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Comparative Evaluation of Traditional Quality Risk Management and AI-Based Dynamic Quality Risk Management in Pharmaceutical Manufacturing

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Abstract : Quality risk management (QRM) is the cornerstone of pharmaceutical manufacturing oversight, guiding decisions that protect patients from harm arising from variability in materials, processes, equipment, and human performance. For nearly two decades, QRM in the industry has been anchored in the International Council for Harmonisation's ICH Q9 guideline, operationalised through structured, largely manual tools such as Failure Mode and Effects Analysis (FMEA), Hazard Analysis and Critical Control Points (HACCP), and Fault Tree Analysis (FTA). While this traditional model has brought discipline and harmonisation to risk decision-making, it is inherently periodic, retrospective, and dependent on subjective expert scoring. The emergence of artificial intelligence (AI), machine learning (ML), the Internet of Things (IoT), and digital twin technology is now enabling a parallel model often described as dynamic or continuous QRM, in which risk is monitored, scored, and mitigated in near real time as manufacturing data are generated. This review synthesises the peer-reviewed and regulatory literature to compare traditional and AI-based dynamic QRM approaches across the dimensions of methodology, data usage, timeliness, objectivity, scalability, regulatory acceptance, and implementation cost. The review finds that AI-based dynamic QRM offers substantial gains in early-warning capability, predictive accuracy, and consistency, but introduces new categories of risk related to data integrity, model transparency, validation burden, and cybersecurity that traditional QRM does not encounter to the same degree. The evidence suggests that the two paradigms are not mutually exclusive: current regulatory thinking from the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA), and the International Society for Pharmaceutical Engineering (ISPE) points toward a hybrid model in which AI-enabled analytics augment, rather than replace, the ICH Q9(R1) risk management framework, with human oversight retained as a decisive control point. The review concludes with recommendations for regulatory science, workforce development, and validation strategy needed to responsibly scale dynamic QRM across the pharmaceutical manufacturing sector.

IndexTerms - quality risk management; ICH Q9; artificial intelligence; machine learning; pharmaceutical manufacturing; digital twin; Pharma 4.0; predictive quality; FMEA; dynamic risk management.

I. INTRODUCTION

Pharmaceutical manufacturing occupies a unique position among industrial sectors: a single undetected deviation in a batch record, a raw-material impurity, or a drifting process parameter can translate directly into patient harm. Quality risk management (QRM) was formalised as an industry-wide expectation with the introduction of the International Council for Harmonisation's ICH Q9 guideline in 2005, which established a systematic process for the assessment, control, communication, and review of risks to product quality across the product lifecycle (European Medicines Agency [EMA], 2006). The guideline rests on two governing principles: risk evaluation should be grounded in scientific

knowledge and linked to patient protection, and the level of formality applied to a risk exercise should be proportionate to the level of risk involved (EMA, 2023).

For close to two decades, this framework has been operationalised chiefly through manual, team-based tools: FMEA, HACCP, and FTA, typically supplemented by qualitative risk matrices. These tools have brought welcome structure and a common vocabulary to risk-based decision-making in a heavily regulated sector. However, a growing body of literature documents their practical shortcomings, particularly the subjectivity inherent in assigning severity, occurrence, and detectability scores, and the fact that a Risk Priority Number computed as the product of three ordinal ratings can mask very different underlying risk profiles (Assyro, 2026; SimplerQMS, 2026). The revised guideline, ICH Q9(R1), explicitly acknowledges these concerns, citing high levels of subjectivity in risk assessments and outputs, and a lack of clarity regarding risk-based decision-making and risk review, as motivations for its revision (FDA, 2024).

In parallel, the wider manufacturing sector has undergone a digital transformation loosely grouped under the label Industry 4.0, and its pharmaceutical-specific counterpart, Pharma 4.0, promoted by the International Society for Pharmaceutical Engineering (ISPE). Pharma 4.0 builds on the ICH Q10 pharmaceutical quality system and adds resources, information systems, organisation and processes, and culture as enabling elements, alongside digital maturity and data integrity by design (Automera, 2026; Sware, 2026). Within this broader digital transformation, artificial intelligence and machine learning have moved from experimental pilots to active deployment in quality control, predictive maintenance, and increasingly, quality risk management itself (Niazi, 2025). AI-enabled systems can ingest continuous streams of data from process analytical technology (PAT) sensors, the Internet of Things (IoT), manufacturing execution systems, and laboratory information management systems, and use these data to generate risk scores that update as manufacturing conditions change, rather than at fixed review intervals (Kodumuru et al., 2025; Zhu, 2025).

This shift raises a central question for the pharmaceutical quality profession: does AI-based dynamic QRM represent a genuine improvement over the traditional ICH Q9 model, and if so, along which dimensions, and at what cost in terms of new categories of risk? This review addresses that question by systematically comparing the two paradigms across methodology, data handling, timeliness, objectivity, validation burden, regulatory acceptance, and total cost of ownership. It further considers how regulatory thinking, exemplified by ICH Q9(R1), the FDA's evolving AI/ML guidance, the position of the European Federation of Pharmaceutical Industries and Associations (EFPIA) on AI in GMP environments, and the GAMP 5 Appendix D11 framework for AI/ML validation, is converging on a hybrid model rather than treating AI as a wholesale replacement for established risk tools.

2. Review Methodology

This is a narrative, comparative review rather than a systematic review with meta-analysis, reflecting the heterogeneous and rapidly evolving nature of the literature on AI applications in pharmaceutical manufacturing quality. Sources were identified through structured searches of regulatory repositories (the FDA, the EMA, and the ICH document databases), peer-reviewed literature indexed in PubMed Central and journal publisher platforms, and industry guidance issued by ISPE, EFPIA, and the GAMP community. Search terms combined quality risk management, ICH Q9, FMEA, artificial intelligence, machine learning, digital twin, predictive quality, Pharma 4.0, and process analytical technology.

Sources were included if they addressed (a) the principles, tools, or limitations of traditional pharmaceutical QRM; (b) the application of AI, ML, digital twins, or related digital technologies to manufacturing quality or risk management; or (c) regulatory or standards-body guidance bearing on either paradigm. Trade and industry commentary was included selectively, where it usefully illustrated implementation practice, but conclusions of regulatory consequence are drawn primarily from peer-reviewed studies and primary regulatory documents. Because this is a fast-moving field in which many primary sources are recent publications, position papers, or preprints, the review privileges recency while cross-checking claims against the underlying ICH Q9(R1) text and FDA/EMA statements wherever possible. Figure 1 summarises the resulting conceptual comparison, and Section 5 presents the synthesised evaluation in tabular form.

3. Traditional Quality Risk Management in Pharmaceutical Manufacturing

3.1 Regulatory Foundation: ICH Q9 and Q9(R1)

ICH Q9, first issued in 2005, provides principles and a toolbox of methods for identifying, evaluating, controlling, communicating, and reviewing risks to pharmaceutical quality across development, manufacturing, and distribution (EMA, 2006). The guideline defines quality risk management as a systematic process for the assessment, control, communication, and review of risks to the quality of the medicinal product across the product lifecycle, and it establishes that the evaluation of risk should ultimately link back to protection of the patient (EMA, 2023).

The 2023 revision, ICH Q9(R1), was motivated by four recognised gaps in the original framework: high levels of subjectivity in risk assessments and their outputs, inadequate management of supply and product-availability risk, a lack of shared understanding of what constitutes appropriate formality in QRM work, and insufficient clarity on risk-based decision-making and risk review (FDA, 2024). The revision explicitly links quality and manufacturing non-compliance to drug shortages and reframes an effective pharmaceutical quality system as an early-warning mechanism for both quality and supply risk (FDA, 2023). Notably, the revision did not change the underlying risk-review expectation itself, but it clarified that risk assessments must be kept current and that review frequency should scale with the level of residual risk (FDA, 2023). Industry commentary on the revision has emphasised that its recurring use of the word "effective" signals an intent to move QRM programmes away from documentation-driven, compliance-only exercises and toward decision-relevant risk management (Coleman, 2026).

3.2 Core Tools and Techniques

ICH Q9(R1) does not mandate a single risk-assessment method; instead it offers a toolbox from which organisations select an approach proportionate to the risk question at hand. Three tools dominate practice.

Failure Mode and Effects Analysis (FMEA) is the most widely used pharmaceutical risk-assessment tool. It systematically decomposes a process into individual failure modes and scores each on severity, occurrence, and detectability, typically on ten-point ordinal scales, before multiplying the three scores into a Risk Priority Number (RPN) used to prioritise mitigation (Assyro, 2026). FMEA is commonly applied to process design, equipment qualification, change-control impact assessment, and supplier risk evaluation (Assyro, 2026).

Hazard Analysis and Critical Control Points (HACCP) and Fault Tree Analysis (FTA) supplement FMEA. HACCP is oriented toward identifying critical control points at which a hazard can be prevented or eliminated, while FTA visualises the combinations of failures that lead to a top-level undesired event and supports quantitative probability estimation when reliable failure-rate data exist (Assyro, 2026). FTA is valued for surfacing critical failure combinations but is time-intensive to construct correctly and can miss failure modes that were not anticipated when the tree was built (Assyro, 2026).

All three tools are typically deployed by cross-functional teams during discrete, scheduled exercises: at process validation, at the introduction of a planned change, during a deviation investigation, or as part of a periodic product quality review. This mode of operation is a defining structural feature of traditional QRM, distinguishing it from the continuously updating risk pictures described in Section 4.

3.3 Strengths of Traditional QRM

The ICH Q9 framework has delivered three durable benefits. First, it created a common, internationally harmonised vocabulary and process for risk-based decision-making that regulators, auditors, and manufacturers across jurisdictions can rely upon, reducing friction in cross-border drug approval and inspection (EMA, 2006). Second, its tools are transparent and auditable: a completed FMEA worksheet shows exactly how a risk score was derived and by whom, which supports inspection readiness and root-cause traceability during deviation investigations (SimplerQMS, 2026). Third, because the methodology depends on structured human judgement rather than a trained statistical model, its outputs do not depend on the availability of large historical datasets, making it applicable even to novel products, first-in-class processes, or low-volume manufacturing lines where an AI model could not be adequately trained or validated.

3.4 Limitations of Traditional QRM

Notwithstanding these strengths, the literature converges on several structural limitations of the traditional model.

Subjectivity and inter-rater variability. Because severity, occurrence, and detectability ratings are assigned by expert judgement, different teams frequently score the same failure mode differently, and the mathematical accuracy of the resulting RPN has repeatedly been questioned in the clinical and manufacturing risk-assessment literature (Bioprocess Tools, 2026). ICH Q9(R1) itself acknowledges that subjectivity can directly affect the effectiveness of risk management activities and the decisions that follow from them (Coleman, 2026).

Mathematical weaknesses in RPN scoring. The multiplicative RPN formula can produce identical scores for very different risk profiles; a failure mode scored 10 × 1 × 1 yields the same RPN as one scored 2 × 2 × 2.5, despite representing qualitatively different hazards (Assyro, 2026). Standard automotive- or electronics-derived FMEA scoring scales also translate poorly to biological systems, which has led specialist practice to develop bioprocess-specific severity, occurrence, and detection scales (Bioprocess Tools, 2026).

Static, point-in-time assessment. A traditional risk assessment reflects the state of process knowledge at the moment it was performed. Once approved, it typically remains unchanged until a triggering event, such as a planned change, a deviation, or a scheduled periodic review, prompts reassessment (FDA, 2023). Between these checkpoints, gradual process drift, equipment wear, or supplier variability can accumulate undetected.

Resource intensity and limited system-level visibility. A rigorous FMEA exercise demands significant cross-functional time and facilitation expertise, and by design it examines failure modes individually, which can obscure complex, multi-factor interactions across a manufacturing system (Assyro, 2026; SimplerQMS, 2026). These limitations do not invalidate the ICH Q9 framework, which remains the regulatory baseline for pharmaceutical QRM worldwide, but they define the specific gaps that AI-based dynamic QRM is being positioned to close.

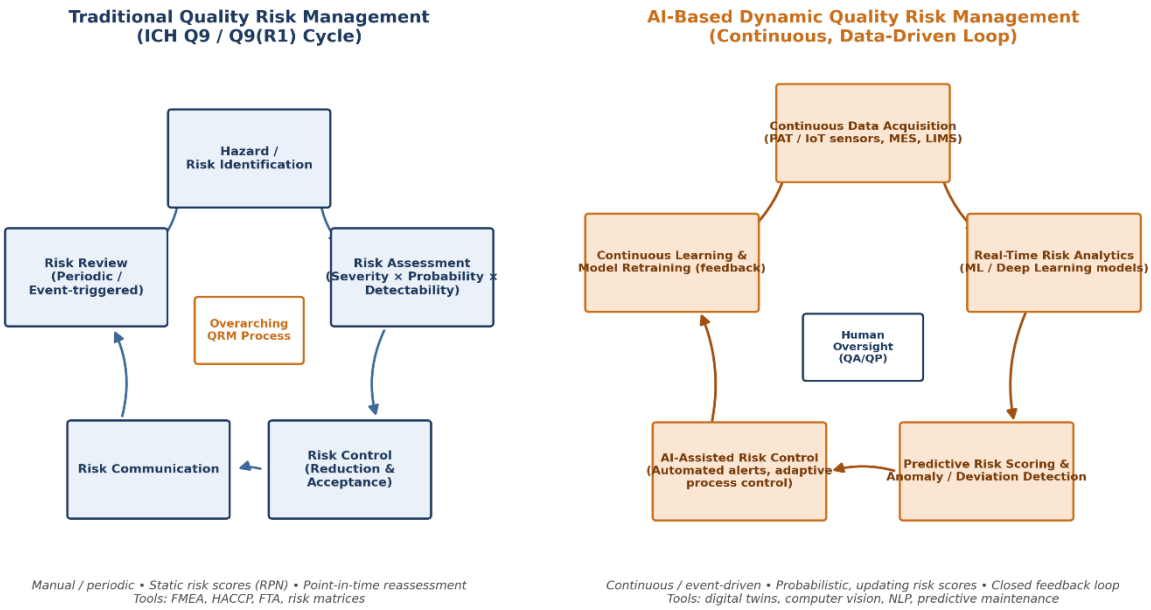

Figure 1. Conceptual comparison of the traditional, cyclic ICH Q9 quality risk management process (left) and an AI-based dynamic, continuous quality risk management loop (right).

4. AI-Based Dynamic Quality Risk Management

4.1 Conceptual Shift: From Static to Dynamic QRM

Dynamic quality risk management does not discard the ICH Q9(R1) process of assessment, control, communication, and review; rather, it changes the cadence and evidentiary basis on which that process operates. Instead of a risk score generated at discrete review points from expert recollection and historical batch records, a dynamic model continuously ingests live process data and recalculates risk as new information arrives (Zhu, 2025). The European Federation of Pharmaceutical Industries and Associations (EFPIA) frames this shift in terms of the underlying technologies rather than a change in regulatory philosophy: AI in a GMP environment is understood as machine learning, natural language processing, and robotics applied within the existing quality management system, with a risk-based approach still governing how much control and validation any given AI application requires (EFPIA, 2024).

This reframes quality risk management as a closed feedback loop rather than a linear or cyclic checklist: data acquisition feeds analytics, analytics generate a predictive risk score, the score triggers a control action (automated or human-mediated), and the outcome of that action becomes new training data that refines the underlying model. Figure 1 illustrates this contrast against the traditional ICH Q9 cycle.

4.2 Enabling Technologies

Several converging technologies make dynamic QRM operationally possible.

Process analytical technology (PAT) and the Internet of Things. The FDA's PAT framework, first issued in 2004, encouraged manufacturers to build quality into the process through timely, often in-line or on-line, measurement of critical process parameters (CPPs) and critical quality attributes (CQAs), rather than relying solely on end-product testing (FDA, 2004; Wikipedia, 2026). PAT remains foundational to in-process analytical strategy and now underpins ICH Q8, Q9, and Q10 (Technology Networks, 2026). IoT-enabled sensors extend this concept by continuously monitoring parameters such as temperature and air quality on the shop floor and feeding that data to AI algorithms that can flag early signs of process deviation (Kodumuru et al., 2025).

Machine learning and deep learning. Predictive models, ranging from random forests and gradient boosting machines to convolutional and deep neural networks, are used to model the nonlinear relationships between CPPs and CQAs, enabling proactive quality assurance rather than reactive end-point testing (Zhu, 2025). Comparative evaluations report that deep learning architectures generally achieve lower prediction error and higher accuracy than classical regression-based Design of Experiments approaches when applied to high-dimensional, industrial-scale process data, although this comes at higher computational and training cost (Zhu, 2025).

Computer vision. Machine-vision systems coupled with deep learning are being used for real-time visual inspection tasks such as coating-thickness measurement and defect detection in film-coated tablets, catching inconsistencies that could compromise safety or efficacy and that human visual inspection might miss (Han & Tao, 2024; Freyr Solutions, 2024).

Natural language processing and explainable AI. Natural language processing (NLP) is applied to unstructured regulatory documentation, batch records, and technical reports, enabling automated extraction of compliance-relevant information (Zhu, 2025). Because regulators and quality units cannot accept opaque risk scores, explainable-AI (XAI) techniques such as SHAP (Shapley Additive Explanations) and LIME (Local Interpretable Model-Agnostic Explanations) are increasingly paired with predictive models to expose which input variables are driving a given risk prediction, supporting both interpretability and the process-understanding expectations embedded in ICH Q8 and the risk-assessment expectations of ICH Q9 (Zhu, 2025).

Digital twins. A digital twin is a live virtual replica of a physical manufacturing process, continuously updated from PAT and sensor data, that can be used for predictive maintenance, virtual (predictive) release testing, and what-if simulation of process changes before they are implemented on the physical line (Sakara Digital, 2026; PharmOut, 2026). Reviews of digital-twin applications across the drug development lifecycle report that coupling digital twins with AI and machine learning amplifies their value for preventive maintenance and manufacturing optimisation, while noting that data integration, model accuracy, and regulatory complexity remain significant barriers to adoption (“Transformative Roles of Digital Twins,” 2025). Digital-twin adoption also carries its own governance burden: a 2026 review of 248 documented data-integrity incidents in digital-twin-enabled continuous manufacturing found that the majority involved non-contemporaneous data capture, underscoring that predictive quality tools must be built on the same ALCOA+ data-integrity foundation required of conventional paper and electronic records (“Data Integrity Failures,” 2026).

4.3 Applications in Manufacturing Quality Risk Management

AI-based dynamic QRM is being applied across several concrete use cases relevant to manufacturing risk. Predictive quality and virtual release testing use digital-twin or model-based predictions of finished-product quality attributes to support or supplement traditional end-of-batch testing, shortening the interval between manufacture and release decision while flagging predicted excursions before they occur (Sakara Digital, 2026). Predictive maintenance uses sensor and equipment-performance data to forecast component failure before it causes an unplanned line stoppage or a deviation, reducing both downtime and the associated quality risk of an abnormal restart (Kodumuru et al., 2025). Real-time deviation and anomaly detection applies statistical or ML-based control limits to streaming process data so that a drift toward an out-of-specification condition is detected while the batch is still in progress, rather than discovered at final testing (Freyr Solutions, 2024). Automated visual quality control uses computer vision to inspect packaging, coating, and fill/finish operations at line speed, improving detection sensitivity relative to manual visual inspection (Freyr Solutions, 2024). Regulatory and documentation support uses NLP to reconcile batch records, deviation reports, and change controls against current regulatory text, reducing the administrative risk of an inconsistent or incomplete quality record (Zhu, 2025).

4.4 Regulatory Perspectives on AI/ML in GMP

Regulators have moved cautiously but deliberately to define expectations for AI/ML used in or adjacent to GMP manufacturing. The FDA's earliest AI/ML framework, the 2021 Artificial Intelligence/Machine Learning-Based Software as a Medical Device Action Plan, was written primarily for AI-enabled medical devices but established principles, including a predetermined change-control plan for models that continue to learn after deployment and a call for Good Machine Learning Practice (GMLP), that have since informed drug-manufacturing-specific thinking (FDA, 2021; Drug Discovery News, 2026). A dedicated FDA discussion paper on AI in drug manufacturing followed in 2023, and a January 2025 draft guidance extended AI-specific expectations across discovery, nonclinical research, clinical research, and manufacturing (Drug Discovery News, 2026).

The Good Automated Manufacturing Practice (GAMP 5) framework, maintained by ISPE, added Appendix D11 in its second edition specifically to address AI/ML validation, prescribing a lifecycle covering concept, project, and operational phases and explicitly extending the traditional validation lens to include model training data, continuous monitoring, and model drift (IntuitionLabs, 2026a, 2026b). Both FDA and international quality bodies increasingly favour Computer Software Assurance (CSA), a risk-based approach that concentrates validation effort on the functions with the greatest potential impact on patient or product quality, over exhaustive, one-size-fits-all testing; under this logic, an AI system that recommends a dosing or release decision would receive materially more rigorous validation than one used for warehouse logistics (IntuitionLabs, 2026a). EFPIA's industry position, developed in coordination with member companies, similarly argues that existing GMP and quality-risk-management frameworks, rather than an entirely new regulatory regime, should be the vehicle for governing AI/ML in biopharmaceutical manufacturing, with the extent of validation scaled to the AI system's context of use and degree of autonomous control (EFPIA, 2024). Across these sources, one theme recurs: AI/ML systems used in manufacturing are expected to be treated as GxP computerised systems subject to ICH Q9(R1)-consistent risk assessment, not as an exemption from it (IntuitionLabs, 2026b).

4.5 Limitations and Emerging Risks of AI-Based QRM

The literature is candid that AI-based dynamic QRM introduces risk categories that traditional QRM does not encounter in the same form.

Data integrity and provenance. Continuous, high-volume data capture from PAT, IoT, and digital-twin sources multiplies the number of electronic records that must satisfy ALCOA+ (attributable, legible, contemporaneous, original, accurate, plus complete, consistent, enduring, and available) expectations. A recent review of documented data-integrity incidents in digital-twin-assisted continuous manufacturing found that the large majority stemmed from non-contemporaneous data capture, non-traceable simulation inputs, or virtual records lost to cloud-synchronisation failures (“Data Integrity Failures,” 2026).

Model transparency and the black-box problem. Deep-learning models in particular can achieve high predictive accuracy while offering limited native insight into why a given prediction was made, a tension the industry is addressing through XAI methods such as SHAP and LIME, but which nonetheless increases both validation effort and the burden of demonstrating process understanding to regulators (Zhu, 2025; IntuitionLabs, 2026a).

Validation and lifecycle burden. Unlike a static software function, a learning model can change its behaviour as it is retrained on new data, which GAMP 5 Appendix D11 addresses through a dedicated AI/ML lifecycle emphasising continuous monitoring, but which nonetheless represents a materially larger

and more continuous validation commitment than a traditional, one-time risk-assessment exercise (IntuitionLabs, 2026b).

Cybersecurity and infrastructure dependence. AI-integrated PAT and digital-twin systems depend on networked sensors, cloud or edge computing infrastructure, and secure data pipelines; unauthorised access, data tampering, or an outage in this infrastructure translates directly into a quality risk, requiring investment in encrypted transmission, access control, and penetration testing that traditional, paper- or spreadsheet-based FMEA programmes did not require (Zhu, 2025).

Cost, talent, and organisational readiness. Digital-twin and AI programmes require substantial upfront investment in infrastructure, data engineering, and specialised talent, and pharmaceutical organisations frequently cite integration with legacy systems and a shortage of cross-trained data-science and quality personnel as barriers to scale-up (Pharm Out, 2026; Freyr Solutions, 2024).

5. Comparative Evaluation

Table 1 synthesises the preceding sections into a structured, dimension-by-dimension comparison of traditional and AI-based dynamic quality risk management. The comparison is deliberately framed as complementary rather than adversarial: as Section 7 argues, the strongest current regulatory and industry position is that the two paradigms should be integrated rather than treated as substitutes for one another.

Table 1

Comparative Evaluation of Traditional and AI-Based Dynamic Quality Risk Management

Dimension	Traditional QRM (ICH Q9)	AI-Based Dynamic QRM
Underlying philosophy	Periodic, checklist-driven assessment tied to defined trigger events (validation, change control, deviation, periodic review)	Continuous, feedback-driven monitoring that recalculates risk as new process data arrive
Primary tools	FMEA, HACCP, FTA, qualitative risk matrices	Machine learning / deep learning, computer vision, NLP, digital twins, PAT/IoT sensor networks
Data basis	Historical records, expert recollection, batch documentation reviewed at a point in time	Live, high-frequency process, sensor, and quality data streams
Timeliness of detection	Deviations typically identified at scheduled review or after batch completion	Deviations and drift can be flagged in near real time, during the batch
Objectivity	Subject to inter-rater variability in severity/occurrence/detectability scoring	Model scores are computed consistently from data, but inherit any bias present in training data
Transparency / explainability	Fully transparent; scoring rationale is documented by the assessment team	Can be limited ("black box") for complex models; mitigated via XAI (SHAP, LIME)
Scalability across sites/products	Labour-intensive; difficult to scale uniformly across large, multi-site networks	Scales well once data pipelines and validated models exist, but requires sufficient training data per product/process
Regulatory basis	ICH Q9 / Q9(R1); decades of established inspection precedent	ICH Q9(R1) plus emerging AI-specific guidance (GAMP 5 Appendix D11, FDA draft AI guidance, EFPIA position)
Validation burden	One-time validation of the assessment exercise and its documentation	Continuous lifecycle validation, including model monitoring for drift and periodic retraining

Dimension	Traditional QRM (ICH Q9)	AI-Based Dynamic QRM
New risk categories introduced	Minimal; risks are largely those of human error or omission	Data integrity of high-volume electronic records, model bias, cybersecurity of connected infrastructure
Applicability to novel/low-data processes	Well suited; does not require historical data volume	Constrained; models need adequate representative training data to be reliable
Implementation cost profile	Lower capital cost; recurring labour cost for facilitation and documentation	Higher upfront capital and data-infrastructure cost; potentially lower marginal cost per assessment at scale

Read together, the rows in Table 1 show a consistent pattern: AI-based dynamic QRM improves timeliness, consistency of computation, and scalability, but it does so by trading the interpretive transparency and low data-dependency of manual tools for a new, and in some respects heavier, validation and data-governance burden. Neither paradigm dominates the other on every dimension, which is itself the strongest argument in the literature for a hybrid approach (EFPIA, 2024; IntuitionLabs, 2026a).

6. Illustrative Industry Examples

Several documented examples illustrate how the comparison in Table 1 plays out in practice. In solid-dosage manufacturing, an AI-powered quality-by-design framework applied at pilot scale to a tablet line integrated real-time critical-process-parameter data (temperature, pressure, and torque) with predictive deep-learning models; the system identified deviations affecting tablet hardness and dissolution before they propagated, and the associated corrective actions reduced out-of-specification batches by approximately 18% across three production cycles (Zhu, 2025). In a sterile fill-finish setting, natural-language-processing modules were used to reconcile batch records and documentation against ICH Q8–Q11 expectations, while an explainable-AI layer identified filling speed and vial-stopper alignment as the dominant process parameters driving sterility failures; the resulting AI-assisted control strategy was associated with a 12% reduction in batch rejections and improved audit traceability (Zhu, 2025).

At the sensor-and-facility level, IoT-enabled continuous monitoring of temperature and air quality, coupled with AI algorithms trained to recognise early signs of process deviation, has been reported in large manufacturing operations as a mechanism for triggering rapid corrective action before a full deviation investigation becomes necessary (Kodumuru et al., 2025). In continuous biomanufacturing, digital twins built around in-line spectroscopic feedback have been proposed as a route toward autonomous operation and real-time release testing for complex modalities such as virus-like-particle and mRNA-based products, directly extending the reach of dynamic QRM into process types that traditional, end-point-testing-oriented QRM handles less efficiently (Sakara Digital, 2026).

These examples share a common structure: AI-based dynamic QRM did not replace the underlying ICH Q9(R1) risk categories of severity, occurrence, and detectability; rather, it changed how quickly and how granularly those categories could be evaluated, while human quality-assurance and qualified-person oversight remained the final control point before a batch disposition decision was made.

7. Toward a Hybrid Quality Risk Management Model

The weight of regulatory and industry opinion reviewed in this paper does not support framing traditional and AI-based dynamic QRM as competing alternatives from which an organisation must choose. Instead, three converging lines of evidence point toward a hybrid model.

First, regulatory guidance treats AI/ML systems as GxP computerised systems that must themselves be risk-assessed using an ICH Q9(R1)-consistent process before and during deployment; in this framing, ICH Q9(R1) is not superseded by AI but becomes the governing framework for validating the AI (IntuitionLabs, 2026a, 2026b; EFPIA, 2024). Second, the Computer Software Assurance philosophy embraced by the FDA and reflected in GAMP 5 Appendix D11 explicitly scales validation rigour to risk, meaning that lower-risk AI applications, such as logistics optimisation, can be validated with lighter-touch methods, while higher-risk applications, such as those informing a batch-release or dosing decision, warrant validation as rigorous as, or more rigorous than, a traditional FMEA (IntuitionLabs, 2026a). Third, the practical case studies reviewed in Section 6 retained human oversight, in the form of quality-assurance review and qualified-person sign-off, as the final control point even where AI substantially accelerated detection and scoring (Zhu, 2025).

A hybrid model, consistent with the ISPE Pharma 4.0 operating model, would use traditional FMEA/HACCP/FTA-based assessment for novel processes, low-data situations, and the qualitative aspects of risk (for example, assessing the severity of patient harm from a given failure mode, which remains a matter of clinical and scientific judgement rather than a quantity a model can learn from data), while using AI-based dynamic monitoring for high-volume, well-characterised, and heavily instrumented processes where continuous data streams already exist and where the marginal value of real-time detection is highest (Automera, 2026; Sware, 2026). Risk communication and risk review, the two ICH Q9(R1) process steps least discussed in the AI literature to date, may be the areas most directly improved by AI-generated dashboards that make an evolving risk picture visible to quality leadership on a continuous basis rather than only at scheduled review meetings (Assyro, 2026, iFactory example).

8. Future Directions and Research Gaps

Several gaps in the current evidence base merit attention from both researchers and regulators. First, there remains a shortage of peer-reviewed, prospective studies quantifying the comparative patient-safety impact of AI-based dynamic QRM against traditional QRM under real manufacturing conditions rather than pilot-scale or retrospective simulation; most of the quantitative performance gains reported in the literature reviewed here, while credible, come from single-site or single-product case studies (Zhu, 2025). Second, regulatory science needs to mature standardised expectations for the validation of continuously learning models, building on GAMP 5 Appendix D11 and the FDA's predetermined change-control-plan concept, so that model retraining does not require a full re-validation cycle each time (IntuitionLabs, 2026b; FDA, 2021). Third, data-integrity frameworks purpose-built for digital-twin and continuous-manufacturing environments, extending ALCOA+ to cover simulation inputs, model versioning, and cloud-synchronisation failure modes, are an active but still-developing area (“Data Integrity Failures,” 2026).

Fourth, the workforce implications of dynamic QRM deserve more systematic study: cross-training quality professionals in basic data science and data-science professionals in ICH Q9(R1) principles is repeatedly cited as a barrier to adoption, but there is limited published evidence on which training models are most effective (Freyr Solutions, 2024; PharmOut, 2026). Finally, small and mid-sized manufacturers, and manufacturers of novel modalities with limited historical process data, need explicit guidance on how far dynamic QRM tools can be responsibly applied when training data are scarce, an area where hybrid statistical/mechanistic modelling approaches may offer a bridge between traditional and fully data-driven methods.

9. Conclusion

Traditional, ICH Q9(R1)-based quality risk management has served the pharmaceutical industry for two decades as a transparent, auditable, and internationally harmonised method for identifying and controlling

risk to product quality. Its central limitations, subjectivity in expert scoring, static point-in-time assessment, and resource intensity, are well documented and are precisely the gaps that AI-based dynamic quality risk management is now positioned to close through continuous data acquisition, predictive analytics, and real-time anomaly detection. At the same time, AI-based approaches introduce their own risks: data-integrity exposure across a much larger volume of electronic records, reduced model transparency, a heavier and more continuous validation burden, and new cybersecurity dependencies. The comparative evaluation presented in this review indicates that neither paradigm is categorically superior; each is better suited to different risk questions, data environments, and stages of the product lifecycle. Current regulatory thinking, from ICH Q9(R1) itself through the FDA's evolving AI guidance, EFPIA's industry position, and the GAMP 5 Appendix D11 framework, converges on treating AI/ML systems as GxP computerised systems that must themselves be subject to ICH Q9(R1)-consistent risk management, effectively nesting the newer paradigm inside the older one rather than replacing it. For pharmaceutical manufacturers, the practical implication is that investment in dynamic QRM technology should proceed hand-in-hand with continued investment in the foundational risk-assessment skills, data-governance infrastructure, and human oversight that traditional QRM has always required, so that the sector captures the genuine safety and efficiency gains AI offers without compromising the transparency and patient-centred rigour that ICH Q9 established.

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