Office of Scientific Investigations & Office of Study Integrity and Surveillance

BIMO Metrics

[Updated: December 2017 ]
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 Bioresearch 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) FACTS database) 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

- 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 December 29, 2017]

- Sponsor (GCP) includes Sponsor/CRO/Sponsor-Investigator
- BEQ Application-Inspections accomplished with 289 FY17 Site Visits
- Good Laboratory Practice and Bioequivalence inspection programs operated by OSIS as of January 2015

*Based on inspection start date – [Complis database as of December 29, 2017]
### Domestic vs. Foreign Application-Inspections Overseen by OSI/OSIS*
(CDER, FY 2013 - FY 2017)

<table>
<thead>
<tr>
<th>Year</th>
<th>Domestic</th>
<th>Foreign</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013</td>
<td>527</td>
<td>72</td>
</tr>
<tr>
<td>2014</td>
<td>104</td>
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<td>2015</td>
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<td>2016</td>
<td>233</td>
<td>52</td>
</tr>
<tr>
<td>2017</td>
<td>261</td>
<td>72</td>
</tr>
</tbody>
</table>

- **Domestic** includes Postmarketing Adverse Drug Experience, Good Laboratory Practice, Bioequivalence, Sponsor (GCP), and Clinical Investigator.
- **Foreign** includes the same categories as Domestic.

*Based on inspection start date – [Complis database as of December 29, 2017]*

- Sponsor (GCP) includes Sponsor/CRO/Sponsor-Investigator
- Good Laboratory Practice and Bioequivalence inspection programs operated by OSIS as of January 2015
Bioreresearch Monitoring Program Inspections*
(CDER, FY 2017)

*Based on inspection start date – [Complis database as of December 29, 2017]
Clinical Investigator Inspections Classified*
(All Centers, FY 2017)

* CDER, CDRH and CBER numbers based on number of classified inspections reported to BIMO Resource Allocation Metrics PAG for FY17.
• CDER: Center for Drug Evaluation and Research. CBER: Center for Biologics Evaluation and Research. CDRH: Center for Devices and Radiological Health.
Clinical Investigator: Data Audit versus Referral*
(CDER, FY 2017)

*Based on inspection start date – [Complis database as of December 29, 2017]*
*Referrals include Complaints, Required Reports, IRB/Sponsor Notifications, and other referrals-internal and external for All OSI Branches*
Clinical Investigator Inspections*
(CDER, FY 2008 – FY 2017)

*Based on inspection start date – [Complis database as of December 29, 2017]
Clinical Investigator Inspections by Location*
(CDER, FY 2017)

*Based on inspection start date – [Complis database as of December 29, 2017]
International Clinical Investigator Inspections*
(CDER, FY 2007 - FY 2017)

*Based on inspection start date – [Complis database as of December 29, 2017]
International Clinical Investigator Inspections by Location*
(CDER, FY 2017)

- Western Europe: 31%
- Eastern Europe: 30%
- Asia/Pacific: 14%
- Canada: 6%
- Australia: 1%
- Latin America: 10%
- Middle East/Central Asia: 5%

161 Inspections

*Based on inspection start date – [Complis database as of December 29, 2017]
Clinical Investigator Inspections Final Classification* (CDER, FY 2017)

*Based on EIR Received date and Final Classification; Includes OAI Untitled Letters, [Complis database as of December 29, 2017]
International Clinical Investigator Inspections Final Class*
(CDER, FY 2017)

142 Inspections

No Action Indicated 76%

Voluntary Action Indicated 24%

Official Action Indicated 0%

*Based on EIR Received date; Includes OAI Untitled Letters, [Complis database as of December 29, 2017]
Frequency of Clinical Investigator-Related Deficiencies Based on Post-Inspection Correspondence Issued* (CDER, FY 2017)

Domestic CI Deficiencies

- Protocol: 26%
- Records: 14%
- Drug Accountability: 3%
- Consent: 2%
- IRB Communication: 2%
- Adverse Events: 1%

Total: 276 Domestic Inspections

Foreign CI Deficiencies

- Protocol: 16%
- Records: 10%
- Consent: 4%
- Adverse Events: 1%
- Other: 1%
- IRB Communication: 1%

Total: 142 Foreign Inspections

*Based on EIR Received date and Classification. Inspections may have multiple deficiencies. Includes OAI untitled letters. [Complis database as of December 29, 2017]

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 2017)

*Based on letter issue date. Inspections may have multiple deficiencies. Includes OAI untitled letters. [Complis database as of December 29, 2017]
Note: this does not denote number of inspections completed, but rather number of inspection reports evaluated and closed.
Referrals Received by OSI*
(CDER, FY 2008 - FY 2017)

*Includes Complaints, Required Reports, IRB/Sponsor Notifications, and internal/external referrals for all branches where evaluation may result in inspection.
[Complis database as of December 29, 2017]
Referral-Related Clinical Investigator Inspections*
(CDER, FY 2008 - FY 2017)

*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 December 29, 2017]
Referral-Related Sponsor Inspections*
(CDER, FY 2008 - FY 2017)

*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 December 29, 2017]
BIMO Warning/NIDPOE Letters*
(CDER, FY 2008 - FY 2017)

*Based on letter issue date [Complis database as of December 29, 2017]
- BIMO = Bioresearch Monitoring (Clinical Investigators, Sponsor/CRO/Sponsor-Investigator (GCP), IRB, BEQ, GLP)
- NIDPOE = Notice of Initiation of Disqualification Proceedings and Opportunity to Explain

Notice of Initiation of Disqualification Proceedings and Opportunity to Explain

Warning Letter

<table>
<thead>
<tr>
<th>Year</th>
<th>BIMO Warning Letters</th>
<th>NIDPOE Letters</th>
</tr>
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<tbody>
<tr>
<td>2008</td>
<td>5</td>
<td>18</td>
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<tr>
<td>2009</td>
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<td>6</td>
<td>3</td>
</tr>
<tr>
<td>2017</td>
<td>6</td>
<td>6</td>
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</table>
Warning Letters*
(CDER, FY 2008 - FY 2017)

*Based on letter issue date [Complis database as of December 29, 2017]

As of June 2011, the Postmarketing Adverse Drug Event inspection program was incorporated into OSI.

Includes Clinical Investigators, Sponsor/CRO/Sponsor-Investigator (GCP), IRB, BEQ, GLP, 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.)
Clinical Investigator Warning/NIDPOE Letters*
(CDER, FY 2008 - FY 2017)

*Based on letter issue date [Complis database as of December 29, 2017]
NIDPOE = Notice of Initiation of Disqualification Proceedings and Opportunity to Explain
Clinical Investigator Regulatory Actions*
(CDER, FY 2007 - FY 2017)

<table>
<thead>
<tr>
<th>Action</th>
<th>FY08</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>
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<td>WL**</td>
<td>12</td>
<td>18</td>
<td>13</td>
<td>13</td>
<td>5</td>
<td>5</td>
<td>11</td>
<td>4</td>
<td>7</td>
<td>4</td>
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<tr>
<td>NIDPOE</td>
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<td>5</td>
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<td>2</td>
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<td>5</td>
<td>3</td>
<td>0</td>
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</tr>
<tr>
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<td>CA-Restricted</td>
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<tr>
<td>CA-Full DQ</td>
<td>6</td>
<td>3</td>
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<tr>
<td>DQ-Hearing/Commissioner</td>
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</tr>
</tbody>
</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 December 29, 2017]

**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 2008 - FY 2017)

*Based on letter issue date [Complis database as of December 29, 2017]

**Posted 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.

<table>
<thead>
<tr>
<th>Program Area</th>
<th>FY08</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>
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<td>0</td>
<td>1</td>
<td>0</td>
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<td>Clinical Investigator</td>
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<td>13</td>
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<td>5</td>
<td>11</td>
<td>4</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Sponsor-Investigator (GCP)</td>
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<td>Sponsor (GCP)</td>
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<tr>
<td>Contract Research Organization (GCP)</td>
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<tr>
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<td>Radioactive Drug Research Committee</td>
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<tr>
<td>Postmarketing Adverse Drug Event***</td>
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<tr>
<td>Risk Evaluation and Mitigation Strategy***</td>
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</tbody>
</table>
IRB/RDRC Inspections*
(CDER, FY 2008 - FY 2017)

*Based on inspection start date [Complis database as of December 29, 2017]
Includes only CDER numbers – previously reported metrics may have used combined data across CDER, CBER and CDRH
IRB Inspection Final Classifications*
(CDER, FY 2017)

- No Action Indicated: 82%
- Voluntary Action Indicated: 18%
- Official Action Indicated: 0%

79 Inspections

*Based on letter issue date, [Complis database as of December 29, 2017]
Frequency of IRB-Related Deficiencies Based on Post-Inspection Correspondence Issued*  
(CDER, FY 2017)

- Records: 7
- Written Procedures: 3
- Suspension or termination: 2

79 IRB Inspections

*Based on letter issue date, [Compls database as of December 29, 2017]
Note that this does not denote number of inspections completed, but rather number of inspection reports evaluated and closed in the fiscal year.
Postmarketing Adverse Drug Experience Inspections*  
(CDER, FY 2017)

- Voluntary Action Indicated: 41%  
- Official Action Indicated: 2%  
- No Action Indicated: 57%

*Based on Log Out Date, [OSI database as of December 29, 2017]
Risk Evaluation and Mitigation Strategies Inspections*
(CDER, FY 2010 - 2017)

*Based on date inspection started, REMS inspection program began in FY10.
Based on inspection start date [Complis database as of December 29, 2017]
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 2017)

*Based on letter issue date [Complis database as of December 29, 2017]
Includes Sponsor-Investigator Inspections

- No Action Indicated: 67%
- Voluntary Action Indicated: 30%
- Official Action Indicated: 3%

57 Inspections
Bioequivalence Site Visits and Applications Inspected*  
(CDER, FY 2014 - FY 2017)

*B Based on inspection Start Date [Complis database as of December 29, 2017] 
*Includes only CDER numbers.
Bioequivalence Site Visit Final Classifications*
(CDER, FY 2017)

No Action Indicated 68%
Voluntary Action Indicated 27%
Official Action Indicated 5%

353 Site Visits

*Based on Logout date and Final Classification, [Complis database as of December 29, 2017]
Frequency of BEQ-Related Deficiencies*
(CDER, FY 2017)

- Validation: 12%
- Stability: 11%
- Records: 11%
- Reserve Samples: 10%
- Chromatograms: 4%
- Dosing: 4%

353 Site Visits Classified

*Based on Logout date and Final Classification, [Complis database as of December 29, 2017]
Note that this does not denote number of inspections completed, but rather number of inspection reports evaluated and closed in the fiscal year.