)

*Based on inspection start date – [Complis database as of January 7, 2019]
International Clinical Investigator Inspections by Location*
(CDER, FY 2018)

- Eastern Europe: 33%
- Western Europe: 25%
- Africa: 2%
- Asia: 2%
- Canada: 5%
- Australia: 3%
- Asia/Pacific: 20%
- Latin America: 10%

167 Inspections

*Based on inspection start date – [Complis database as of January 7, 2019]
Clinical Investigator Inspections Final Classification*
(CDER, FY 2018)

- No Action Indicated: 67.2%
- Voluntary Action Indicated: 31.3%
- Official Action Indicated: 1.5%

591 Inspections Classified

*Based on LogOut Date and Final Classification; Includes OAI Untitled Letters, [Complis database as of January 7, 2019]
International Clinical Investigator Inspections Final Class*
(CDER, FY 2018)

No Action Indicated 79%
Voluntary Action Indicated 21%

Official Action Indicated 0%
169 Inspections Classified

*Based on LogOut Date; Includes OAI Untitled Letters, [Complis database as of January 7, 2019]
Frequency of Clinical Investigator-Related Deficiencies Based on Post-Inspection Correspondence Issued* (CDER, FY 2018)

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### Domestic CI Deficiencies
- Protocol: 29%
- Records: 14%
- Consent: 4%
- Drug Accountability: 3%

395 Domestic Inspections

### Foreign CI Deficiencies
- Protocol: 14%
- Records: 10%
- IRB Communication: 2%
- Consent: 2%

198 Foreign Inspections

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*Based on LogOut Date and Classification. Inspections may have multiple deficiencies. Includes OAI untitled letters. [Complis database as of January 7, 2019]*

Note: this does not denote number of inspections completed, but rather number of inspection reports evaluated and closed.
Frequency of Clinical Investigator Related Deficiencies Based on Post-Inspectional Correspondence Issued: Official Action Indicated (OAI) Final classification* (CDER, FY 2018)

- Records: 40%
- Drug Accountability: 40%
- Submission of False Info: 20%
- Protocol: 20%

5 OAI Inspections

*Based on letter issue date. Inspections may have multiple deficiencies. Includes OAI untitled letters. [Complis database as of January 7, 2019] Note: this represents the number of inspection reports evaluated and closed which differs from the number of inspections performed.
Referrals Received by OSI*  
(CDER, FY 2009 - FY 2018)

*Includes Complaints, Required Reports, IRB/Sponsor Notifications, and internal/external referrals for all branches where evaluation may result in inspection.
[Complis database as of January 7, 2019]
Referral-Related Clinical Investigator Inspections*
(CDER, FY 2009 - FY 2018)

*Based on inspection start date; Referrals include Complaints, Required Reports, IRB/Sponsor Notifications, and other referrals-internal and external for All Branches
[Complis database as of January 7, 2019]
Referral-Related Sponsor Inspections*
(CDER, FY 2009 - FY 2018)

*Based on inspection start date; Referrals include Complaints, Required Reports, IRB/Sponsor Notifications, and other referrals-internal and external for All Branches
[Complis database as of January 7, 2019]
*Based on letter issue date [Complis database as of January 7, 2019]*

- **BIMO** = Bioresearch Monitoring (Clinical Investigators, Sponsor/CRO/Sponsor-Investigator (GCP), IRB, BEQ, GLP)
- **NIDPOE** = Notice of Initiation of Disqualification Proceedings and Opportunity to Explain

**BIMO Warning/NIDPOE Letters**

(CDER, FY 2009 - FY 2018)
• As of June 2011, the Postmarketing Adverse Drug Event and Risk Evaluation and Mitigation Strategy programs were incorporated into OSI.

• Includes Clinical Investigators, Sponsor/CRO/Sponsor-Investigator (GCP), IRB, BEQ, GLP, REMS, Adverse Drug Event (ADE) and Postmarketing Requirements (PMR) Warning Letters.

• PMR includes all required studies and clinical trials that are mandated by statute (e.g., section 505(o)(3) of FDCA, PREA, Animal Rule and 21 CFR 314 and 601 Subparts H and E, respectively.

*Based on letter issue date [Complis database as of January 7, 2019]
Clinical Investigator Warning/NIDPOE Letters*
(CDER, FY 2009 - FY 2018)

*Based on letter issue date [Complis database as of January 7, 2019]
NIDPOE = Notice of Initiation of Disqualification Proceedings and Opportunity to Explain
### Clinical Investigator Regulatory Actions*
(CDER, FY 2009 - FY 2018)

<table>
<thead>
<tr>
<th>Action</th>
<th>FY09</th>
<th>FY10</th>
<th>FY11</th>
<th>FY12</th>
<th>FY13</th>
<th>FY14</th>
<th>FY15</th>
<th>FY16</th>
<th>FY17</th>
<th>FY18</th>
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<td>18</td>
<td>13</td>
<td>13</td>
<td>5</td>
<td>5</td>
<td>11</td>
<td>4</td>
<td>7</td>
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<tr>
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</table>

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 January 7, 2019]  
**WLs 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 2009 - FY 2018)

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<th>Program Area</th>
<th>FY09</th>
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*Based on letter issue date [Complis database as of January 7, 2019]
**Posted Bioavailability/ Bioequivalence OAI untitled letters.
***As of June 2011, Postmarketing Adverse Drug Event and Risk Evaluation and Mitigation Strategies inspection programs incorporated into OSI.
^Postmarketing Requirements (PMR) includes all required studies and clinical trials that are mandated by statute (e.g., section 505(o)(3) of FDCA, PREA, Animal Rule and 21 CFR 314 and 601 Subparts H and E, respectively.
IRB/RDRC Inspections*
(CDER, FY 2009 - FY 2018)

*Based on inspection start date [Complis database as of January 7, 2019]
Includes only CDER numbers – previously reported metrics may have used combined data across CDER, CBER and CDRH
IRB Inspection Final Classifications*
(CDER, FY 2018)

No Action Indicated 71%
Voluntary Action Indicated 28%
Official Action Indicated 1%

104 Inspections

*Based on letter issue date, [Complis database as of January 7, 2019]
Frequency of IRB-Related Deficiencies Based on Post-Inspection Correspondence Issued*
(CDER, FY 2018)

*Based on letter issue date, [Complis database as of January 7, 2019]
Note: this represents the number of inspection reports evaluated and closed which differs from the number of inspections performed.
Postmarketing Adverse Drug Experience Inspections*
(CDER, FY 2018)

- NAI (62%)
- VAI (38%)

71 Inspections

*Based on Close/Log Out Date, [OSI database as of January 7, 2019]
Risk Evaluation and Mitigation Strategies Inspections*
(CDER, FY 2010 - 2018)

*Based on date inspection started, REMS inspection program began in FY10.
*Based on inspection start date [Complis database as of January 7, 2019]
The Sponsor/CRO distribution shifted for FY09-12 in previous releases due to data corrections in the Complis Database.
GCP-Related Sponsor/Contract Research Organization Inspections Final Classification*
(CDER, FY 2018)

- No Action Indicated: 77%
- Voluntary Action Indicated: 23%

*Based on letter issue date [Complis database as of January 7, 2019]
Includes Sponsor-Investigator Inspections
Bioavailability/Bioequivalence Site Visits and Applications Inspected*
(CDER, FY 2014 - FY 2018)

*Based on inspection Start Date [Complis database as of January 7, 2019]
Includes only CDER numbers.
Bioavailability/Bioequivalence Site Visit Final Classifications*
(CDER, FY 2018)

*Based on Logout date and Final Classification, [Complis database as of January 7, 2019]
Frequency of BA/BE-Related Deficiencies*
(CDER, FY 2018)

- **Stability**: 24%
- **Validation**: 10%
- **Chromatograms**: 9%
- **Calibration Curve**: 8%

78 Analytical Classified Site Visits

163 Clinical & Clin End Pt Classified Site Visits

- **Record Keeping**: 7%
- **Blinding Code**: 3%
- **SOPs**: 2%
- **Inclusion/Exclusion Criteria**: 2%
- **Adverse Events**: 2%

*Based on Logout date and Final Classification, [Complis database as of January 7, 2019]*

Note that this does not denote number of inspections completed, but rather number of inspection reports evaluated and closed in the fiscal year.
Bioavailability/Bioequivalence Analytical Site Visit Final Classifications and Application Types*
(CDER, FY 2018)

78 Analytical Site Visits
208 Application-Inspections covering 204 unique applications

*Based on Logout date and Final Classification, [Complis database as of January 7, 2019]
Bioavailability/Bioequivalence Clinical Site Visit Final Classifications and Application Types*
(CDER, FY 2018)

*Based on Logout date and Final Classification, [Complis database as of January 7, 2019]
Bioavailability/Bioequivalence Clinical End Point Site Visit Final Classifications*
(CDER, FY 2018)

- No Action Indicated: 85%
- Official Action Indicated: 3%
- Voluntary Action Indicated: 12%

60 Clinical End Point Site Visits
62 Application-Inspections covering 24 unique applications

*ANDA Applications based on Logout date and Final Classification, [Complis database as of January 7, 2019]