PRACTICAL GMP TOOL

OOS Investigation Decision Guide & Workbook

Preserve the evidence. Test hypotheses scientifically. Reach a conclusion that can support the batch decision.

USE THIS WORKBOOK TO

01	02	03	04
Secure original data and preparations	Conduct the immediate laboratory assessment	Pre-authorise hypothesis tests and retesting	Connect the conclusion to batch impact

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DECISION GUIDE

The controlled route from result to conclusion

An OOS result is a result outside an established specification or acceptance criterion. Treat the original result as valid unless a scientifically demonstrated cause supports invalidation. A later passing result does not erase the original result.

Decision point	If yes	If no / not demonstrated
Is the result genuinely outside the applicable specification?	Register the OOS and preserve evidence.	Correct a verified transcription or specification-selection issue transparently.
Did the immediate assessment demonstrate a specific laboratory cause?	Document and, where appropriate, test the hypothesis before invalidating.	Expand the investigation beyond the laboratory.
Is additional testing scientifically justified?	Use a pre-approved protocol defining purpose, number of tests and evaluation logic.	Do not test merely to obtain a passing result.
Does the evidence invalidate the original result?	Retain all data and evaluate valid replacement results according to procedure.	The original OOS remains relevant to batch evaluation.
Could other batches, products or systems be affected?	Expand scope and assess common materials, equipment, methods, people and time periods.	Document the evidence supporting a limited scope.

STOP RULE	Do not discard preparations, delete injections, overwrite audit trails, average the OOS with passing results, or begin repeated testing without an approved scientific purpose.

Suggested stage gates

Gate 1: evidence secured and immediate assessment authorised. Gate 2: laboratory phase conclusion approved. Gate 3: any additional testing protocol approved. Gate 4: manufacturing and scope review complete. Gate 5: Quality approves the final conclusion and disposition.

SECTION 1

OOS intake and evidence preservation

OOS reference / date and time detected

Product / material / batch / sample / test

Specification, acceptance criterion and observed result

Immediate preservation check	Yes / No / N/A	Evidence / location
Original electronic and paper raw data protected		
Sample, preparations, standards and reagents retained where stable		
Chromatograms, spectra, calculations and audit trails retained		
Instrument, sequence and equipment state documented		
Potentially affected batches or operations identified		
Quality and responsible supervisor notified		

Immediate containment and business continuity actions
Do not prejudge the batch decision. Record any hold, segregation, notification or pause in testing.

SECTION 2

Immediate laboratory assessment

Reconstruct what was done and what was observed. Interview the analyst promptly and review original evidence rather than relying on recollection alone.

Assessment area	Questions and evidence	Finding / reference
Method and calculation	Approved version, steps, times, temperatures, dilutions, units, formulas and specification.	
Sample and preparation	Identity, sampling, storage, homogeneity, weighing, extraction, filtration, stability and hold time.	
Standards and reagents	Identity, potency, preparation, expiry, storage, traceability and suitability.	
Equipment and system	Calibration, maintenance, alarms, suitability, sequence, audit trail, integrations and configuration.	
Environment and execution	Conditions, interruptions, observations, technique and departures from the method.	
Complete data set	All injections, repeats, aborted runs, calculations, metadata and unofficial records considered.	

Analyst account - factual observations at the time

Supervisor conclusion and next gate
Specific laboratory hypothesis demonstrated / hypothesis requires testing / no assignable laboratory cause.

SECTION 3

Hypothesis-testing protocol

PURPOSE	Additional laboratory work should test a stated hypothesis. A passing answer alone does not demonstrate the hypothesis.

Observed evidence supporting the suspected cause

Specific hypothesis
Example: incomplete extraction caused low recovery in the original preparation.

Predicted observation if the hypothesis is correct

Controlled experimental plan
Define retained preparation or sample, variables, controls, analyst, equipment and sequence.

Predefined interpretation logic
State what result would support, contradict or leave the hypothesis unresolved.

Approval before execution	Name / role	Signature / date
Laboratory supervisor		
Quality approval		

SECTION 4

Retesting and resampling authorisation

Retesting uses another portion of the original homogeneous sample. Resampling obtains a new sample from the batch. They answer different questions and must not be used interchangeably.

Control question	Retest	Resample
What question is being answered?	Repeat measurement or preparation from the original sample under an approved plan.	Whether the original sample was unrepresentative or a defined sampling issue exists.
Required justification	Scientific basis, predefined number of tests and evaluation of all results.	Evidence of sampling error or a justified need to assess batch representation.
What it cannot do	It cannot erase the original OOS merely because later tests pass.	It cannot substitute a fresh sample simply to obtain a passing result.

Purpose and scientific justification

Number of tests / sample locations / analysts

Method for evaluating all individual results
Do not average an OOS with passing results when individual results must meet the specification.

Stopping and escalation rules

Authorisation	Name / role	Signature / date
Laboratory supervisor		
Quality approval		

SECTION 5

Expanded manufacturing and scope investigation

When a clear laboratory cause is not demonstrated, assess whether the result reflects the process, material, product, sampling or a wider quality-system issue.

Evidence stream	Reviewed evidence and finding	Impact / reference
Manufacturing and packaging	Parameters, alarms, yields, holds, interventions, deviations and operator observations.	
Materials and suppliers	Lots, certificates, variability, storage, dispensing and supplier changes.	
Equipment and utilities	Status, calibration, maintenance, cleaning, environment, water and support systems.	
Sampling	Plan, locations, technique, containers, transport, storage and representativeness.	
Product and batch history	Other tests, trends, stability, complaints, rejects, deviations and related batches.	
Method and process capability	Suitability, variability, specification relationship and known failure modes.	

Scope rationale
Define products, batches, materials, equipment, methods, sites and time period included or excluded.

Potential patient, product and regulatory impact

SECTION 6

Additional-testing and evidence log

Record every result, including failures, atypical observations, aborted activity and results that contradict the working hypothesis.

Date / test / sample	Purpose and protocol reference	Result and observation	Interpretation

Deviations from the approved testing plan

Overall interpretation of the complete data set

REMINDER	Selective use of passing data creates false confidence. Explain inconsistencies and uncertainty; do not hide them.

SECTION 7

Conclusion, batch impact and follow-up

Conclusion category	Select	Evidence expectation
Confirmed laboratory error	[ ]	A specific cause is demonstrated and the original result is scientifically invalidated.
Manufacturing / product cause	[ ]	Evidence connects the result with process, material, sampling or product failure.
No assignable cause	[ ]	The investigation cannot scientifically invalidate the original OOS result.
Inconclusive	[ ]	Evidence limitations prevent a firm cause conclusion; uncertainty and risk are explicit.

Cause conclusion and supporting evidence

Disposition and batch-impact rationale
Include related batches, materials, stability, distributed product and regulatory reporting where applicable.

Corrective / preventive actions and linked references

Residual risk, trend category and effectiveness-check plan

Final approval	Name / role	Signature / date
Laboratory management		
Manufacturing / technical reviewer		
Quality Unit		

CLOSEOUT CHECK

Before the investigation is approved

Confirm	Yes / No / N/A	Reference
The original OOS and complete raw-data history are retained		
Every additional test had an approved scientific purpose		
Retesting and resampling were distinguished and justified		
All results were evaluated without selective reporting		
The investigation expanded beyond the laboratory when required		
Scope includes related batches, materials, methods and systems		
The conclusion states both what is known and what remains uncertain		
The batch decision follows the evidence and approved procedure		
CAPA, trend review and effectiveness verification are defined		

Primary references

FDA, Investigating Out-of-Specification (OOS) Test Results for Pharmaceutical Production, Level 2 Revision, May 2022.
https://www.fda.gov/media/158416/download

European Commission, EudraLex Volume 4, Chapter 6: Quality Control.
https://health.ec.europa.eu/document/download/c74c8720-27bf-4252-808f-d65a206a90bb_en

WHO, Good Practices for Pharmaceutical Quality Control Laboratories.
https://www.who.int/publications/m/item/annex-1-trs-957

EDUCATIONAL USE	This workbook does not replace approved procedures, product-specific scientific assessment, quality-unit authority or applicable regulatory requirements.