Postmarketing Adverse Drug Experience (PADE) Inspections - Part IV

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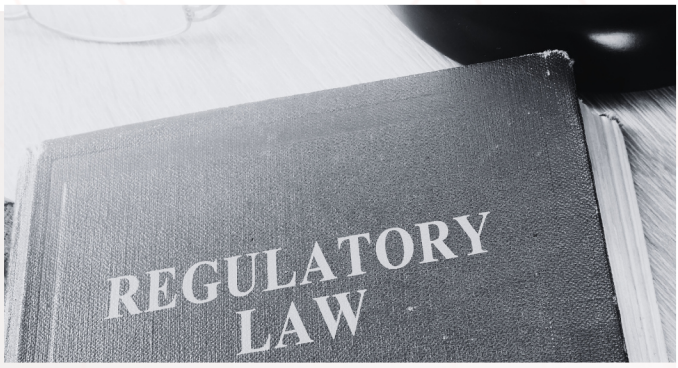
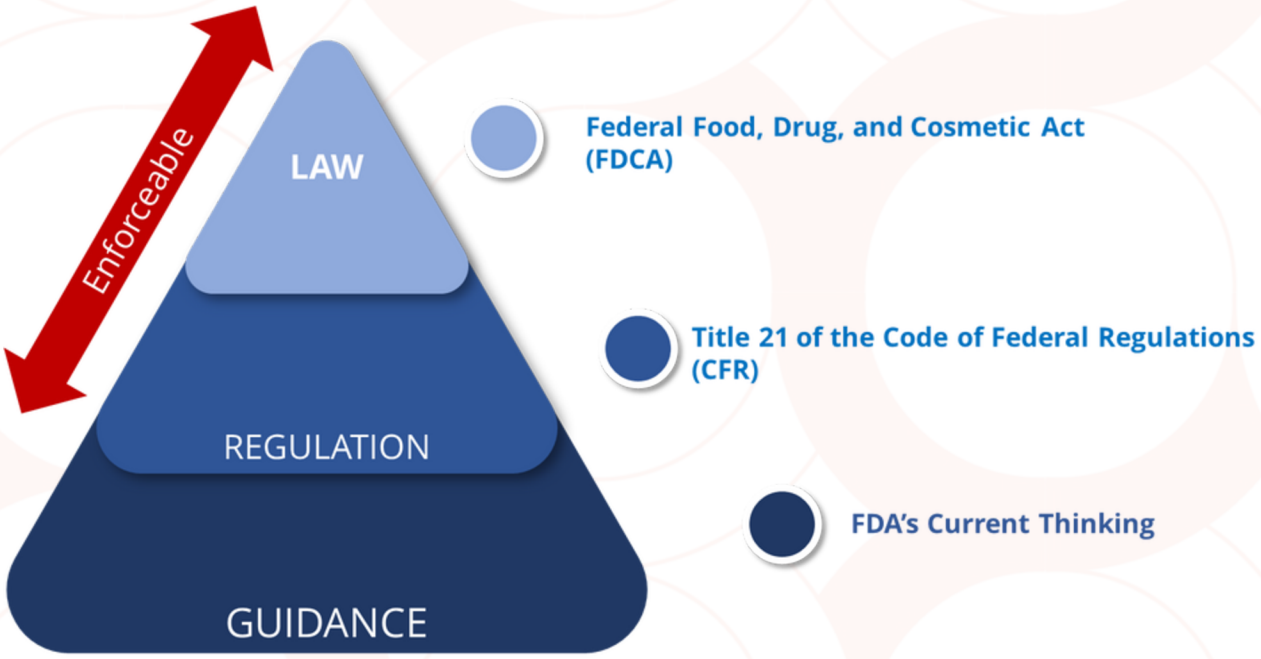
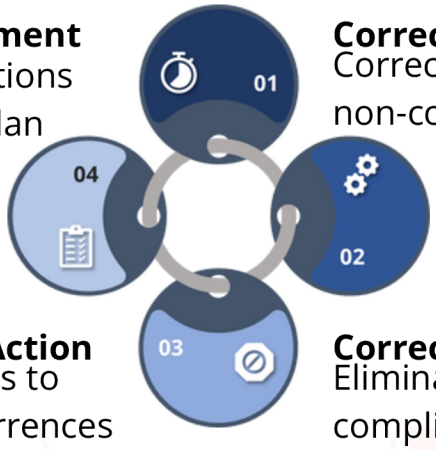


Legal Framework of PADE Inspections



Good Corrective Action Plan



Assessment
Verify timeliness of actions and effectiveness of plan

Correction
Correct instances of non-compliance

Preventative Action
Implement measures to prevent future occurrences

Corrective-Action
Eliminate causes of non-compliance

Four Reasons to Submit a Complete and Timely Written Response

- Determine if safety report submissions are in an electronic format that FDA can process, review, and archive, as required.
- Review system-generated delivery confirmation notices from either the Electronic Submission Gateway (ESG) or the Safety Reporting Portal (SRP) and determine if the firm has a procedure for correcting and resubmitting any submission for which the message delivery notice (MDN) indicated that the submission was not accepted.
- Determine if the firm has a corrective action for each late submission to the Agency, according to the MDN.
- Determine if MDNs are being retained.

Points to Consider for Written Responses to the FDA

Include a commitment from senior leadership

Address each observation separately

Note whether you agree or disagree

Provide both corrective and preventive actions

Provide both completed and planned actions

Provide timelines for completion

Provide a method of verification or monitoring the effectiveness of the actions

Submit documentation (training, SOPs, CAP, records)

SUBMIT THE RESPONSE WITHIN 15 WORKING DAYS

Inspection Reporting: FORM FDA 483, Inspectional Observations

No Action Indicated (NAI)

No objectionable conditions or practices were found during an inspection (or the objectionable conditions found do not justify further regulatory action).

Voluntary Action Indicated (VAI)

Objectionable conditions or practices were found, but do not rise to the level warranting OAI classification.

Official Action Indicated (OAI)

Objectionable conditions or practices were found, whose scope, severity, or pattern warrants the recommendation for a regulatory action.

Warning Letters

The issuance of a Warning Letter (WL) may be warranted when the inspection uncovers significant objectionable conditions related to noncompliance with PADE requirements. The CDER PVC Team and OSI management will evaluate all inspections classified as OAI by OBIMO on a case-by-case basis.

Untitled Letters

An Untitled Letter (UL) may be warranted when the deficiencies found at the firm are severe enough to justify a formal letter to the firm, but do not meet the threshold of regulatory significance for a WL.
Factors that influence the issuance of a WL or UL include the nature and extent of the violations (for example, if they are repeated or deliberate), the compliance history of the inspected firm, and the corrective actions implemented by the firm.

Inspection Reporting: FORM FDA 483, Inspectional Observations

Enforcement Actions

Generally, FDA may take the following enforcement actions if the firm does not implement adequate corrective actions and continues to violate PADE regulations or the FD&C Act following the issuance of a WL or UL.

1. **Injunction:** Injunction should be considered when follow-up inspection(s) show that the firm has a continuing pattern of significant and substantial deviations, despite previous attempts by FDA to obtain compliance.

2. **Seizure:** Seizure for failure to comply with postmarketing adverse drug experience reporting regulations would be possible only if the approval of the application for the product has first been withdrawn (FD&C Act, section 304(a)(1)). Seizure would then be based on distribution of an unapproved drug product.

3. **Prosecution:** Evidence that a firm is submitting false information, not submitting required reports for serious postmarketing adverse events, or withholding important information, the submission of which may have resulted in the Agency requiring labeling changes or withdrawing an application, should be referred to the Office of Criminal Investigations (OCI) for consideration of prosecution.

Selected References

- https://www.fda.gov/
- Number of 483 issued from the System* Inspections ending between 10/1/2022 and 9/30/2023 https://www.fda.gov/inspections-compliance-enforcement-andcriminal-investigations/inspection-references/inspection-observations
- Postmarketing Drug Safety Compliance: 2019 Inspection Findings April 29, 2020 (Live Webinar) Center for Drug Evaluation and Research – Small Business and Industry Assistance, Center for Drug Evaluation and Research, US Food and Drug Administration
- Postmarketing Drug Safety and Inspection Readiness June 19, 2018 Center for Drug Evaluation and Research (CDER) Small Business and Industry Assistance (SBIA) Webinar
- Postmarketing Drug Safety and Inspection Readiness June 19, 2018 Center for Drug Evaluation and Research (CDER) Small Business and Industry Assistance (SBIA) Webinar
- CHAPTER 53 – Postmarketing Surveillance and Epidemiology: Human Drug and Therapeutic Biological Products, fda.gov

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Dr. Sumit Verma is a medical graduate with specialization in anesthesiology and has more than 15 years of experience in the pharmaceutical industry, clinical medicine, clinical research, and pharmacovigilance. He has built teams that have consistently delivered and exceeded customer expectations across pharmacovigilance domains such as case processing, signal management, risk management, aggregate reports, and clinical safety. He has co-authored two books – one on pharmacovigilance and another on pharmacology.

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Disclaimer

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