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AI ARCHITECTURE FOR REAL-TIME RELEASE TESTING USING RAMAN SPECTRA AND TABLET MANUFACTURING SIGNALS

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ABSTRACT

Real-time release testing promises faster and more robust quality assurance for pharmaceutical tablets by shifting quality assessment from delayed laboratory testing to continuous process understanding. Current PAT models, however, often treat chemical spectra and manufacturing signals as separate information streams rather than parts of one integrated quality system. Existing RTRT models are frequently centered on spectroscopy for chemical CQAs or on threshold-based monitoring of tablet press behavior. This separation limits the ability to capture multivariate interactions among formulation chemistry, compression behavior, and final tablet performance. This article proposes an AI architecture that ingests Raman spectra and tablet press signals in real time, fuses them within a multimodal model, and outputs a comprehensive quality statement. The architecture is intended to support predictions for assay, content uniformity, hardness, and dissolution as part of real-time batch release decisions. The proposed system includes a Raman preprocessing and chemometric feature extractor, a tablet press signal encoder, a multimodal fusion layer, and a multi-head quality predictor. It also includes a decision-support module with uncertainty handling and a model-monitoring layer for detecting drift and sensor degradation. Such an architecture would provide a holistic quality assessment of tablets during manufacture rather than after batch completion. It could support a transition from laboratory-centered release to in-line, evidence-based release decisions within regulated manufacturing systems. An AI-driven, multivariable RTRT system could transform tablet manufacturing from a batch-tested process to a continuously assured, data-driven quality model. Its value would depend on robust validation, lifecycle management, and alignment with pharmaceutical quality systems.

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Introduction

Real-time release testing represents a shift from retrospective confirmation of product quality toward prospective assurance based on process understanding and in-line evidence. In continuous and advanced tablet manufacturing, PAT systems can support this shift by connecting process measurements to critical quality attributes during production rather than after batch completion [1]. Raman-enabled monitoring of continuous blending and tableting has shown how spectroscopic measurements can be embedded into manufacturing flows, making it conceptually suitable for release-oriented control [2]. Model-risk considerations are also central because RTRT decisions must be supported by traceable models whose limitations are understood before they influence batch disposition [3].

Raman spectroscopy is especially relevant to tablet RTRT because it provides chemically specific information about formulation composition, API distribution, and solid-state characteristics. Applications of Raman and related spectroscopic approaches have supported dissolution prediction, assay-related modeling, and chemical imaging of tablets [4, 5]. Tablet press signals provide a complementary view because compression behavior, tablet weight control, and mechanical response are linked to physical CQAs such as hardness and dissolution behavior [6]. The challenge is that chemical spectra and press-derived signals are often modeled separately, even though tablet quality emerges from their combined effects [7].

The evolution of AI and machine learning in pharmaceutical PAT has created a foundation for architectures that can integrate heterogeneous data streams. Deep spectral models, artificial neural networks, and machine-learning frameworks have been

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explored for pharmaceutical spectra, dissolution prediction, and manufacturing process understanding [8-10]. Data fusion studies have further shown that combining multiple PAT instruments can improve the representational completeness of process monitoring, even when the exact architecture must be adapted to each unit operation [11, 12]. However, a validated multimodal architecture that joins Raman spectra with tablet press signals for routine RTRT remains a system-level gap.
The thesis of this AIF article is that an AI architecture fusing Raman spectra with tablet press data could provide a unified, real-time release decision with quantified confidence. Such a system would map chemical and physical process evidence to multiple CQAs, including assay, content uniformity, hardness, and dissolution, rather than treating each attribute as an isolated prediction problem [7]. Intelligent tablet press concepts and deep-learning-enabled press monitoring indicate that machine signals can become part of an in-line quality decision layer rather than only a control or alarm layer. When embedded within lifecycle-managed PAT practice, this architecture would be expected to strengthen RTRT implementation without replacing the need for scientifically justified validation [1, 3].

Background

Real-Time Release Testing (RTRT) in Pharmaceutical Manufacturing

RTRT in pharmaceutical manufacturing can be understood as a quality assurance strategy in which release decisions are supported by process understanding, validated models, and in-process measurements rather than solely by end-product testing. Regulatory experience with continuous manufacturing and dissolution-related RTRT demonstrates that such approaches require clear links among process parameters, PAT signals, CQAs, and control strategy [1]. Continuous tableting examples using in-line Raman spectroscopy illustrate how spectral measurements can be placed close to the manufacturing operation that generates quality-relevant variation [2]. The paradigm shift is therefore not merely analytical but architectural, because release assurance depends on a connected system of sensors, models, decision rules, and quality governance [3].

Raman Spectroscopy as a PAT Tool for Tablets

Raman spectroscopy is a strong PAT candidate for tablets because it is non-destructive, chemically specific, and capable of detecting API-related and solid-form-related spectral signatures in pharmaceutical matrices. Raman mapping and fast Raman imaging have been used conceptually to connect spatial chemical information with dissolution behavior, suggesting a route from spectral evidence to product performance attributes [4, 5]. Raman and near-infrared comparisons also show that Raman can complement other vibrational spectroscopy methods when the target attribute depends on chemical distribution or formulation-specific spectral features [13]. Practical implementation must still consider fluorescence, sample presentation, and probe-condition effects, which can degrade spectral quality and require automated preprocessing and sensor-health monitoring [12].

Tablet Press Signals as Quality Indicators

Tablet press signals provide a physical-process perspective on quality because compression force, ejection behavior, machine speed, and related process variables reflect how powder is consolidated into a tablet. Compression force has been framed as a PAT-relevant signal for tablet weight uniformity and in-line control, showing that press data can participate directly in quality assurance rather than only equipment monitoring [6]. Machine-learning models for breaking force, disintegration, and tableting behavior further support the idea that press and formulation variables can inform mechanical and performance-related CQAs [14, 15]. For an RTRT architecture, these signals should be synchronized with Raman measurements so that chemical and mechanical evidence can be interpreted together.

Machine Learning and Data Fusion in Pharmaceutical PAT

Machine learning in pharmaceutical PAT has evolved from linear chemometric methods toward neural networks and deep learning architectures capable of learning nonlinear relationships in spectra and process signals. Artificial neural networks have been applied to dissolution prediction and PAT-based decision support, indicating that learned representations can connect process measurements to product-performance attributes [8, 16]. Data fusion work has shown that low-level, mid-level, and high-level fusion can integrate complementary PAT instruments, with the appropriate strategy depending on signal type, timing, interpretability, and validation burden [11, 12]. The current architectural gap is not the absence of algorithms, but the lack of a clearly specified RTRT system that fuses Raman and tablet press signals into one regulated decision engine. **Figure 1** illustrates the conceptual gap between available machine-learning and PAT data-fusion methods and the need for a clearly specified regulated RTRT decision engine that integrates Raman spectroscopy and tablet press signals into one validated release-support architecture.

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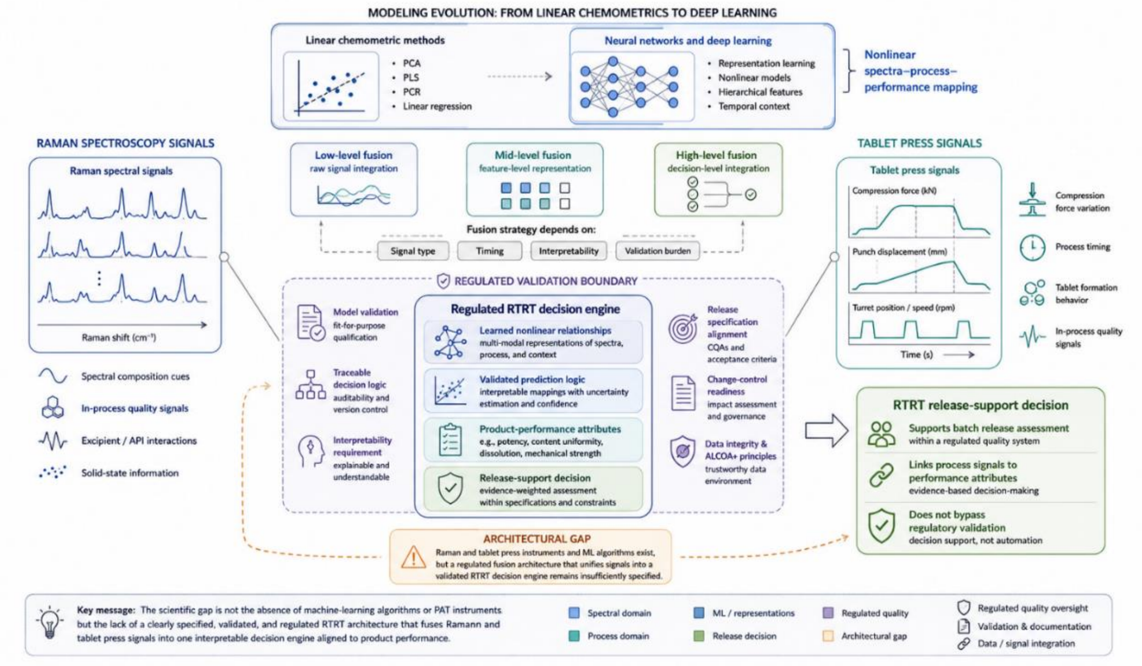

Figure 1. Regulated data-fusion architecture for raman–tablet press rtrt decision support.

Model Lifecycle and Drift Management in Regulated Environments

Model lifecycle management is essential in regulated PAT because spectral response, raw material attributes, equipment condition, and operating context can change over time. Reviews of artificial neural networks in pharmaceutical manufacturing emphasize that model maintenance, interpretability, and robustness must be treated as ongoing obligations rather than one-time development tasks [10]. Model-risk frameworks for pharmaceutical manufacturing further indicate that models used in quality decisions require defined monitoring, change control, and evidence of continued suitability [3]. In an AI-driven RTRT architecture, drift detection should therefore be integrated from the start, with recalibration and validation pathways aligned to continuous process verification expectations.

System Architecture Overview

High-Level Design

The proposed architecture begins with synchronized acquisition of Raman spectra and tablet press signals for each tablet or for a scientifically justified representative stream. Raman data would pass through a spectral conditioning and feature-extraction branch, while tablet press data would pass through a time-series encoding branch designed to capture compression and ejection behavior [6]. These branches would feed a multimodal fusion layer that maps combined chemical and physical representations to predicted CQAs, following the logic of prior spectroscopy-plus-process-input dissolution modeling [7]. A decision engine would then determine whether the tablet stream or batch meets acceptance criteria, with holds triggered when uncertainty or signal integrity prevents reliable release judgment [1].

Figure 2 presents the proposed multimodal RTRT architecture linking synchronized Raman spectra and tablet press signals to fused CQA prediction, uncertainty-aware release logic, and GMP lifecycle governance.

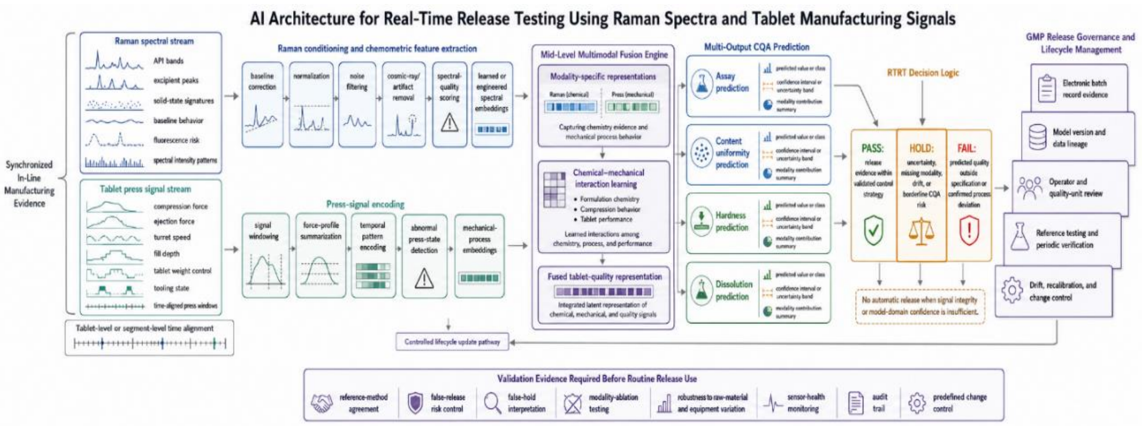

Figure 2. AI Architecture for real-time release testing using raman spectra and tablet manufacturing signals.

Core Inputs and Outputs

The core inputs would include Raman spectra containing API bands and excipient-related peaks, together with tablet press signals such as compression force, press speed, ejection force, and other machine-derived indicators. Spectroscopy-based models have already been used to connect Raman and near-infrared information with dissolution or assay-related attributes, supporting the inclusion of chemically rich spectral inputs [13, 17]. Press-based and intelligent-tablet-press studies support the parallel inclusion of mechanical and machine-state indicators as quality-relevant inputs [6]. The outputs would include predicted assay, content uniformity, hardness, dissolution behavior, and a release status expressed as pass, fail, or hold with an associated confidence statement.

Table 1 maps each evidence stream to the specific quality information it contributes, showing why Raman spectra and tablet press signals should be fused rather than modeled as isolated RTRT inputs.

Table 1. Modality-to-CQA evidence map for multimodal real-time release testing

Evidence domain	Representative input variables	Primary quality information captured	Most directly supported CQA predictions	Why the modality alone is insufficient	Added value in multimodal fusion
Raman spectral chemistry	API bands, excipient peaks, spectral intensity patterns, solid-state signatures, baseline behavior, fluorescence tendency	Chemical composition, API distribution, formulation-specific spectral features, potential solid-form information	Assay; content uniformity; dissolution-related chemical contributors	Raman may be sensitive to probe condition, tablet presentation, fluorescence, sampling geometry, and spectral artifacts	Provides chemically specific evidence that helps distinguish true compositional variation from purely mechanical press variation
Raman spectral quality metadata	Signal-to-noise indicators, abnormal baselines, cosmic-ray artifacts, probe-condition indicators, spectral-domain shift	Whether the spectral evidence is reliable enough for release-supporting prediction	Supports all CQA predictions indirectly by determining whether Raman-derived evidence is admissible	Quality metadata does not directly predict tablet performance; it only qualifies the trustworthiness of spectral inputs	Enables uncertainty-aware hold decisions when chemical evidence is degraded or outside the validated spectral domain
Tablet press compression behavior	Main compression force, precompression force, force–time profile, dwell-related descriptors, compaction signatures	Powder consolidation behavior, mechanical response, compaction consistency, potential mechanical quality variation	Hardness; dissolution-related physical contributors; indirect support for content uniformity and assay when linked to process state	Press signals cannot directly observe chemical identity, API distribution, or spectral composition	Adds physical-process context so that the model can learn how compression behavior modifies chemically derived quality risk
Tablet press machine-state signals	Turret speed, fill depth, ejection force, tooling condition, feeder behavior, machine alarms, production segment timing	Equipment state, process stability, tablet formation conditions, possible sources of manufacturing variability	Hardness; tablet weight-related consistency; dissolution-related manufacturing effects	Machine signals may detect process disturbance without explaining chemical CQA changes	Helps separate sensor noise from process-related variation and supports exception handling when equipment state compromises release confidence
Time-alignment and synchronization layer	Tablet-level timestamps, segment identifiers, batch position, sensor-matching rules, press-to-spectra linkage	Whether Raman and press evidence refer to the same tablet unit or representative production interval	All CQA predictions, especially multi-output release decisions	Misaligned signals can create false associations between chemistry and process behavior	Protects model validity by ensuring that chemical and mechanical features are fused only when scientifically matched
Multimodal fused representation	Raman embeddings, press-signal embeddings, modality contribution summaries, interaction terms	Joint chemical–mechanical quality state of the tablet stream	Assay; content uniformity; hardness; dissolution; release status	Fused representations can become opaque without interpretability and validation controls	Captures interactions that neither Raman-only nor press-only models can adequately represent

Uncertainty and model-domain indicators	Prediction confidence, domain applicability, missing-modality flags, drift scores, modality disagreement	Reliability of the predicted CQA and release recommendation	Pass, fail, or hold decision; escalation pathway	Uncertainty does not replace reference validation or quality-unit judgment	Converts AI outputs into regulated decision support by preventing unjustified automatic release under incomplete evidence

Design Principles

The architecture should be real-time capable, modular, and robust to sensor variation while maintaining data integrity suitable for GMP decision-making. Modularity is important because additional PAT streams, such as near-infrared spectroscopy or machine vision, may later be incorporated without redesigning the entire system [18, 19]. Robustness is equally important because spectral models may be affected by sample presentation, instrument response, and manufacturing variability, while press signals may be affected by tooling, calibration, and operating state [3, 12]. The architecture should therefore be validated as a lifecycle-managed system rather than as an isolated predictive model.

Raman Spectral Data Acquisition and Preprocessing

In-Line Raman Acquisition and Signal Conditioning

In-line Raman acquisition could be positioned at the feed frame, after compression, or at another justified point where the signal is representative of the material state relevant to the target CQA. Continuous blending and tableting work using Raman spectroscopy illustrates that spectral probes can be integrated into a manufacturing train to support monitoring and feedback concepts [2]. For coated or finished tablets, Raman and near-infrared approaches have been used to predict coating-related and tablet-performance attributes, supporting the broader concept of post-compression spectral assessment. Signal conditioning should include automatic handling of exposure, fluorescence tendencies, and acquisition stability so that spectra entering the AI model remain suitable for quality decisions.

Spectral Preprocessing and Feature Extraction

Spectral preprocessing would include baseline correction, normalization, noise filtering, and other transformations selected through scientifically justified development rather than convenience. Chemometric and neural approaches to pharmaceutical spectra show that both engineered spectral features and end-to-end learned representations can support CQA prediction, depending on the intended use and validation strategy [9, 10]. Raman imaging and convolutional neural network concepts further support automated feature learning when spatial or high-dimensional spectral information is available [5]. In this architecture, the Raman branch could therefore support either interpretable chemometric features or learned spectral embeddings, provided that the chosen representation can be explained and monitored.

Monitoring Sensor Health and Spectral Quality

Spectral-quality monitoring should be embedded before release prediction so that unreliable Raman measurements are not silently converted into release-supporting outputs. Data fusion and PAT reviews emphasize that sensor degradation, inconsistent sample presentation, and instrument variability can compromise model robustness if not detected early [10, 12]. Automated checks would be expected to flag low signal quality, abnormal baselines, cosmic-ray artifacts, or probe-condition issues before the spectrum enters the decision engine. When a spectral-quality alert occurs, the system should shift from automatic release support to exception handling rather than relying on a potentially degraded prediction [3].

Tablet Press Signal Integration and Multimodal Fusion

Encoding Compression and Ejection Signals

Tablet press signals should be represented as time-aligned windows associated with individual tablets or defined production intervals, allowing the model to capture the process context in which each unit is formed. Compression-force-based PAT and tablet press monitoring studies support the idea that press signals carry information about weight control, compaction behavior, and mechanical quality [6]. Machine-learning frameworks for tableting processes further suggest that relationships between process variables and tablet performance may be nonlinear and formulation-dependent [14, 15]. The signal encoder should therefore extract both summary descriptors and temporal patterns rather than reducing press behavior to fixed alarm limits.

Mid-Level Fusion Architecture

A mid-level fusion architecture would use separate branches for Raman and press data before joining the learned representations in a shared fusion layer. Data fusion studies in PAT indicate that intermediate representations can preserve modality-specific information while allowing the model to learn interactions across sensor streams [11, 12]. A Raman branch could use chemometric features or a convolutional encoder, while a press-signal branch could use dense or temporal encoders, depending on the sampling structure and intended explainability [9]. The fused representation would then support multi-output prediction, allowing chemical and physical evidence to jointly inform release-relevant CQAs.

Handling Missing or Degraded Signals

The architecture should be designed to handle temporary missingness or degradation in one modality without producing unjustified automatic release decisions. Data fusion frameworks highlight that multimodal PAT systems require explicit strategies for sensor failure, unequal data quality, and modality-specific uncertainty [12]. If press sensors are unavailable, the system could rely more heavily on Raman-derived evidence only when the intended use and validation package justify that fallback; similarly, if Raman quality is degraded, press-based evidence alone should not be treated as sufficient for chemical CQAs [19]. Exception handling should therefore include operator alerts, audit-trail documentation, and hold decisions when the remaining evidence is incomplete for release assurance [3].

Table 2 shows the key strategies for managing missing or degraded data in multimodal PAT systems to ensure safe and reliable release decisions.

Table 2. Strategy for handling multimodal data missingness and degraded sensor inputs in PAT systems

Scenario	System Response	Decision Logic	Risk Control Measure
Temporary absence of press sensor data	Increase reliance on Raman spectroscopy data where validated	Use Raman evidence only within validated fallback boundaries	Prevent over-reliance on a single modality without justification
Degraded Raman signal quality	Reduce weighting of Raman-derived outputs	Do not allow press data alone to confirm chemical CQAs	Avoid false assurance from incomplete modality coverage
Unequal or inconsistent data quality	Apply modality-specific weighting or uncertainty adjustment	Combine evidence only when minimum quality thresholds are met	Maintain robustness in multimodal fusion
Sensor failure or dropout	Trigger system alert and flag data gap	Suspend automated release decision if evidence is insufficient	Ensure human intervention in uncertain conditions
Incomplete multimodal evidence	Default to conservative decision pathway	Hold batch or require operator review	Prevent unjustified release decisions
All-modality uncertainty condition	Escalate to operator and log exception event	No automated decision permitted	Ensure full auditability and regulatory compliance

AI Decision Engine for Real-Time Release

Multi-Output Quality Predictor

The AI decision engine would receive the fused Raman–press representation and route it into separate prediction heads for assay, content uniformity, hardness, and dissolution. This multi-output structure is consistent with the broader movement from single-attribute chemometric models toward integrated pharmaceutical machine-learning systems that support several linked quality judgments [20]. Dissolution-focused neural models and spectroscopy-based dissolution prediction studies indicate that product-performance CQAs can be represented as model outputs when the reference relationship is scientifically justified [8, 16]. For tablet manufacturing, the predictor should be interpreted as a decision-support layer that connects validated measurements to CQA estimates rather than as a substitute for process understanding.

Real-Time Release Decision Logic

The release decision module would compare predicted CQAs and their uncertainty statements against the product specification, returning a pass, fail, or hold status for the batch or defined production segment. Regulatory experience with continuous manufacturing and RTRT for dissolution shows that such decisions must be embedded in a control strategy where model use, model limits, and confirmatory testing expectations are clearly defined [1]. A system-level control approach has also been proposed for complex tablet manufacturing workflows, supporting the idea that AI and PAT outputs should feed structured decision rules rather than uncontrolled automation. In this architecture, release would be supported only when chemical and physical CQAs are jointly consistent with the predefined control strategy.

Uncertainty Quantification and Risk-Based Hold Decisions

Uncertainty handling would be essential because RTRT decisions involve quality risk, not merely point prediction. Model-risk frameworks for pharmaceutical manufacturing emphasize that models used in quality decisions should include mechanisms for identifying when predictions are outside their reliable operating space [3]. Deep-learning applications in manufacturing and acoustic process monitoring also illustrate the need to distinguish normal process variation from potential process upset before acting on model outputs [21]. Borderline or uncertain cases should therefore trigger a hold for laboratory confirmation or quality review rather than automatic release or rejection.

Model Monitoring, Drift Handling, and Lifecycle Management

Continuous Model Performance Monitoring

Continuous model monitoring would compare AI predictions with periodic reference measurements, manufacturing trends, and sensor-health indicators to detect loss of model suitability. Calibration transfer, drift, and data-fusion challenges in PAT suggest that even well-developed models may degrade when raw material lots, probes, equipment states, or production contexts change [12]. Reviews of machine learning in pharmaceutical development also emphasize that lifecycle monitoring is necessary when models are intended to support decisions across changing manufacturing conditions [20]. The monitoring layer should therefore track residual patterns, spectral-domain shifts, and press-signal changes as triggers for investigation rather than relying on a static validation event.

Model Update and Validation in a GMP Environment

Any model update should follow a predefined change-control pathway that documents the reason for revision, the data used for evaluation, and the intended effect on release decisions. Artificial neural network reviews in PAT and model-risk frameworks both indicate that validation, interpretability, and traceability must be maintained throughout the model lifecycle [3, 20]. Retrospective quality-by-design modeling of tablet manufacturing demonstrates how archived development and manufacturing data can support structured model understanding, although prospective GMP validation would still be required before release use [22]. In this architecture, model updating would be treated as a regulated lifecycle activity rather than routine software optimization.

Table 3 shows the key elements required for managing model updates within a controlled and regulated lifecycle framework.

Table 3. Structured Framework for Regulated Model Update and Lifecycle Management

Aspect	Description	Purpose in Model Lifecycle
Change-control documentation	Formal recording of the reason for model updates, data used, and expected changes in output behavior	Ensures transparency and regulatory accountability
Model validation	Evaluation of model performance before and after updates using relevant datasets	Confirms reliability and consistency of predictions
Interpretability	Ability to explain model behavior and decision drivers in a meaningful way	Supports user trust and regulatory acceptance
Traceability	Clear linkage between data, model versions, and outputs across the lifecycle	Enables auditability and reproducibility
Pre-deployment testing	Structured assessment before model is used in operational decision-making	Reduces risk of unsafe or incorrect outputs
Lifecycle governance	Treating model updates as a controlled, regulated process rather than ad hoc changes	Maintains long-term model integrity and compliance

Integration into Manufacturing Execution and Quality Systems

Embedding in the Manufacturing Execution System (MES)

The AI module would operate within the manufacturing execution and quality system environment, receiving sensor streams, generating CQA predictions, and writing release-relevant evidence to the electronic batch record. Continuous blending and tableting studies show that PAT signals can be integrated close to the manufacturing process, while real-time release work indicates that the resulting model outputs must be connected to batch disposition logic [1, 2]. Near-infrared, Raman, and machine-vision approaches further suggest that multiple sensor types can contribute to a broader quality system when their roles are clearly defined [18, 19]. The MES interface should therefore preserve timing, data lineage, model version, sensor status, and operator actions for auditability.

Operator Dashboard and Exception Handling

The operator dashboard would translate model outputs into a controlled human-machine interface that displays current predicted CQAs, quality trends, sensor status, and release or hold recommendations. Intelligent tablet press concepts and color-space-based RTRT work both point toward practical operator-facing systems that transform in-line observations into interpretable production decisions. The dashboard should not hide uncertainty; instead, it should show whether a hold was driven by spectral quality, press-signal abnormality, model-domain warning, or CQA risk. Exception handling should preserve a full audit trail so that quality units can review the basis for release, hold, or additional testing.

Evaluation Strategy

Analytical Accuracy of CQA Predictions

The evaluation strategy should examine whether predicted assay, content uniformity, hardness, and dissolution are analytically suitable for their intended RTRT role without presenting the model as universally valid. Spectroscopic tablet characterization and dissolution-prediction studies provide a conceptual basis for comparing model outputs with reference laboratory methods, including chemical assays and off-line physical tests [7, 23]. Raman and near-infrared imaging comparisons also support evaluating whether each modality contributes distinct information for specific CQAs [13]. Accuracy assessment should therefore be framed around intended use, bias behavior, agreement with reference methods, and suitability across representative manufacturing conditions rather than around isolated headline performance values.

Release Decision Performance

Release decision evaluation should test whether the architecture reaches the same quality disposition that would be expected from the approved laboratory-based control strategy, while also identifying cases where the AI appropriately recommends a hold. Regulatory experience with RTRT for dissolution emphasizes that release decisions must be justified by a scientifically supported relationship between in-process measurements and product quality [1]. Machine-learning studies in tablet development and manufacturing show that algorithmic predictions can support quality understanding, but their deployment as release logic requires more stringent evaluation than development-stage modeling [20, 24]. The release-decision assessment should therefore focus on false-release risk, false-reject behavior, and escalation pathways in conceptual terms, without relying on unsupported numerical claims.

Robustness and Drift Resilience

Robustness evaluation should challenge the architecture against expected sources of variation, including raw material changes, tablet presentation effects, sensor condition, equipment state, and normal process variability. Hot-melt extrusion and broader process-monitoring reviews show that machine-learning models in pharmaceutical manufacturing must be evaluated for continued suitability as processes evolve over time [25]. Data fusion and neural PAT reviews further indicate that multimodal systems require specific checks for modality imbalance, signal degradation, and model drift [10, 12]. The goal would be to demonstrate that the system detects uncertainty and degradation early enough to support quality risk management rather than silently extending beyond its validated domain.

Table 4 consolidates the validation, governance, and failure-control requirements that determine whether the proposed AI-driven RTRT architecture could move from conceptual design to regulated manufacturing use.

Table 4. Validation, Governance, and Failure-Control Framework for AI-Driven RTRT Deployment

RTRT system layer	Key validation question	Required evidence before release use	Principal failure mode if under-controlled	Risk-control mechanism	Quality-system implication
Raman acquisition and preprocessing	Are Raman spectra representative, stable, and suitable for CQA prediction under intended manufacturing conditions?	Probe-placement justification, preprocessing rationale, spectral-quality thresholds, robustness testing across presentation and instrument conditions	Degraded or artifact-contaminated spectra are converted into apparently confident release predictions	Automated spectral-quality gates, artifact detection, probe-health monitoring, and hold decisions for unusable spectra	Raman data must be treated as controlled quality evidence, not as an unqualified sensor feed
Tablet press signal encoding	Do press signals capture tablet formation behavior relevant to physical and performance CQAs?	Time-window definition, signal-calibration checks, force-profile validation, equipment-state coverage, process-range challenge testing	Machine-state variation is mistaken for product-quality assurance or ignored when it affects tablet performance	Press-signal plausibility checks, abnormal-state detection, equipment calibration review, and operator alerts	Press data become part of the quality control strategy and must be traceable to batch evidence
Raman–press synchronization	Are the chemical and physical signals correctly linked to the same tablet unit or justified production interval?	Timestamp integrity, tablet or segment matching rules, representative sampling justification, data-lineage verification	Misaligned evidence creates false chemical–mechanical relationships and unreliable CQA predictions	Synchronization checks, missing-link flags, batch-position tracking, and audit-trail documentation	Data integrity depends on defensible linkage between sensor streams and manufacturing units
Multimodal fusion model	Does fusion improve quality understanding beyond single-modality models without creating unacceptable opacity?	Modality-ablation studies, interaction analysis, interpretability summaries, comparison with Raman-only and press-only baselines	The model appears accurate during development but relies on unstable or non-causal cross-modal shortcuts	Ablation testing, modality contribution reporting, domain applicability limits, and periodic performance review	Fusion must be justified scientifically and maintained as a validated model component
Multi-output CQA predictor	Are assay, content uniformity, hardness, and dissolution predictions accurate enough for their intended RTRT role?	Agreement with reference methods, bias analysis, representative manufacturing coverage, CQA-specific error characterization	Strong performance for one CQA masks weak or unsafe performance for another	CQA-specific acceptance criteria, separate prediction heads, reference-method comparison, and conservative release rules	Multi-output prediction should not imply uniform readiness across all CQAs
Release decision logic	Does the pass, fail, or hold decision	Decision-rule specification, false-	AI output bypasses quality	Predefined decision thresholds,	RTRT should function as

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	align with the approved control strategy and quality risk expectations?	release risk assessment, false-hold analysis, borderline-case testing, quality-unit review procedure	judgment or releases product outside validated confidence limits	uncertainty-aware hold rules, escalation pathways, and human quality review	controlled decision support within GMP, not as uncontrolled automation
Missing or degraded modality handling	What happens when Raman, press, or synchronization evidence is incomplete?	Missing-data scenarios, sensor-failure simulations, fallback-use justification, modality-specific confidence limits	The system releases product using evidence insufficient for the claimed CQA decision	Missing-modality flags, restricted fallback modes, automatic hold status, and documented exception handling	Incomplete evidence must trigger quality review unless a validated fallback pathway exists
Drift and lifecycle monitoring	Does the model remain suitable as raw materials, equipment, sensors, and process conditions change?	Drift metrics, periodic reference testing, residual monitoring, sensor-health trends, recalibration triggers	A once-valid model silently becomes unsuitable for release decisions	Continuous monitoring, controlled recalibration, change-control review, and revalidation requirements	AI-driven RTRT requires lifecycle governance comparable to other GMP-critical systems
MES and electronic batch record integration	Are model outputs, sensor status, and operator actions traceable in the manufacturing record?	Data-lineage mapping, model-version capture, audit-trail testing, batch-record integration, role-based access controls	Release decisions cannot be reconstructed or defended during quality review or inspection	Electronic batch record linkage, timestamped model outputs, operator annotations, and version-controlled evidence	RTRT evidence must be inspection-ready and tied to the approved manufacturing control strategy

Limitations

Dependency on Sensor and Sample Presentation Consistency

The proposed architecture would depend strongly on consistent Raman sampling geometry, stable probe condition, controlled tablet presentation, and reliable synchronization with tablet press signals. Raman-based dissolution and imaging studies show that spectral information can be quality-relevant, but they also imply sensitivity to measurement context and sample representation [4, 5]. Data fusion does not eliminate these dependencies; it can instead propagate sensor artifacts if signal-quality controls are weak [12]. Therefore, engineering controls around probe placement, environmental interference, calibration state, and tablet handling would remain essential.

Current Scope Limited to Chemical and Basic Physical CQAs

The architecture is intentionally scoped to assay, content uniformity, hardness, and dissolution-related decision support, because these attributes can be conceptually linked to Raman spectra and press behavior. More complex CQAs, such as disintegration mechanisms, specialized release profiles, or coating-specific functional behavior, may require additional modalities or product-specific model structures [14]. Machine vision and other PAT tools could extend the system toward visual defects, geometry, and surface features that Raman and press signals may not fully capture [18]. As a result, this AIF should be understood as a modular RTRT framework rather than a universal tablet quality platform.

Conclusion

An AI architecture that fuses Raman spectra with tablet press signals offers a system-oriented path toward real-time release testing in tablet manufacturing. By combining chemical information with physical manufacturing signals, the architecture could support a more complete view of quality than either modality can provide alone.

The main strength of the proposed framework is its holistic structure. It connects in-line sensing, multimodal feature learning, multi-output CQA prediction, uncertainty-aware decision logic, and lifecycle monitoring into one release-supporting system.

Important challenges remain before such an architecture could be used routinely in GMP manufacturing. Robust calibration transfer, sensor-health management, explainable model governance, regulatory acceptance, and prospective validation would all need to be addressed through disciplined development and quality-system integration.

Collaborative pilot studies among equipment vendors, AI developers, PAT scientists, and pharmaceutical manufacturers would help establish shared best practices. Such work could build the scientific and regulatory precedent needed for AI-driven RTRT to become a practical part of modern tablet manufacturing.

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