Postmarketing Adverse Drug Experience (PADE) Inspections - Part III

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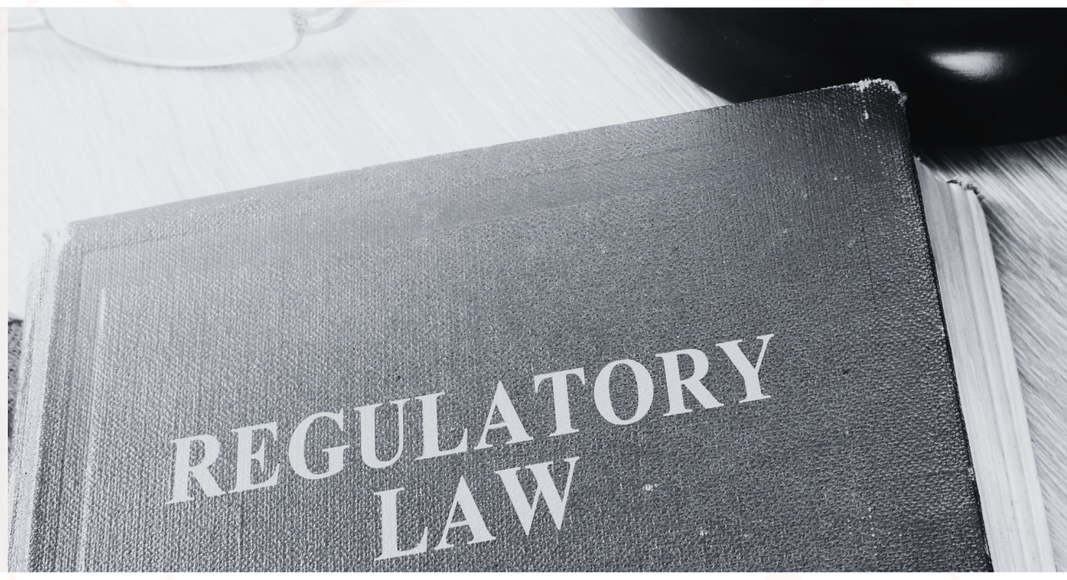
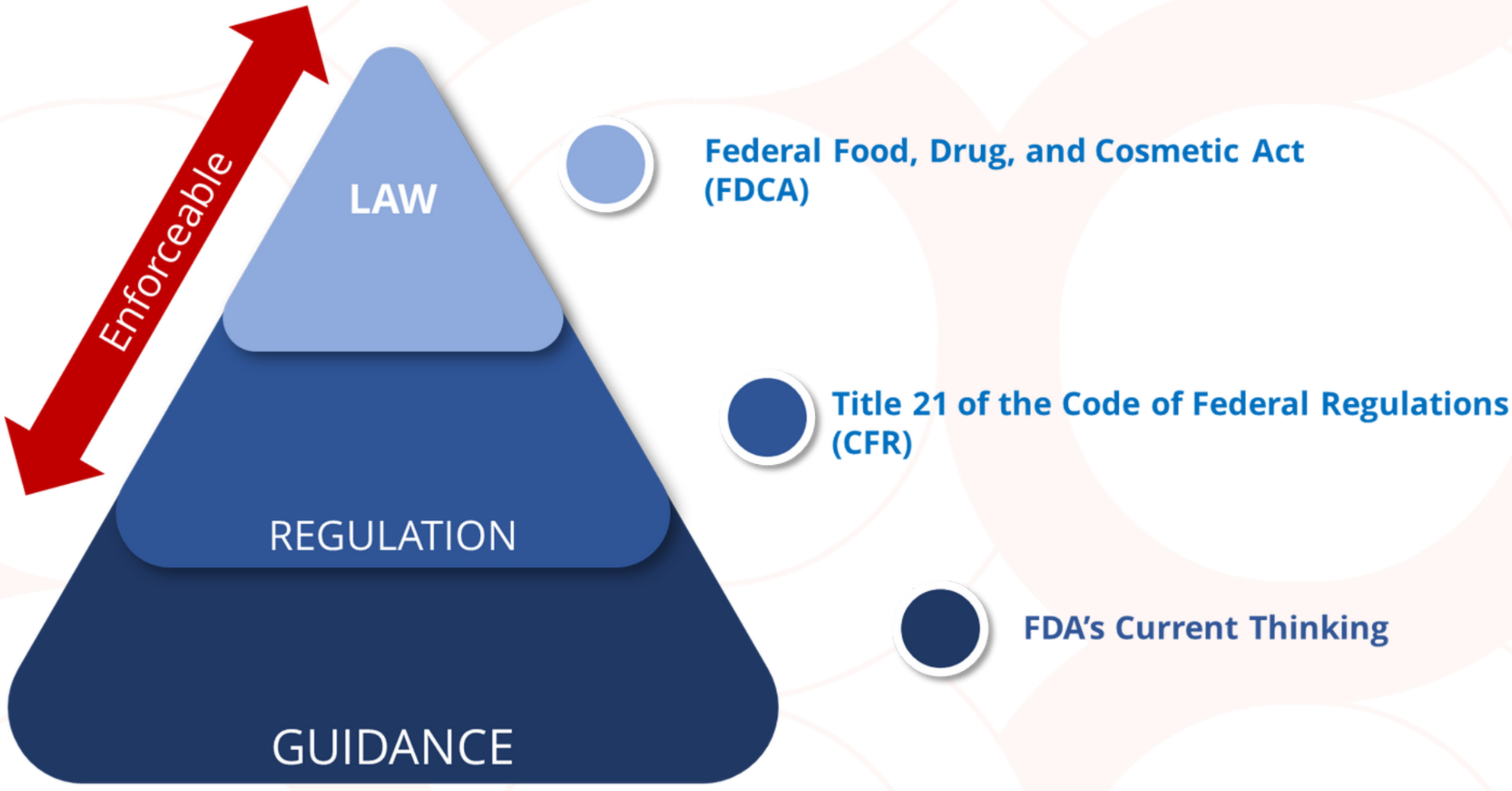


Legal Framework of PADE Inspections



Scientific Literature Reports

Determine:

- If the firm reviews scientific literature and the frequency of the review.
- If the applicant or non-applicant is submitting expedited ICSRs for adverse experiences obtained from the published scientific and medical literature that are both serious and unexpected.
- If the applicant or non-applicant is submitting a copy of the published article as an ICSR attachment for each expedited ICSR of an adverse experience obtained from the published scientific and medical literature. Foreign language articles should be accompanied by an English translation of the abstract.

FOREIGN POSTMARKETING ADVERSE EXPERIENCE REPORTING

Determine:

- If written procedures address the surveillance, receipt, evaluation, and reporting of adverse experiences from affiliates, subsidiaries, contractors, and business partners outside the United States.

- If serious and unlabeled (i.e., unexpected) adverse experiences from foreign sources have been submitted to FDA within 15 calendar day.

SOLICITED SAFETY DATA

Determine:

- How the firm identifies and monitors all sources of solicited safety information including, but not limited to, postmarketing studies, nonapplicant-sponsored clinical data obtained by the firm, and patient engagement programs, to ensure that the firm's pharmacovigilance personnel receive all potential adverse experiences. The identification and monitoring of solicited safety data should be addressed in the firm's written procedures.

- If the firm is monitoring its firm-sponsored internet and social media sites, and the frequency of the monitoring.

- If solicited safety data has been assessed for seriousness, unexpectedness, and causality.

- If solicited safety data that has been assessed as serious, unexpected, and possibly related to the suspect product has been submitted to FDA within 15 days of receipt of the information

- During inspection, auditor may select several Annual Reports and confirm that the status of the firm's postmarketing studies is included in the reports.

Aggregate Safety Reports

The reporting interval is quarterly for the first three years following the approval of the application or license, and annually thereafter, unless FDA instructs the firm otherwise.

Determine:

- If the PADER or PAER contains all the required content as described in 21 CFR 314.80(c)(2) or 21 CFR 600.80(c)(2), respectively.
- If the PADER or PAER has been submitted within the required regulatory timelines.
- Several Annual Reports may be selected to confirm that the status of the firm's postmarketing studies is included in the reports, as required by 21 CFR 314.81.
- All reports must be submitted in electronic format, as described in 21 CFR 314.80(g) and 21 CFR 600.80(h).

Contractor Oversight

- Oversight of outsourced services may include a broad range of activities to ensure that all outsourced services and activities associated with postmarketing safety are performed according to applicable FDA regulations.
- Identify the name, business location, and contact information for any contractor involved in the surveillance, receipt, evaluation, or reporting of adverse experiences to FDA, including all domestic and foreign locations where safety information is processed.
- If the applicant or non-applicant has written procedures for obtaining and processing safety information from its contractors.
- Assess how the applicant or non-applicant ensures that its contractors develop written procedures.
- Determine the contractor's specific responsibilities. Determine how the applicant or non-applicant ensures that its contractors fulfill their responsibilities. Applicants or non-applicants may outsource some or all of their postmarketing safety obligations, but remain responsible for complete, accurate, and timely reporting to FDA.

- Determine how the contractor documents its receipt date for obtaining the minimum dataset for a valid ICSR and how it communicates this information to the applicant or non-applicant. The clock for expedited reporting starts as soon as the minimum information for a valid ICSR has been received by the contractor or its representatives.

Electronic Submissions

- 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.

Waivers and Record Keeping

- A copy of the waiver for any regulatory requirement pertaining to postmarketing safety, may be requested to determine compliance with the terms of the waiver.
- For approved drugs or biologics, if all records containing information relating postmarketing safety reports (whether or not submitted to FDA) have been maintained for a period of 10 years, or for combination products, the longest retention period applicable.
- Anyone marketing a prescription drug for human use without an approved new drug application or abbreviated new drug application must comply with the recordkeeping and reporting requirements of 21 CFR 310.305.

Selected References

- Good practice guide on recording, coding, reporting and assessment of medication errors: 23 October 2015, EMA/762563/2014, Pharmacovigilance Risk Assessment Committee (PRAC).
- Good practice guide on risk minimization and prevention of medication errors: 18 November 2015, EMA/606103/2014, Pharmacovigilance Risk Assessment Committee (PRAC)
- Global burden of preventable medication-related harm in health care - A systematic review: WHO (World Health Organization)
- MedDRA Coding of Medication Errors – General Principles
- Product images taken from -Medication Errors: A CDER Perspective- Yelena Maslov, Pharm.D. (Team Leader), Division of Medication Error Prevention and Analysis Office of Medication Error Prevention and Risk Management Office of Surveillance and Epidemiology, June 25, 2015
- National Coordinating Council for Medication Error Reporting and Prevention. Available at: www.nccmerp.org.
- www.fda.com and www.ema.europa.eu

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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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