

From Regulatory Warning to Product Recall: An Integrated Quality Risk and Data Integrity Framework for Preventing Pharmaceutical Quality Failures in Indian Manufacturing and Testing Laboratories

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Abstract

Pharmaceutical product recalls and regulatory warning letters are important indicators of weaknesses within pharmaceutical quality systems. While recalls represent market-level corrective actions, warning letters frequently reveal deficiencies in manufacturing, laboratory controls, data integrity, investigations, documentation, CAPA, and Quality Unit oversight that may precede product-quality failures. The present study integrates data from two researcher-provided documents addressing pharmaceutical recalls and FDA warning letters involving Indian pharmaceutical organizations and contract testing laboratories. Recall cases included Glenmark Pharmaceuticals, Sun Pharmaceutical Industries, Zydus Pharmaceuticals, and Dr. Reddy's Laboratories, while warning-letter cases included Shiva Analyticals Private Limited and Tentamus India Private Limited. Additional contemporary FDA information was examined to broaden the regulatory analysis. A retrospective, document-based approach was used to evaluate the nature of quality failures, regulatory concerns, company responses, and potential preventive interventions. Recurring deficiencies involved impurities, degradation, labeling, OOS investigations, data integrity, documentation, CAPA, Quality Unit oversight, and management responsibility. The findings indicate that recalls and warning letters represent different manifestations of a broader pharmaceutical quality-failure continuum. Based on the integrated analysis, the authors propose a Regulatory Warning–Recall Prevention framework emphasizing early detection of quality signals, scientifically sound investigations, data-integrity assurance, assessment of related products and batches, effective CAPA, Quality Unit independence, and management-level quality intelligence. The study highlights the need to shift from reactive quality management toward predictive and continuously improving pharmaceutical quality systems.

Keywords: pharmaceutical recalls, FDA warning letters, Indian pharmaceutical industry, CGMP, data integrity, OOS investigation, CAPA, Quality Unit, regulatory compliance, pharmaceutical quality system, product quality, quality risk management.

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1. Introduction

The pharmaceutical industry has a fundamental responsibility to ensure that medicines supplied to patients consistently meet predetermined requirements for identity, strength, quality, purity and safety. Pharmaceutical quality is therefore not limited

to the successful completion of finished-product testing. It depends on the combined performance of manufacturing processes, raw materials, analytical laboratories, equipment, computerized systems, packaging operations, documentation practices,

personnel, Quality Units and management systems. When any of these components becomes ineffective, the resulting quality failure may remain undetected or may progress through several stages before becoming visible as a regulatory observation, market complaint or product recall[1].

Product recalls represent one of the most visible consequences of pharmaceutical quality failure. A recall may result from contamination, impurity formation, degradation, particulate matter, sterility concerns, incorrect potency, packaging defects, labeling errors or other circumstances in which a product no longer meets the required quality or safety expectations. The supplied recall document identifies several important examples from the Indian pharmaceutical industry during 2025, including recalls involving Glenmark Pharmaceuticals, Sun Pharmaceutical Industries, Zydus Pharmaceuticals and Dr. Reddy's Laboratories. The cases demonstrate that quality problems can arise from substantially different mechanisms and that even large and internationally established pharmaceutical organizations remain exposed to quality-system failures[2].

Regulatory warning letters provide a complementary perspective. Unlike a recall, which is generally associated with a specific product or market action, a warning letter can expose underlying weaknesses in the systems used to manufacture or test pharmaceutical products. The supplied analysis of the FDA warning letter issued to Shiva Analyticals Private Limited describes deficiencies involving OOS investigations, Quality Unit responsibilities, documentation, discarded analytical records and electronic data integrity. The analysis of the Tentamus India warning letter similarly identifies deficiencies involving data integrity, laboratory documentation, record retention, deviation investigation, contemporaneous documentation and Quality Unit oversight[3].

These cases are particularly important because a laboratory result may form the basis for a manufacturer's decision to release a batch. If the analytical data are incomplete, manipulated, inadequately investigated or not scientifically reliable, the organization may make an incorrect decision regarding the quality of a pharmaceutical product. The consequences may extend beyond the laboratory itself to manufacturing operations, regulatory submissions, batch release decisions and ultimately patient safety.

The relationship between warning letters and recalls is therefore an important area for pharmaceutical regulatory research. A warning letter does not necessarily mean that a particular product will subsequently be recalled, and a recall does not

necessarily establish that a prior warning letter caused the recall. However, both regulatory events can provide evidence of weaknesses within the pharmaceutical quality lifecycle. The present study therefore does not attempt to establish a direct causal relationship between individual warning letters and individual recalls. Instead, it examines the recurring quality-system failures across the documented cases and asks whether these failures could serve as early-warning signals for organizations seeking to prevent future product-quality events[4].

The central premise of this study is that a recall should not be viewed merely as the point at which a defective product is removed from the market. Rather, it may represent the final visible stage of a longer quality-failure process that began with a weak signal, inadequate investigation, ineffective CAPA or failure of management oversight. The purpose of integrating recall and warning-letter data is therefore to identify where intervention could have occurred earlier.

2. Rationale of the Study

The rationale for the present study arises from the observation that pharmaceutical quality failures often involve interconnected systems rather than isolated technical errors. Recall cases demonstrate impurity, degradation, manufacturing, and labeling problems, while FDA warning letters reveal weaknesses in OOS investigations, documentation, data integrity, CAPA, and Quality Unit oversight. The Shiva and Tentamus cases particularly highlight how inadequate investigation, discarded records, and ineffective CAPA can compromise data reliability and allow recurring problems to persist. Therefore, the study emphasizes treating OOS results, deviations, stability failures, labeling errors, CAPA recurrence, and data-integrity concerns as early-warning signals requiring systematic evaluation. Early identification and intervention may help prevent quality-system weaknesses from progressing to product recalls or significant regulatory action[5].

3. Aim

The present study aimed to integrate pharmaceutical product recalls and FDA warning-letter observations involving Indian pharmaceutical companies and contract testing laboratories to identify recurring quality-system failures, evaluate company responses, assess opportunities for prevention, and propose strategies to reduce future pharmaceutical quality failures, regulatory actions, and product recalls.

4. Materials and Methods

The study adopted a retrospective, document-based analytical approach using two researcher-provided documents as the principal sources. The first contained pharmaceutical recall information, including products, companies, recall quantities,

reasons, and regulatory classifications. The second included analyses of FDA warning letters involving Shiva Analyticals Private Limited and Tentamus India Private Limited, focusing on OOS investigations, Quality Unit responsibilities, data integrity, documentation, deviations, and CAPA.

The researcher-provided information formed the basis of the case analysis and was supplemented by publicly available FDA regulatory records to verify selected details and incorporate recent regulatory developments. Additional cases involving Indian pharmaceutical facilities, including Cdymax India Pharma Private Limited, Zydus Lifesciences Limited, Intas Pharmaceuticals Limited, and Shimoga Chemicals, were reviewed to identify relevant quality-system concerns.

Cases were qualitatively analyzed across key domains, including product quality, impurities, degradation, labeling, contamination, sterility assurance, OOS investigations, data integrity, documentation, CAPA, Quality Unit oversight, and management responsibility. Because cases were purposively selected rather than statistically sampled, the study did not estimate the incidence of recalls or warning letters across the Indian pharmaceutical industry. Instead, the analysis focused on identifying recurring quality-system failures and developing a preventive conceptual framework.

Where complete root-cause investigations or CAPA effectiveness data were unavailable, this limitation was acknowledged. Recommendations and the proposed preventive framework represent the authors' analysis and are not attributed to the companies or FDA.

5. Results and Integrated Case Analysis

5.1 Glenmark Pharmaceuticals and the Atomoxetine Recall

Glenmark Pharmaceuticals provides an example of an impurity-related pharmaceutical quality failure. According to the researcher-provided recall material, the company voluntarily recalled approximately 1.48 million bottles of atomoxetine capsules manufactured at its Goa facility after elevated N-nitroso atomoxetine levels were detected. The recall involved multiple strengths and was classified by the FDA as Class II.

The immediate response included recalling affected lots, quarantining stock, removing products from distribution, and communicating with relevant stakeholders. While these measures help prevent further patient exposure, the case also highlights the need to address how impurity risks are identified and controlled before product release. A detailed public Glenmark-specific root-cause and CAPA report was not available in the reviewed material; therefore, no specific cause should be inferred. From a preventive

perspective, the case emphasizes the importance of incorporating nitrosamine-risk assessment throughout the product lifecycle, considering raw materials, excipients, manufacturing conditions, process chemistry, storage, and potential degradation pathways rather than relying solely on finished-product testing.

5.2 Sun Pharmaceutical Industries and Product Quality Failures

The researcher-provided material identifies Sun Pharmaceutical Industries among the Indian pharmaceutical companies experiencing recalls during the study period. The dataset includes approximately 10,000 bottles of morphine sulfate extended-release tablets recalled in February 2025 and approximately 24,624 bottles of fluocinolone acetonide topical solution recalled in December 2025 due to failure to meet impurity and stability specifications. The latter recall was classified as Class III. These cases highlight the importance of lifecycle-based quality monitoring, particularly stability and impurity control. Stability programs should identify emerging trends in product quality and determine whether observed changes reflect broader formulation, manufacturing, packaging, or storage-related issues. The significance is further strengthened by FDA observations concerning OOS investigations at Sun Pharmaceutical Industries. The 2024 FDA warning letter questioned the scientific basis of an OOS investigation and the handling of invalidated OOS results. Together, these observations demonstrate that OOS events should be treated as potential indicators of underlying quality-system weaknesses rather than merely isolated laboratory deviations.

5.3 Zydus Pharmaceuticals and Nelarabine

Zydus Pharmaceuticals provides an example of an impurity- and degradation-related quality failure involving an oncology injectable. According to the supplied material, Zydus Pharmaceuticals (USA) initiated a voluntary recall on February 13, 2025 involving 38,871 vials of nelarabine, manufactured at its Alidac facility in Ahmedabad. The recall was initiated after the product failed impurity and degradation specification testing. The case highlights the importance of stability monitoring for injectable anticancer products, where degradation may affect product quality and patient safety. Stability failures should therefore prompt assessment beyond the affected batch, including formulation, manufacturing conditions, container-closure integrity, storage conditions, analytical methods, and potential product-quality trends. For sterile injectables, the risk assessment should additionally consider the consequences associated with direct administration to patients.

5.4 Dr. Reddy's Laboratories and Levetiracetam Mislabeling

The Dr. Reddy's levetiracetam case represents a labeling-related pharmaceutical quality failure. According to the supplied FDA-related material, the infusion bag was labeled as containing 500 mg/100 mL, whereas the actual product contained 1,000 mg/100 mL. The affected lot was distributed between November 4 and 6, 2024, after which distributors, wholesalers, hospitals, and pharmacies were instructed to stop use and quarantine the product. The case demonstrates that a product may meet chemical specifications while still presenting a significant patient-safety risk because of incorrect labeling. The discrepancy could result in an unintended double dose, particularly in patients receiving intravenous treatment. The preventive lesson extends beyond analytical testing and includes artwork approval, packaging-line clearance, reconciliation, barcode verification, electronic master-data controls, and final packaging inspection. Labeling and packaging should therefore be treated as critical quality and patient-safety processes. Investigation should address both the immediate labeling error and the broader systems that could allow similar errors to occur.

6. FDA Warning-Letter Analysis

6.1 Shiva Analyticals Private Limited

Shiva Analyticals Private Limited, a contract testing laboratory in Hoskote, Bengaluru, received FDA Warning Letter 320-25-96 dated July 23, 2025, following an inspection conducted in January 2025. The supplied material identified significant deficiencies involving OOS investigations, Quality Unit oversight, documentation, discarded records, and electronic data integrity. FDA observed that unexplained OOS results were not adequately investigated and that repeat results were used to invalidate original results without sufficient scientific justification. Investigations also did not adequately assess potentially affected previously tested batches, while recurring human errors continued without effective CAPA. The case demonstrates that an initial OOS result should not be invalidated solely because a repeat test passes; investigations must scientifically evaluate potential laboratory and, where relevant, manufacturing causes.

Significant documentation deficiencies included disposal of original CGMP records such as analytical balance and pH meter printouts. FDA also identified electronic activities involving modification or deletion of chromatographic data in the MassLynx system, raising concerns regarding data reliability, traceability, access controls, and audit-trail management.

FDA recommended involvement of a qualified CGMP consultant. However, remediation

responsibility remains with the organization's management and Quality Unit. Overall, the case demonstrates how weaknesses in OOS investigation, record retention, data governance, and Quality Unit oversight can collectively undermine the reliability of pharmaceutical testing and quality decisions.

6.2 Tentamus India Private Limited

Tentamus India Private Limited, a contract testing laboratory in Hyderabad, received FDA Warning Letter 320-26-47 dated March 3, 2026, following an inspection in August 2025. The supplied material identified significant deficiencies involving Quality Unit oversight, discarded records, laboratory deviations, CAPA, and contemporaneous documentation.

FDA investigators reportedly found discarded analytical records, chromatographic reports, validation worksheets, and handwritten laboratory notes, compromising the traceability of laboratory activities. A microbiological discrepancy involving missing sample plates had also been identified during an internal audit but was not entered into the deviation and CAPA system, demonstrating a missed opportunity to address an early quality signal. Additional concerns included pre-signed preventive-maintenance records and backdated analytical reconciliation documents. Although the company reportedly suspended the personnel involved, initiated independent review, and retrained staff, these actions alone may not demonstrate effective systemic remediation. Root-cause evaluation should also examine how such practices occurred, whether similar deficiencies existed elsewhere, and whether Quality Unit oversight and electronic controls were adequate. Overall, the case demonstrates how weak documentation practices, failure to formally escalate deviations, and ineffective CAPA can undermine laboratory data integrity and prevent early identification of recurring quality-system failures.

7. Comparative Analysis of Recall and Warning-Letter Cases

When considered together, the cases reveal an important distinction between product-level and system-level quality failures. Recall cases primarily represent product-level manifestations, including impurity and degradation risks in Glenmark and Zydus, labeling risk in Dr. Reddy's, and impurity and stability concerns in Sun Pharma. In contrast, the Shiva and Tentamus warning letters highlight system-level weaknesses involving OOS investigations, documentation, data integrity, CAPA, and Quality Unit oversight. The cases support a conceptual quality-failure pathway in which an isolated deviation or abnormal laboratory result may become a recurring signal when inadequately investigated. Repeated signals may develop into systemic weaknesses when

CAPA fails to address underlying causes, potentially leading to regulatory intervention or product recalls. However, warning letters and recalls should not be considered a direct causal sequence. Not every warning letter results in a recall, and not every recall follows a warning letter. The relationship is better understood as a quality-system continuum, in which recurring quality events and regulatory observations can serve as early-warning indicators of broader systemic weaknesses.

8. Analysis of Company Responses

Company responses described in the supplied material generally included immediate measures such as voluntary recalls, product quarantine, stakeholder notification, investigation, retraining, consultant engagement, and CAPA. Glenmark initiated a voluntary recall following detection of N-nitroso atomoxetine, while Dr. Reddy's instructed stakeholders to stop distribution and quarantine the affected lot. Tentamus reportedly suspended the supervisor involved, initiated third-party review, and retrained personnel. However, immediate correction does not necessarily ensure systemic prevention. A recall removes affected products but may not prevent recurrence, while retraining may not address weaknesses in supervision, system design, workload, access controls, or organizational culture. Similarly, SOP revision and CAPA documentation demonstrate planned actions but do not establish effectiveness without subsequent verification.

Accordingly, the authors propose evaluating company responses across four levels: (1) immediate correction, (2) root-cause correction, (3) systemic prevention, and (4) effectiveness verification. This framework provides a more meaningful basis for assessing whether corrective actions are capable of preventing recurrence.

9. Authors' Critical Analysis: What Should Be Done to Prevent Recalls and Warning Letters?

The analysis supports several recommendations for strengthening pharmaceutical quality systems.

1. **Trend quality events rather than treating them as isolated incidents.** Recurring OOS results, deviations, documentation errors, or equipment- and analyst-related events should trigger trend analysis and broader investigation.
2. **Strengthen OOS investigations.** A passing repeat test should not automatically invalidate an initial OOS result. The original result should remain part of the investigation, with laboratory causes scientifically established before invalidation; otherwise, the assessment should extend to manufacturing and product history.

3. **Strengthen data integrity controls.** Original records should be preserved, electronic access should follow least-privilege principles, audit trails should be routinely reviewed, and suspicious activities should be investigated. Data integrity should remain an integral component of the quality system.
4. **Strengthen Quality Unit authority.** The Quality Unit should independently challenge inadequate investigations, require appropriate scope expansion, prevent inappropriate release decisions, and escalate systemic concerns to senior management.
5. **Implement horizontal CAPA.** When a quality problem is identified, organizations should assess whether the same vulnerability exists across other batches, products, equipment, processes, or facilities rather than restricting corrective action to the affected batch.
6. **Measure CAPA effectiveness.** Effectiveness checks should use objective evidence, such as recurrence monitoring, audit findings, documentation compliance, or audit-trail reviews, to demonstrate sustained improvement.
7. **Strengthen management review.** Senior management should routinely review trends in OOS results, deviations, complaints, stability failures, rejected batches, CAPA recurrence, supplier issues, audit findings, and data-integrity events. This converts quality data into proactive management intelligence rather than relying on regulatory inspections or recalls to identify systemic weaknesses.

10. Proposed Regulatory Warning–Recall Prevention Framework

Based on the integrated findings, the authors propose a Regulatory Warning–Recall Prevention (RWRP) Framework as an original conceptual model. It is not an FDA-validated or regulatory instrument but is intended to connect emerging quality signals with early intervention before they progress to regulatory enforcement or product recall.

The framework comprises seven stages:

1. **Quality Signal Detection:** Collect and integrate OOS/OOT results, deviations, complaints, stability data, environmental monitoring, rejected batches, supplier issues, audits, and CAPA trends.
2. **Risk-Based Escalation:** Escalate recurring or high-risk signals, including repeated OOS events, human errors, CAPA failures, data-integrity concerns, labeling errors, and

potential patient-safety risks, to the Quality Unit and senior management.

3. **Scientific Investigation:** Determine whether the event originates from laboratory error, manufacturing variability, materials, equipment, analytical methods, documentation, or other causes. Where laboratory error cannot be established, extend the investigation to manufacturing and product history.
4. **Systemic Impact Assessment:** Evaluate whether other batches, products, equipment, suppliers, methods, or facilities may be affected.
5. **CAPA Implementation:** Address both immediate and systemic causes, with the objective of preventing recurrence rather than merely closing the deviation.
6. **Effectiveness Verification:** Require objective evidence demonstrating that implemented CAPA has effectively reduced or eliminated recurrence before closure.
7. **Management Review and Continuous Monitoring:** Incorporate lessons learned into quality metrics, training, procedures, risk assessments, and process improvements, creating a continuous feedback loop.

Thus, the RWRP Framework represents a closed-loop preventive quality model in which quality signals are detected, risk-assessed, investigated, corrected, verified, and continuously monitored before they escalate into regulatory action or product recall.

12. Proposed Quality Failure Early-Warning Model

As an additional analytical contribution, the authors propose a Quality Failure Early-Warning Model based on five conceptual dimensions: severity, occurrence, detectability, recurrence and systemic impact. The model is not intended to replace established regulatory risk-management systems and has not been statistically validated. Its purpose is to provide a structured way for pharmaceutical organizations to determine when a quality event should be escalated.

An event with limited patient impact, isolated occurrence, high detectability and no evidence of recurrence may remain a routine quality-system event. In contrast, a repeated unexplained OOS result associated with poor documentation, inappropriate retesting and recurring CAPA would represent a much more serious systemic risk. Similarly, a single labeling discrepancy should be investigated immediately, but repeated labeling errors across different products should be interpreted as evidence of a broader packaging and master-data control problem. The central concept of the model is that

recurrence and systemic impact should increase the urgency of intervention even when the immediate event appears clinically minor. This is important because quality systems should prevent serious events rather than wait until patient harm occurs.

13. Discussion

The integrated analysis demonstrates that pharmaceutical quality failure is multidimensional and cannot be attributed solely to manufacturing, laboratory, or packaging functions. The Glenmark case highlights impurity-risk management, the Zydus nelarabine case emphasizes stability and degradation monitoring, and the Dr. Reddy's case demonstrates the importance of labeling and packaging controls. The Shiva and Tentamus cases further show that reliable laboratory data, documentation, and Quality Unit oversight are essential to pharmaceutical quality assurance.

A key finding is the importance of missed early signals. The Tentamus case describes an internal audit finding that was not incorporated into the formal deviation and CAPA system, while recurring human errors reportedly continued at Shiva without effective CAPA. These observations support the need to recognize recurring events and convert individual quality observations into organizational learning. The findings also demonstrate that quality culture is closely linked to regulatory compliance. Training alone may be insufficient when organizational practices or incentives discourage accurate reporting, investigation, or documentation. Responsibility therefore extends from individual personnel to supervisors, Quality Units, and senior management. Contemporary FDA enforcement further supports this approach. The 2026 warning letter to Shimoga Chemicals called for retrospective assessment of data-integrity deficiencies, patient-risk evaluation, and comprehensive management remediation. This reinforces the principle that quality failures should be evaluated for their historical and systemic impact rather than treated as isolated incidents.

14. Implications for the Indian Pharmaceutical Industry

The findings have particular significance for Indian pharmaceutical organizations because many companies operate within highly internationalized supply chains and manufacture products for markets with stringent regulatory expectations. A quality-system failure at an Indian manufacturing or testing facility can therefore have consequences extending beyond the local market to international product supply, regulatory approvals, contract relationships and organizational reputation. The present analysis does not support the simplistic conclusion that Indian pharmaceutical products are inherently of lower quality. Rather, it demonstrates that internationally

distributed pharmaceutical manufacturing requires continuous investment in quality systems, data governance, scientific investigation and management oversight. The presence of regulatory actions involving established companies should be interpreted as evidence of the complexity of pharmaceutical quality management rather than as a basis for generalizing about an entire national industry. The appropriate response is therefore stronger quality intelligence. Pharmaceutical organizations should identify patterns earlier, use data more effectively, strengthen laboratory governance, improve CAPA effectiveness and create organizational cultures in which quality concerns can be escalated without fear.

15. Future Research

The proposed framework should be subjected to prospective validation in pharmaceutical manufacturing and contract testing organizations. Future studies could collect longitudinal data on OOS frequency, deviation recurrence, CAPA effectiveness, complaints, stability failures, data-integrity events, audit observations and product recalls. Statistical analysis could then determine whether combinations of these indicators predict subsequent regulatory findings or market actions. A larger multicenter dataset could also allow development of a statistically validated early-warning score. Machine-learning methods could potentially be applied to quality-event databases to identify relationships that are difficult to detect through conventional review. Such research could ultimately support predictive quality management in which organizations identify increasing risk before a regulatory inspection or product recall occurs.

16. Limitations

The study has several limitations. The analysis is based primarily on researcher-provided documents and publicly available regulatory information rather than confidential company quality records. The selected cases were purposively examined and therefore cannot be interpreted as a statistically representative sample of all Indian pharmaceutical manufacturers. Public recall notices frequently provide information about the immediate product-quality concern but do not disclose the complete root-cause investigation or CAPA effectiveness assessment. Similarly, a warning letter identifies regulatory concerns but does not necessarily establish that the cited deficiencies directly caused a particular product recall. The proposed RWRP framework and Quality Failure Early-Warning Model are conceptual contributions of the authors and have not yet undergone prospective statistical validation. These limitations should be considered when interpreting the findings.

17. Conclusion

The integrated analysis demonstrates that pharmaceutical quality failures are systemic rather than isolated technical events. Recall cases highlight impurity, degradation, stability, and labeling failures, while FDA warning letters reveal weaknesses in OOS investigations, data integrity, documentation, Quality Unit oversight, and CAPA. The study emphasizes that recall prevention depends on recognizing early warning signals such as recurring OOS results, deviations, data-integrity concerns, stability trends, and repeated CAPA failures. The proposed Regulatory Warning–Recall Prevention (RWRP) Framework integrates early detection, risk-based escalation, scientific investigation, systemic assessment, CAPA, effectiveness verification, and management review. The Pharmaceutical organizations should shift from reactive “detect, correct and recall” approaches toward proactive “detect early, investigate, prevent and continuously improve” quality management.

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