AI for Batch Record Review by Exception: The Future of Pharmaceutical Batch Release?

A Practical GMP Perspective on AI Batch Review, Electronic Batch Records, and Quality Oversight

Batch record review is one of the most important and time-sensitive activities in pharmaceutical Quality Assurance. Before a batch can be released or distributed, the Quality Unit must review production and control records to determine whether the batch was manufactured according to approved procedures and whether any discrepancies, deviations, or failures were properly investigated.

This is not optional. FDA requires batch production and control records to be prepared for each batch and to include complete information related to the production and control of that batch, including equipment used, components, in-process and laboratory control results, yields, labeling records, sampling, checks, and investigations where applicable (FDA, 21 CFR 211.188). FDA also requires all drug product production and control records, including packaging and labeling records, to be reviewed and approved by the Quality Control Unit before batch release or distribution (FDA, 21 CFR 211.192).

The challenge is that traditional batch record review is slow, repetitive, and heavily dependent on human attention. Reviewers must examine pages of entries, signatures, calculations, timestamps, corrections, attachments, alarms, deviations, equipment IDs, reconciliation records, and procedural confirmations. In paper or hybrid systems, this can take hours or days per batch. Even in electronic batch record systems, reviewers may still spend significant time verifying routine steps that were already executed within validated workflows.

This is where review by exception becomes attractive. Instead of manually reviewing every routine entry with equal intensity, QA focuses on exceptions: deviations, missing entries, invalid signatures, parameter excursions, yield discrepancies, unapproved interventions, late entries, alarm events, reconciliation mismatches, and unusual process patterns.

AI could take this concept further by helping detect anomalies, prioritize batch review risks, correlate process data, and identify records that deserve deeper QA attention. But AI should not become the batch release decision-maker. In GMP, batch disposition remains a Quality Unit responsibility.

What Is Batch Record Review?

Batch record review is the process of verifying that the batch was manufactured, processed, packed, tested, and documented according to approved procedures and specifications.

Review Area	Examples
Manufacturing steps	Verification that each required step was completed
Equipment and line use	Correct equipment ID, line clearance, cleaning status, setup

Materials and components	Correct lot numbers, quantities, reconciliation, expiry status
Process parameters	Temperature, pressure, speed, time, mixing, hold times
In-process controls	Fill weight, pH, bioburden, appearance, torque, hardness
Laboratory results	Finished product testing, in-process testing, stability if applicable
Yield reconciliation	Actual yield, theoretical yield, acceptable yield range
Packaging and labeling	Label reconciliation, specimen labels, coding, line clearance
Deviations	Investigation, product impact, CAPA, batch disposition support
Signatures and checks	Operator entries, supervisor checks, QA verifications
Data integrity	Corrections, late entries, audit trails, missing data, unexplained changes

The purpose is not paperwork perfection. The purpose is documented assurance that the batch was made correctly and that any unexplained discrepancy or failure was investigated before release.

Why Traditional Batch Record Review Is So Difficult

Traditional batch review is difficult because it combines compliance review, technical review, documentation review, and product quality assessment.

Challenge	Practical Impact
Large record volume	QA spends time reviewing routine entries instead of focusing on risk
Paper-based records	Manual page-by-page review increases cycle time
Hybrid records	Paper, MES, LIMS, SCADA, QMS, and spreadsheets must be reconciled
Human fatigue	Reviewers may miss small but important errors
Manual calculations	Yield, reconciliation, and in-process calculations may be error-prone
Late deviations	Issues may be found at final QA review instead of during manufacturing
Missing attachments	Cleaning records, labels, printouts, or logs may delay release
Audit trail review burden	Electronic data require meaningful audit trail review
Unclear exceptions	Not all deviations carry equal product risk
Release pressure	Commercial demand may create pressure to complete review quickly

The problem is not that QA reviewers are careless. The problem is that batch records contain a large volume of repetitive data, while the most important risks may be hidden in small exceptions.

What Is Review by Exception?

Review by exception is a quality review model where routine, compliant, system-verified entries receive less manual attention, while exceptions receive focused review.

In an electronic batch record environment, review by exception may involve system rules such as:

- Required field not completed
- Step performed out of sequence
- Parameter outside approved range
- Missing electronic signature
- Unauthorized user action
- Late entry
- Manual override
- Equipment not qualified or available
- Material lot not approved
- Yield outside expected range
- Alarm during critical step
- Deviation linked to batch
- Audit trail event requiring review

Instead of asking QA to manually confirm every expected entry, the system highlights what is unusual, incomplete, or potentially GMP-impacting.

```
Manufacturing executes batch
        ↓
Electronic system captures steps, parameters, signatures, and timestamps
        ↓
System applies predefined exception rules
        ↓
Exceptions are flagged in real time or during review
        ↓
Manufacturing/QA resolve or investigate exceptions
        ↓
QA reviews exception summary plus required critical records
        ↓
Quality Unit approves or rejects batch disposition
```

This model can reduce review time, but only if the system is validated, the exception rules are scientifically justified, and QA retains final release authority.

Why AI Could Improve Review by Exception

Traditional review-by-exception systems depend on predefined rules. These rules are valuable, but they often detect only known issues. AI can potentially strengthen review by exception by detecting unusual patterns that may not be captured by fixed rules.

Traditional Rule	AI-Enhanced Detection
Temperature exceeded limit	Temperature remained within limit but showed abnormal oscillation
Yield outside range	Yield within range but trending lower across recent batches
Step completed late	Multiple small delays occurred in the same process phase
Deviation opened	Similar near-miss patterns occurred without formal deviation
Alarm triggered	Alarm pattern resembles prior batch failure signature
Manual override used	Override occurred under unusual

	operator/equipment/context pattern
Missing signature	Signature present but timing pattern suggests review after-the-fact
In-process result within limit	Result is within specification but statistically unusual for this product

The value of AI is not simply faster review. The value is more intelligent review: helping QA focus attention where product quality risk may be higher.

AI Anomaly Detection in Batch Records

AI anomaly detection can identify batch record events or data patterns that differ from expected behavior.

Anomaly Type	Example
Process anomaly	Mixing time normal, but torque profile unusual
Timing anomaly	Step duration significantly longer than historical norm
Operator anomaly	Unusual number of corrections by one operator or shift
Equipment anomaly	Higher frequency of minor alarms on same filling line
Material anomaly	Specific component lot linked to repeated adjustments
Documentation anomaly	Entries completed unusually late compared with process timestamps
Yield anomaly	Yield still within limits but drifting downward over multiple batches
Audit trail anomaly	Repeated value changes before final entry acceptance

For example, a batch may have no formal deviation and all parameters may remain within approved limits. However, AI may detect that the batch required more manual interventions than typical batches, had longer setup time, and showed slightly increased yield loss. Individually, these may not trigger exceptions. Together, they may justify deeper review.

That is the realistic value of AI in batch record review: identifying combinations of weak signals.

Electronic Batch Records and AI

AI works best when batch data are structured, time-stamped, and electronically available. Electronic batch record systems can capture data from:

- MES
- EBR workflows
- LIMS
- SCADA
- PLCs
- Equipment historians
- Weighing and dispensing systems
- Barcode systems
- Labeling systems
- Environmental monitoring systems

- QMS deviations and CAPAs
- CMMS and calibration systems

A mature AI-assisted review-by-exception program could analyze:

Data Source	AI Review Use
MES/EBR	Step execution, signatures, timing, sequence
LIMS	In-process and finished product test results
SCADA/historian	Process parameter profiles and alarms
QMS	Deviations, investigations, CAPAs linked to batch
CMMS	Equipment maintenance history relevant to batch
Calibration system	Instrument status during batch execution
EM system	Environmental conditions during sterile manufacturing
Labeling system	Label reconciliation and coding verification
ERP/material system	Material status, supplier lot, inventory movement

The major challenge is integration. If systems do not share clean master data, AI may connect the wrong equipment, batch, room, material, or process step. AI for batch review depends heavily on good data governance.

Manufacturing Examples

Example 1: AI Flags a Subtle Filling Line Pattern

A sterile filling batch has no critical deviations. Fill weights are within limits. However, AI detects that the line had more micro-stoppages than usual, increased operator interventions during stopper feeding, and a slightly wider fill-weight distribution than the product baseline.

QA reviews the AI signal and requests additional review of interventions, EM data, equipment alarms, and rejected units. No product impact is identified, but engineering opens a maintenance work order for stopper bowl adjustment.

GMP value: AI identifies a weak operational signal before it becomes a deviation trend.

Example 2: AI Detects a Documentation Timing Issue

An EBR shows all required signatures completed. AI compares process timestamps with signature timestamps and flags that multiple checks were signed significantly later than expected, all by the same shift.

QA reviews the audit trail and determines whether this represents acceptable delayed documentation, a procedural gap, or a data integrity concern.

GMP value: AI supports meaningful review of documentation behavior, not just completion status.

Example 3: AI Connects Yield Drift With Equipment History

A tablet compression process remains within yield limits, but AI detects a downward yield trend across five batches. It correlates the trend with increased reject counts and a recent tooling change.

QA and manufacturing review batch data, equipment setup, and change control records. The issue is corrected before a batch falls outside expected yield.

GMP value: AI strengthens review by exception by detecting trends that are not yet formal exceptions.

Example 4: AI Prioritizes Batch Review Workload

A QA team has ten batches awaiting review. AI ranks them based on exception count, deviation severity, audit trail events, parameter anomalies, and unresolved linked records.

Batches with no exceptions and low-risk profiles are reviewed efficiently. Batches with unusual patterns receive deeper QA review.

GMP value: AI helps allocate reviewer attention based on risk.

Regulatory Analysis: FDA Expectations

AI-assisted batch review must begin with the basic regulatory expectation: batch production and control records must be complete and reviewed before release.

FDA's 21 CFR 211.188 requires batch production and control records for each batch and lists required record content such as equipment used, component lots, weights and measures, in-process and lab results, packaging and labeling inspection, yields, labeling records, sampling, checks, and investigations (FDA, 21 CFR 211.188).

FDA's 21 CFR 211.192 requires all drug product production and control records, including packaging and labeling records, to be reviewed and approved by the Quality Control Unit before a batch is released or distributed. It also requires unexplained discrepancies or batch/component failures to be thoroughly investigated, even if the batch has already been distributed (FDA, 21 CFR 211.192).

That means AI can assist review, but it cannot remove the Quality Unit's responsibility. A company must still demonstrate:

- Required records exist
- Records are complete
- Exceptions are identified
- Discrepancies are investigated
- Product impact is assessed
- Batch disposition is justified
- Quality Unit approval occurs before release

AI may help make this review more efficient, but it does not weaken the regulatory obligation.

Data Integrity and Audit Trail Implications

Batch record review by exception becomes more complex when records are electronic. FDA Part 11 establishes requirements for electronic records and electronic signatures, including controls intended to ensure records are trustworthy and reliable (FDA, 21 CFR Part 11).

FDA's data integrity guidance also emphasizes that CGMP records must be complete and accurate, and the guidance is specifically focused on data integrity and compliance with drug CGMP (FDA, 2018).

Data Integrity Question	Why It Matters

What source data did AI review?	QA must know whether EBR, LIMS, SCADA, QMS, and audit trails were included
Was source data complete?	Missing historian or LIMS data could hide exceptions
Was the AI output retained?	Batch review rationale must be reconstructable
Were AI flags accepted or rejected?	Human review decisions should be documented
Was the model version controlled?	Different model versions may flag different exceptions
Were audit trail events reviewed?	AI should not replace required audit trail review strategy
Can inspectors see the evidence?	Inspection readiness requires traceability

A strong AI review system should preserve original records, AI-generated findings, human reviewer decisions, and final batch disposition rationale.

EMA and EU GMP Considerations

EU GMP Annex 11 applies to computerized systems used as part of GMP-regulated activities. It was revised in response to increased use and complexity of computerized systems (European Commission, Annex 11). If an AI-enabled EBR or review-by-exception tool is part of GMP batch review, Annex 11 expectations around validation, control, access, data integrity, and system lifecycle should be considered.

EMA's reflection paper on AI states that AI/ML tools can support acquisition, transformation, analysis, and interpretation of data when developed and used correctly. It also emphasizes a risk-based approach for development, deployment, and performance monitoring, and states that risk depends not only on the technology and data quality, but also on context of use and the degree of influence the AI exerts (EMA, 2024).

AI Use	**Regulatory Risk**
AI highlights possible exceptions for QA review	Moderate, if controlled and validated
AI prioritizes review workload	Moderate, depending on impact
AI drafts batch review summary	Moderate to high, if used in release documentation
AI determines whether a deviation is needed	High
AI recommends batch release	Very high
AI automatically releases batch	Not appropriate under current GMP expectations

The closer AI gets to batch disposition, the stronger the validation, governance, and human oversight requirements must be.

Validation Requirements for AI Batch Review

An AI-assisted batch review system should be validated according to intended use and risk.

Validation Element	**Practical Question**
Intended use	Is AI advisory, prioritizing, summarizing, or decision-making?
Data inputs	Which systems feed the model: MES, LIMS, QMS, SCADA, CMMS?
Data mapping	Are batch IDs, equipment IDs, material lots, and timestamps correctly linked?

Exception rules	Are rule-based exceptions scientifically justified and tested?
AI anomaly detection	Can the model detect known historical anomalies?
False negatives	Could AI miss a critical exception?
False positives	Could excessive alerts create review fatigue?
Audit trail	Are AI outputs and human decisions retained?
Model version control	Are model/configuration updates controlled?
Access control	Can only authorized personnel approve batch review?
Electronic signatures	Are signatures compliant with applicable requirements?
Periodic review	Is performance monitored after deployment?

The validation approach should be proportional. An AI tool used only for optional dashboard visualization is lower risk than an AI tool that determines review status or generates batch disposition recommendations.

Risk Assessment Table

AI Batch Review Use Case	GMP Risk	Potential Impact	Required Control
AI flags missing entries	False negative misses incomplete record	Batch released with incomplete documentation	Rule validation and QA review
AI detects process anomaly	False positive creates unnecessary investigation	Release delay and investigation burden	SME triage and alert thresholds
AI ranks batches by review priority	High-risk batch incorrectly ranked low	QA attention misallocated	Conservative ranking rules and reviewer override
AI reviews audit trail patterns	Important audit trail event missed	Data integrity issue overlooked	Defined audit trail review strategy
AI drafts batch release summary	Summary omits key exception	Misleading disposition rationale	Human verification against source records
AI links deviations to batch	Incorrect linkage	Wrong product impact assessment	Validated data mapping
AI predicts batch quality risk	Overreliance on prediction	Incorrect release confidence	Advisory-only use and QA approval
AI recommends release	AI conclusion accepted without review	Serious GMP compliance risk	Do not allow autonomous release

The safest model is AI-assisted review, not AI batch disposition.

Practical AI-Assisted Batch Review Workflow

```
Batch executed in MES/EBR
        ↓
Data captured from EBR, LIMS, SCADA, QMS, and related systems
        ↓
System applies predefined exception rules
        ↓
AI performs anomaly detection and pattern comparison
        ↓
Exception dashboard generated
        ↓
Manufacturing resolves operational/documentation exceptions
        ↓
```

```
QA reviews critical records, exceptions, deviations, audit trails, and AI findings
        ↓
QA accepts/rejects AI findings with rationale
        ↓
Any discrepancy is investigated under approved procedure
        ↓
Quality Unit approves or rejects batch release
        ↓
AI model performance reviewed periodically
```

This workflow keeps the Quality Unit in control while making the review process more targeted.

Future Adoption Barriers

AI batch review by exception sounds attractive, but adoption will not be easy.

Barrier	Explanation
Paper batch records	AI needs structured electronic data to perform well
Hybrid systems	Data spread across paper, EBR, LIMS, QMS, and spreadsheets
Poor master data	Inconsistent equipment, material, and batch identifiers
Weak exception definitions	System cannot flag risk if rules are poorly designed
Validation burden	AI tools require intended-use-based validation
Regulatory uncertainty	Companies may hesitate to use AI near batch release
Data integrity concerns	AI outputs must be traceable and reviewable
Cultural resistance	QA may not trust automated review support
Vendor black boxes	Explainability and documentation may be limited
Alert fatigue	Too many AI findings can slow review instead of improving it

The best path is gradual adoption: start with advisory exception dashboards and anomaly detection, not AI release recommendations.

FAQ: AI for Batch Record Review by Exception

Can AI release pharmaceutical batches?

No. AI should not independently release pharmaceutical batches. FDA requires production and control records to be reviewed and approved by the Quality Control Unit before release or distribution (FDA, 21 CFR 211.192). AI can support review, but the Quality Unit must retain batch disposition authority.

What is review by exception?

Review by exception means focusing QA review on exceptions, discrepancies, missing data, deviations, parameter excursions, audit trail concerns, and unusual patterns rather than manually reviewing every routine compliant entry with the same intensity.

Is review by exception allowed in GMP?

Review by exception can be used when the system is validated, records remain complete, exceptions are properly defined, discrepancies are investigated, and the Quality Unit still reviews and approves

the batch before release. The company must be able to demonstrate control and compliance with applicable GMP requirements.

What is the best first AI use case for batch review?

The best first use case is AI-assisted anomaly detection or exception prioritization in an electronic batch record environment. AI can flag unusual patterns for QA review without making release decisions.

Does Part 11 apply to AI batch review?

Part 11 may apply if the system creates, modifies, maintains, retrieves, or transmits electronic records required under FDA regulations, or uses electronic signatures. AI-enabled EBR workflows should be assessed for Part 11 applicability and validated accordingly (FDA, 21 CFR Part 11).

What is the biggest risk?

The biggest risk is overreliance. If QA assumes “no AI exception” means “no problem,” critical issues may be missed. Traditional GMP review responsibilities and human judgment must remain active.

Can AI help with audit trail review?

Yes, AI can help identify unusual audit trail patterns, late entries, repeated corrections, or unexpected changes. However, the company still needs a defined audit trail review strategy and human review for GMP significance.

Conclusion: AI Can Improve Batch Review, but Batch Release Must Remain a Human GMP Decision

AI for batch record review by exception is one of the most practical and high-impact applications of artificial intelligence in pharmaceutical quality operations. Batch review is repetitive, data-heavy, time-sensitive, and vulnerable to reviewer fatigue. AI can help identify exceptions, detect unusual process patterns, prioritize review workload, and connect batch records with process monitoring, deviations, audit trails, and equipment data.

But AI does not replace the Quality Unit. FDA requires complete batch production and control records and Quality Unit review and approval before release or distribution (FDA, 21 CFR 211.188; FDA, 21 CFR 211.192). EMA’s AI reflection paper also reinforces that AI risk depends on context of use and the degree of influence the system exerts (EMA, 2024).

The realistic future is not autonomous batch release. The realistic future is smarter QA review: fewer hours spent checking routine compliant entries, more attention on exceptions that actually matter, and stronger traceability for batch disposition decisions.

For AIforQA.org, this is a strong cornerstone topic because it addresses a major operational pain point in pharmaceutical QA: how to release batches faster without lowering the standard of GMP review.

References

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