Postmarketing Adverse Drug Experience (PADE) Inspections – Part I

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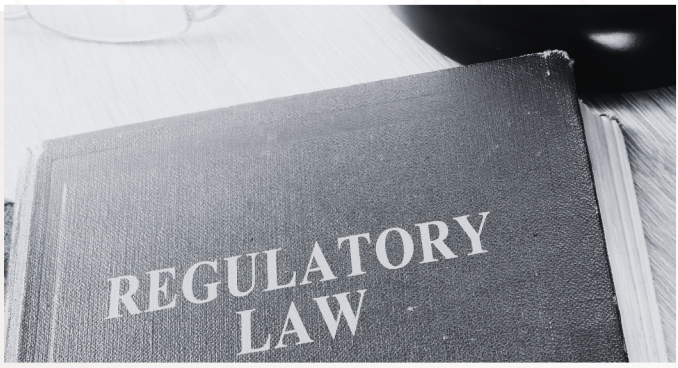
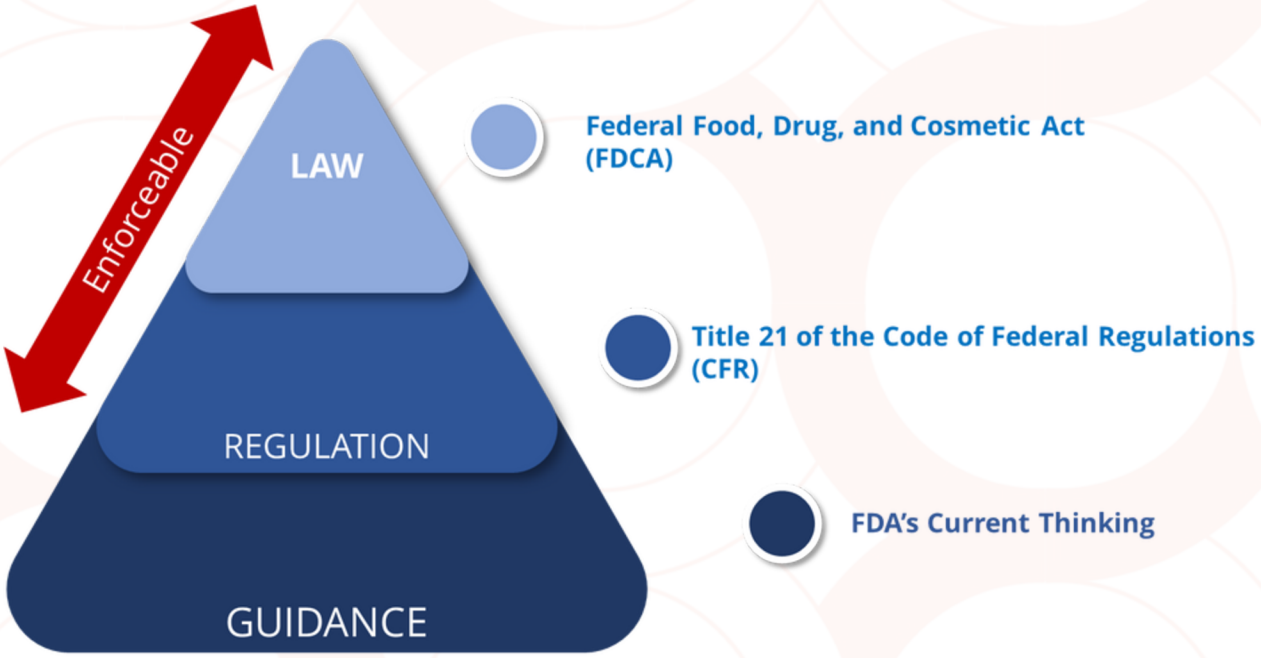


Legal Framework of PADE Inspections



PADE STATUTORY PROVISIONS / REGULATIONS: PRESCRIPTION DRUG PRODUCTS FOR HUMAN USE

#	FD&C Act, subchapter V, part A, section 505 (21 U.S.C. 355)	Comments
1	21 CFR 310.305	New Drugs: Records and reports concerning adverse drug experiences (ADEs) for marketed prescription drugs for human use without an approved new drug application
2	21 CFR 314.80	New drug applications: Postmarketing reporting of ADEs

3	21 CFR 314.81(b)(2)	New drug applications: Annual reports
4	21 CFR 314.90	New drug applications: Waivers
5	21 CFR 314.98	Abbreviated applications: Postmarketing reports
6	21 CFR 314.540	Accelerated approval of new drugs for serious or life-threatening illnesses: Postmarketing safety reporting
7	21 CFR 314.630	Approval of new drugs when human efficacy studies are not ethical or feasible: Postmarketing safety reporting
8	21 CFR part 4, subpart B	Postmarketing safety reporting for combination products

APPROVAL VS. MARKETING

✔ Once a drug is approved, applicant holders MUST receive, evaluate, and report adverse drug experiences (ADEs) to FDA, even if the drug is not marketed.

PADE Inspection - Scope

- Written procedures
- Product list (approval date, status, etc.)
- Late or Missing Periodic Reports or Annual Reports
- Late, missing, incomplete, or inaccurate 15-day reports
- ADEs from all sources
- Root cause analyses and corrective actions for deviations
- Confirmations for electronic submissions
- Training Documents
- Safety Contracts, Agreements, and Business Partners
- Organization, roles, and responsibilities
- Waivers

Who can be inspected for PADE Compliance?

Application holders

Applicants with approved drugs and therapeutic biologics (prescription and non-prescription)

- New Drug Application (NDA)
- Abbreviated New Drug Application (ANDA)
- Biologics License Application (BLA)

Non- Applicants

Manufacturers, packers, distributors, retailers, and certain others named on product labels (responsibilities vary based on product type)

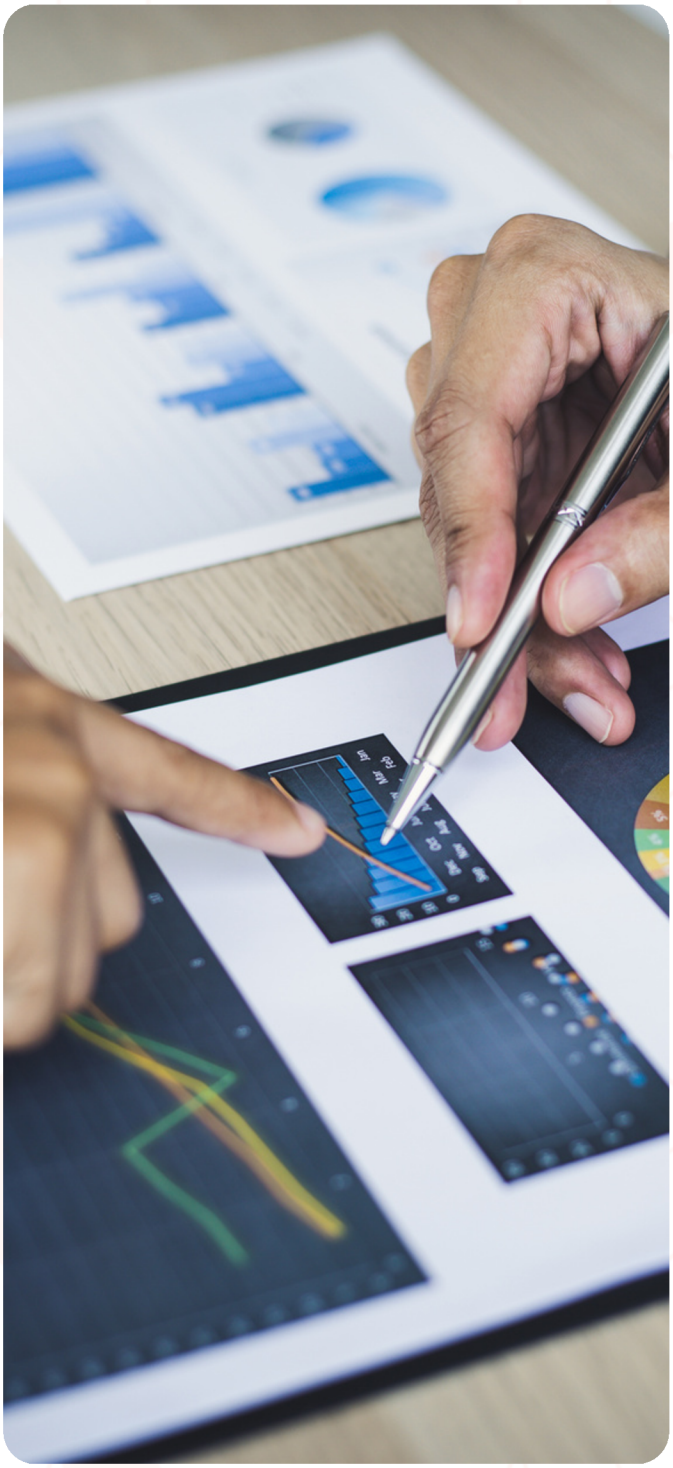
- Approved prescription and non-prescription drugs and therapeutic biologics (NDA, ANDA, BLA)
- Unapproved prescription drugs
- Unapproved non-prescription drugs

Third parties

Contractors, vendors, and other third parties
Pharmacovigilance activities conducted on behalf of application holders or non-applicants

Risk Based Selection for PADE Inspection

- Determine if the firm is monitoring potential sources of adverse event information
- Determine if the firm is surveilling both foreign and domestic sources.
- Determine if the firm is promptly reviewing all postmarketing safety information received from any source



Inspection History

- Compliance and inspection history
  - Never inspected for PADE compliance
  - Inspection findings from other program areas
- Firm's written responses to previous PADE inspections

Firm Information

- Corporate changes
- Portfolio (type and number of products)
- Complaints
- Internal FDA information
- Information from other health authorities

Product Portfolio

- New molecular entities
- High-risk
- Patient exposure
- Recalls
- Submissions to FDA
  - Individual Case Safety Reports (ICSRs)
  - Annual reports
  - Periodic report

Selected References

1. https://www.fda.gov/
2. Number of 483 issued from the System* Inspections ending between 10/1/2022 and 9/30/2023 https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/inspection-references/inspection-observations
3. 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
4. Postmarketing Drug Safety and Inspection Readiness June 19, 2018 Center for Drug Evaluation and Research (CDER) Small Business and Industry Assistance (SBIA) Webinar
5. Postmarketing Drug Safety and Inspection Readiness June 19, 2018 Center for Drug Evaluation and Research (CDER) Small Business and Industry Assistance (SBIA) Webinar
6. 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

The scenario described in this post is entirely hypothetical. It is not based on real-world patient data or individual case safety reports. All pharmacological mechanisms and regulatory references are cited to support discussion only. This post is intended to facilitate dialogue on signal detection and does not imply new safety findings, labeling recommendations, clinical guidance or clinical relevance.

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