

# How AI Could Transform GMP Document Review and Approval Workflows

*A Practical Pharmaceutical QA Perspective on AI-Assisted SOP Review, Document Consistency, and Approval Bottlenecks*

GMP document review is one of the most important quality assurance activities in pharmaceutical manufacturing, but it is also one of the most repetitive, delayed, and error-prone workflows in the quality system. SOPs, forms, batch records, validation protocols, reports, specifications, work instructions, logbooks, and policies all require careful review before approval. Each document must be technically accurate, aligned with current procedures, compliant with GMP expectations, properly version-controlled, and understandable to the people who will use it.

That is a lot to ask from human reviewers who may already be overloaded with deviations, CAPAs, change controls, audits, batch release, APR/PQR work, training, and inspection readiness.

Artificial intelligence could help transform GMP document review by acting as a structured review assistant. AI can support cross-reference checks, consistency review, duplicate content detection, regulatory reference verification, review comment generation, and comparison against similar procedures. But AI should not approve GMP documents independently. The final responsibility must remain with qualified human reviewers, document owners, subject matter experts, and the Quality Unit.

FDA requires written production and process control procedures to be drafted, reviewed, and approved by appropriate organizational units and reviewed and approved by the Quality Control Unit; it also requires those procedures to be followed and deviations recorded and justified (FDA, 21 CFR 211.100).

That regulatory expectation creates the foundation for any AI-assisted document workflow: AI may help reviewers work better, but it cannot replace formal GMP review and approval.

## Why GMP Document Review Is So Difficult

In theory, GMP document review sounds straightforward: read the document, verify accuracy, add comments, route for approval, train users, and implement the effective version. In practice, document review is difficult because controlled documents are connected to almost every part of the pharmaceutical quality system.

A single SOP may affect:

Document Element	Possible GMP Dependency
Equipment names or IDs	Qualification, calibration, PM, asset database

Room numbers	Cleaning procedures, EM plans, pressure cascade, area classification
Material names	Specifications, suppliers, incoming testing, batch records
Process steps	Validation, batch record execution, training, deviations
Acceptance criteria	Specifications, methods, regulatory filings, APR/PQR trends
Forms	Data integrity, record retention, review expectations
Roles/responsibilities	Training, job descriptions, access permissions
References	Other SOPs, regulations, guidance, validation reports
Effective date	Training completion, superseded version control

This is why SOP review bottlenecks are so common. A reviewer is not only checking grammar. They are checking whether the procedure remains technically correct, GMP-compliant, and aligned with the broader quality system.

## Common Problems in Traditional GMP Document Review

Traditional GMP document review is heavily dependent on manual attention. That creates predictable weaknesses.

Review Challenge	Practical Impact
Reviewer fatigue	Important details may be missed after repeated review cycles
Approval bottlenecks	SOPs sit in routing for weeks while operations wait
Cross-reference errors	SOP refers to obsolete document numbers, forms, or sections
Conflicting instructions	Two procedures describe the same activity differently
Version control gaps	Users may follow outdated instructions or forms
Regulatory reference errors	Document cites outdated or incorrect regulation/guidance
Over-commenting	Review cycles become inefficient and unfocused
Under-commenting	Critical technical or GMP issues remain unresolved
Inconsistent review standards	Different reviewers apply different expectations
Poor readability	Technically correct SOPs remain hard for operators to follow

These issues are not only administrative problems. Poor document control can lead to deviations, training failures, audit findings, batch record errors, data integrity issues, and inspection observations.

## Where AI Fits in GMP Document Review

AI is best used as a review support layer, not an approval authority.

A useful AI document review system could help answer:

- Does this SOP conflict with other approved procedures?
- Are all referenced SOPs, forms, attachments, and sections still current?

- Are defined terms used consistently?
- Are responsibilities clearly assigned?
- Are acceptance criteria consistent with specifications or validation documents?
- Are revision reasons aligned with the actual document changes?
- Does the procedure contain ambiguous instructions?
- Does the document contain uncontrolled language such as “as needed,” “if required,” or “usually” without defined criteria?
- Are regulatory references current and applicable?
- Does the procedure contain missing steps based on similar procedures?

EMA’s AI reflection paper notes that AI/ML tools can support acquisition, transformation, analysis, and interpretation of data when developed and used correctly, while emphasizing risk-based development, deployment, and performance monitoring (EMA, 2024). That principle applies well to GMP document review: AI can support interpretation and review, but the risk depends on how much influence the AI output has over the final decision.

## AI-Assisted Document Consistency Checks

One of the most valuable AI use cases is consistency checking.

For example, AI could compare a revised SOP against related approved documents and flag inconsistencies such as:

AI-Detected Issue	Example
Conflicting frequency	SOP A says clean weekly; SOP B says clean monthly
Obsolete reference	SOP cites Form F-002 Rev. 03, but current version is Rev. 05
Inconsistent equipment ID	Procedure uses old equipment number no longer active
Terminology mismatch	“Critical alarm” and “major alarm” used interchangeably
Missing definition	New term introduced without definition
Inconsistent role	Task assigned to QA in one SOP and Production in another
Different acceptance criteria	Validation report says <=10 ppm residue; SOP says <=20 ppm
Training mismatch	SOP revision changes task, but training impact says “No retraining required”

This kind of AI support would be especially useful in large pharmaceutical sites where documents have been revised for years by different authors, departments, and reviewers.

## Detection of Conflicting Instructions

Conflicting instructions are one of the most dangerous document control problems because each individual SOP may look acceptable in isolation.

Example:

SOP-001 says operators must sanitize gloves before every intervention. SOP-002 says operators must sanitize gloves before critical interventions. A training slide deck says operators must sanitize gloves every 15 minutes. A batch record instruction says “sanitize gloves as needed.”

A human reviewer may only see one document during routing. AI can compare instructions across the document ecosystem and flag the conflict for QA review.

This is not only a formatting issue. In sterile manufacturing, laboratory testing, cleaning, calibration, or batch record execution, conflicting instructions can directly create inconsistent behavior.

## Cross-Reference Verification

Cross-reference verification is another high-value AI use case.

AI could automatically check whether:

- Referenced SOP numbers exist
- Referenced forms are current
- Section numbers are still valid
- Attachment names match the document control system
- External standards are still active
- Validation reports cited in the SOP are approved
- Obsolete forms are not embedded in the procedure
- Hyperlinks point to controlled locations
- Document titles match the document master list

This would reduce a common source of document review frustration: the endless back-and-forth over references, attachments, and minor version issues.

In electronic systems, these references may also become regulated electronic records. Part 11 applies to electronic records created, modified, maintained, archived, retrieved, or transmitted under FDA records requirements, and it sets criteria for electronic records and signatures to be considered trustworthy and reliable (FDA, 21 CFR Part 11). If AI assists with controlled document records, the system must support traceability, validation, and inspection readiness.

## AI-Generated Review Comments

AI could also generate draft review comments for human reviewers.

Document Text	AI-Suggested Comment
“Clean the equipment as needed.”	Define specific cleaning trigger or frequency. “As needed” may be ambiguous.
“QA may review the form.”	Clarify whether QA review is required or optional.
“Use the current form.”	Identify form number and revision control expectation.
“Record the result.”	Specify where the result is recorded and whether second-person verification is required.
“Notify management.”	Define role, timing, and documentation method for

	notification.
“Repeat the test if necessary.”	Define criteria for repeat testing and investigation requirements.

This could help junior reviewers learn what good GMP comments look like. It could also improve consistency across reviewers.

However, AI-generated comments carry risks. The AI may over-comment, misunderstand the process, apply generic logic, or recommend changes that conflict with validated processes. For that reason, AI comments should be treated as draft suggestions only.

## Regulatory Reference Verification

Many SOPs include references to regulations, guidance documents, pharmacopeial chapters, internal policies, or industry standards. These references often become outdated.

AI could help identify:

- Incorrect CFR references
- Retired guidance documents
- Superseded internal policies
- Missing Annex 1 references for sterile manufacturing procedures
- Incorrect Part 11 language in electronic record procedures
- References that do not support the requirement stated in the SOP
- Regulatory references copied from old templates but no longer applicable

For example, if a procedure governs electronic signatures in a document management system, AI could flag that Part 11 controls may be relevant because Part 11 applies to electronic records and electronic signatures under FDA records requirements. The AI should not decide the regulatory strategy, but it can prompt the reviewer to confirm that the right regulation is considered.

## Human Reviewer Fatigue and Approval Bottlenecks

One of the biggest practical benefits of AI is reducing reviewer fatigue.

A QA reviewer may receive a 40-page SOP revision after a long day of deviation review, meetings, batch release pressure, and urgent production questions. The reviewer is expected to catch technical errors, GMP gaps, cross-reference errors, formatting inconsistencies, missing definitions, training impact, data integrity concerns, regulatory issues, incorrect responsibilities, and version control problems.

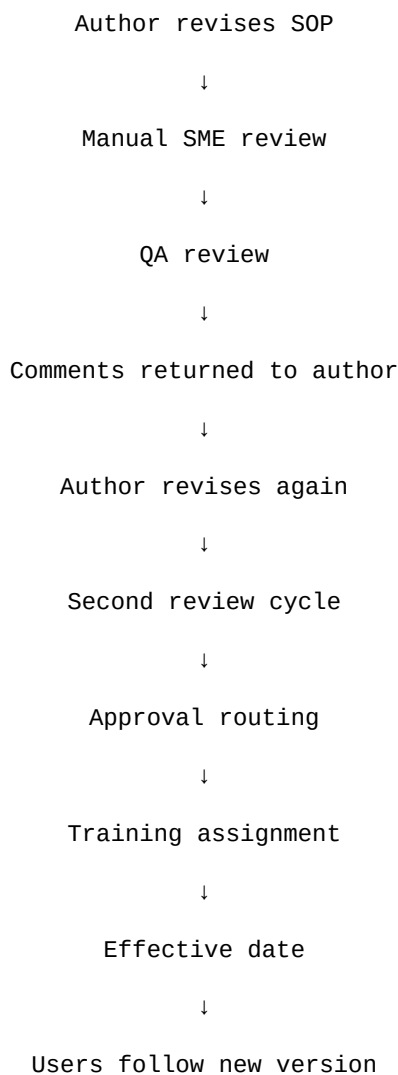
AI can pre-screen the document and highlight likely issues before the human review starts. That does not make the review effortless, but it makes it more targeted.

Instead of reading blindly, the reviewer receives a structured review package:

- Summary of major changes
- List of impacted documents
- Cross-reference check results
- Conflicting instruction alerts
- Ambiguous wording highlights
- Possible training impact
- Possible validation or Part 11 impact
- Suggested review comments
- Source links for every AI finding

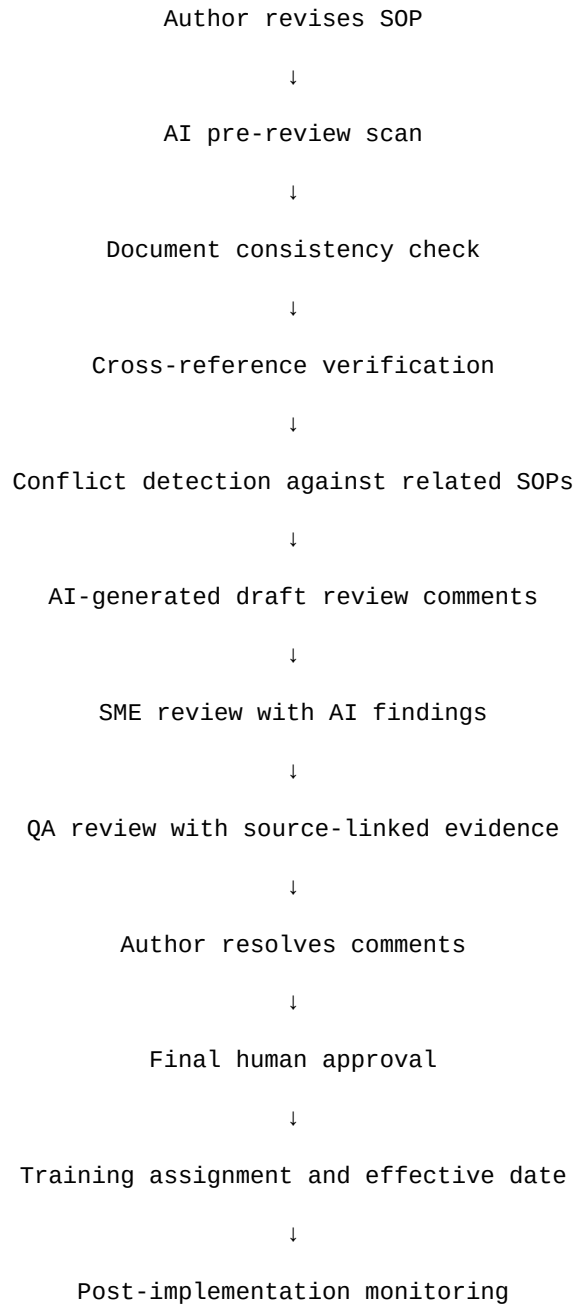
That is a much better starting point than a blank review screen.

## Workflow Diagram: Traditional SOP Review



Traditional workflows often become slow because problems are detected late. A cross-reference issue may not be found until QA review. A training impact may not be recognized until approval. A conflicting instruction may not be noticed until a deviation occurs.

## Workflow Diagram: AI-Assisted GMP Document Review



The key difference is that AI moves issue detection earlier in the workflow.

## Real-World GMP Review Scenarios

### Scenario 1: SOP Revision Conflicts With a Batch Record

A manufacturing SOP is revised to change the mixing hold time from “not more than 2 hours” to “not more than 4 hours.” The author believes this is acceptable based on recent process experience.

AI compares the SOP against the master batch record, process validation report, and regulatory commitment summary. It identifies that the batch record and validation report still state a 2-hour maximum hold time.

The change is routed to validation and regulatory affairs before approval.

GMP value: AI prevents an SOP from being approved with instructions that conflict with validated process controls.

### Scenario 2: Cleaning SOP Has Ambiguous Language

A cleaning SOP states, “Visually inspect the equipment and repeat cleaning if necessary.”

AI flags “if necessary” as ambiguous and suggests defining acceptance criteria for visual inspection, documentation requirements, and escalation if residue is observed.

QA agrees and asks the author to clarify visual inspection criteria.

GMP value: AI improves procedural clarity and reduces inconsistent operator decisions.

### Scenario 3: Obsolete Form Reference

A calibration SOP references a legacy calibration form that was replaced six months earlier.

AI checks the document master list and flags the obsolete form reference. The author updates the SOP before approval.

GMP value: AI prevents a version control issue from reaching implementation.

### Scenario 4: AI Generates an Incorrect Review Comment

An AI tool flags a sterile gowning SOP and recommends removing a redundant glove sanitization step because it appears repetitive.

The microbiology reviewer rejects the suggestion because the repeated sanitization step is intentional and risk-based.

GMP lesson: AI may identify apparent inefficiency without understanding contamination control rationale. Human expertise must remain final.

## Risk Analysis for AI in GMP Document Review

AI Use Case	Potential Risk	GMP Impact	Required Control
Cross-reference checking	AI misses obsolete reference	Wrong form or SOP used	Human verification and document master list integration
Consistency checking	AI flags false conflict	Unnecessary review burden	SME triage and relevance assessment
AI review comments	AI recommends technically wrong change	Procedure becomes inaccurate	Human approval required before comment acceptance
Regulatory reference	AI cites wrong or outdated	Misleading compliance	Regulatory/QA verification

check	guidance	rationale	
SOP summary generation	AI oversimplifies critical steps	Users misunderstand procedure	Summary cannot replace controlled SOP
Version comparison	AI misses meaningful change	Training or validation impact missed	Change owner and QA review remain required
Workflow routing	AI sends document to wrong reviewers	Missing SME review	Predefined routing rules and QA oversight
AI model update	Review output behavior changes	Validated state may be affected	Change control and revalidation assessment

The most important control is simple: AI findings must be reviewable, traceable, and rejectable by humans.

## Validation and Part 11 Considerations

If AI is embedded in a GMP electronic document management system, the system may fall under computerized system validation and Part 11 expectations.

Part 11 requires that electronic records and electronic signatures be trustworthy, reliable, and generally equivalent to paper records and handwritten signatures (FDA, 21 CFR Part 11). It also states that computer systems, controls, and documentation maintained under Part 11 must be available for FDA inspection.

For an AI-assisted document review system, validation should consider:

Validation Element	Practical Question
Intended use	Is AI advisory only, or does it affect approval routing or release?
Source data	Does AI search only controlled, approved, and current documents?
Traceability	Can reviewers see why AI made a recommendation?
Audit trail	Are AI outputs, human decisions, and overrides recorded?
Access control	Can only authorized users approve documents?
Electronic signatures	Are approvals linked to users, meaning, date, and record?
Model version	Is the AI model or configuration version controlled?
Testing	Can the system detect known cross-reference and consistency issues?
Change control	Are AI model updates assessed before implementation?
Periodic review	Is AI performance reviewed over time?

The higher the AI's influence, the greater the validation burden. An AI tool that only highlights possible wording issues is lower risk than an AI tool that automatically routes approval, determines training impact, or blocks document release.

EMA's reflection paper emphasizes that risk depends not only on the AI technology and data quality, but also on context of use and the degree of influence the AI exerts. It also states that manufacturers using AI/ML technology are expected to manage relevant risks from early development to

decommissioning and ensure algorithms, models, datasets, and processing pipelines are fit for purpose and aligned with GxP standards (EMA, 2024).

## Data Integrity Concerns

AI-assisted document review creates new data integrity questions.

A compliant workflow should be able to reconstruct:

- Which document version was reviewed
- Which AI tool and model version were used
- Which source documents were searched
- What findings AI generated
- Which findings were accepted, rejected, or modified
- Who made each decision
- When each decision was made
- What final document was approved
- Which training was assigned
- When the document became effective

This matters because AI output can influence the review record. If a reviewer accepts an AI-generated comment or relies on AI to confirm that no conflicting procedures exist, the system should retain enough evidence to support that decision during inspection.

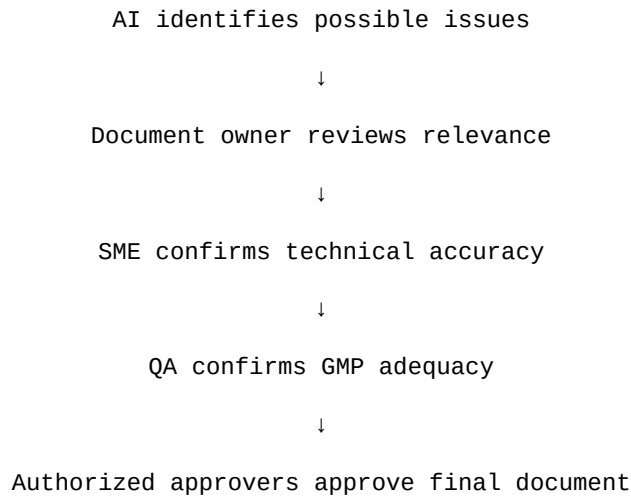
## AI Governance Requirements for Document Review

Governance Area	Requirement
Intended use	Define what AI may and may not do
Human approval	AI cannot approve GMP documents independently
Source control	AI should distinguish approved, obsolete, draft, and archived documents
Traceability	AI findings should link to source documents and sections
Model control	AI model/configuration changes require assessment
Role-based permissions	AI should not expose documents to unauthorized users
Review standards	AI comments should align with approved company SOP standards
Escalation	High-risk findings route to QA, validation, regulatory, or SME review
Periodic review	Performance, false positives, and missed findings should be evaluated
Supplier oversight	Vendor controls, cybersecurity, validation support, and data handling must be assessed

AI governance should be written into procedures. Otherwise, AI becomes an informal reviewer operating outside the quality system.

## Human Oversight Requirements

The safest operating model is:



AI should never become the final reviewer. Human oversight is especially important for sterile manufacturing procedures, cleaning procedures, batch records, critical utilities, validation protocols and reports, analytical methods, specifications, regulatory commitments, data integrity procedures, and Part 11 and computerized system procedures.

## Implementation Roadmap

### Step 1: Start With Low-Risk Review Support

Begin with AI-assisted formatting, cross-reference checks, and consistency checks. Avoid automated approval decisions.

### Step 2: Build a Controlled Document Knowledge Base

Connect AI to approved SOPs, forms, policies, validation documents, training matrices, and document metadata. Clearly separate approved, draft, obsolete, and archived content.

### Step 3: Define Review Rules

Create standard AI checks for cross-references, form numbers, revision history alignment, ambiguous language, responsibilities, training impact, regulatory references, conflicting instructions, data integrity wording, and validation impact.

### Step 4: Validate the Tool

Test the AI against known historical document issues. Confirm it can detect obsolete references, conflicting wording, missing definitions, and incorrect form numbers.

### Step 5: Pilot With Selected SOP Types

Start with moderate-risk SOPs before applying AI to sterile manufacturing, batch records, validation, or release-critical documents.

## **Step 6: Require Source-Linked Output**

AI should not simply say, “Conflict found.” It should show the source document, section, and text that triggered the finding.

## **Step 7: Train Reviewers**

Train QA, document control, SMEs, and authors on what AI can do, what it cannot do, and how to document acceptance or rejection of AI suggestions.

## **Step 8: Monitor Performance**

Track number of findings generated, accepted vs rejected AI comments, missed issues discovered later, review cycle time, post-approval corrections, deviations linked to document errors, and user feedback.

## **Step 9: Expand Gradually**

Only expand to high-risk documents after the system demonstrates value, control, and acceptable performance.

## **FAQ: AI in GMP Document Review**

### **Can AI approve GMP documents?**

No. AI should not independently approve GMP documents. FDA requires appropriate organizational units and the Quality Control Unit to review and approve written procedures and changes (FDA, 21 CFR 211.100). AI can support review, but approval must remain with authorized human personnel.

### **Is AI useful for SOP review?**

Yes. AI is useful for cross-reference checks, consistency checks, conflict detection, review comment drafting, regulatory reference checks, and comparison against related procedures. It is especially helpful when documents are long, interconnected, and frequently revised.

### **Can AI replace QA reviewers?**

No. AI cannot understand full GMP context, product risk, site history, contamination control rationale, validation strategy, or regulatory commitments the way qualified humans can. AI should reduce reviewer burden, not replace QA.

### **Does AI-generated review output need to be retained?**

If AI output influences a GMP document review, the organization should retain enough evidence to reconstruct the decision. That includes the reviewed document version, AI findings, source references, human decisions, and approval history.

### **Does Part 11 apply to AI-assisted document review?**

Part 11 may apply if the system creates, modifies, maintains, archives, retrieves, or transmits electronic records required under FDA regulations, or uses electronic signatures. Part 11 sets criteria for electronic records and signatures to be trustworthy, reliable, and generally equivalent to paper records and handwritten signatures.

## What is the best first use case?

The best first use case is AI-assisted cross-reference and consistency checking. It provides clear value, is relatively easy to verify, and avoids letting AI make final GMP decisions.

## What is the biggest risk?

The biggest risk is overreliance. AI may generate confident but incorrect suggestions. A reviewer may accept the suggestion without understanding the process context. That is why human review, traceability, and governance are essential.

## Conclusion: AI Can Improve GMP Document Review, but It Must Stay Under Quality Control

AI could significantly improve GMP document review and approval workflows by reducing reviewer fatigue, identifying cross-reference errors, detecting conflicting instructions, improving consistency, and helping reviewers focus on higher-risk issues.

The strongest use case is not automatic SOP approval. It is smarter pre-review.

AI can scan documents faster than humans, compare procedures across large document libraries, and generate useful review prompts. But GMP document approval remains a regulated quality activity. FDA requires written procedures and changes to be reviewed and approved by appropriate organizational units and the Quality Control Unit (FDA, 21 CFR 211.100). Part 11 requirements may apply when electronic records and electronic signatures are used in GMP documentation workflows.

The realistic future is not AI replacing QA documentation review. The realistic future is AI helping QA reviewers catch more issues earlier, reduce approval bottlenecks, and make document workflows more consistent and inspection-ready.

For AIforQA.org, this is a strong cornerstone article because it targets a real pain point in pharmaceutical QA: documents are not just paperwork - they are the instructions that control GMP behavior. If AI can help make those instructions clearer, more consistent, and better reviewed, it can provide real quality value.

## References

1. **FDA. 21 CFR 211.100 - Written Procedures; Deviations.** Requires written production and process control procedures, including changes, to be drafted, reviewed, and approved by appropriate organizational units and reviewed and approved by the Quality Control Unit. It also requires procedures to be followed and deviations to be documented and justified.  
<https://www.ecfr.gov/current/title-21/chapter-I/subchapter-C/part-211/subpart-F/section-211.100>
2. **FDA. 21 CFR Part 11 - Electronic Records; Electronic Signatures.** Defines criteria under which electronic records and electronic signatures are considered trustworthy, reliable, and generally equivalent to paper records and handwritten signatures. It applies to electronic records created,

modified, maintained, archived, retrieved, or transmitted under FDA records requirements.

<https://www.ecfr.gov/current/title-21/chapter-I/subchapter-A/part-11>

3. **European Medicines Agency. Reflection Paper on the Use of Artificial Intelligence in the Medicinal Product Lifecycle.** Discusses AI/ML use across the medicinal product lifecycle, including risk-based development, deployment, performance monitoring, data integrity, governance, and manufacturer responsibility for algorithms, models, datasets, and data pipelines. [https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-use-artificial-intelligence-ai-medicinal-product-lifecycle\\_en.pdf](https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-use-artificial-intelligence-ai-medicinal-product-lifecycle_en.pdf)
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5. **PIC/S. PIC/S GMP Guide Part I.** Provides internationally harmonized GMP expectations for pharmaceutical quality systems, documentation, production, quality control, outsourced activities, complaints, recalls, deviations, self-inspection, and related GMP procedures. <https://picscheme.org/docview/6606>