Standard Operating Procedure REF

SOP Title: Regulatory Reference Library
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Background & Source Documentation:

-- Root-Cause Analysis (RCA) Tools: "5 Whys" & Fishbone (Ishikawa) Diagram

Tool	Original Developer / First Publication	Key Reference Documents & Standards	Typical Use in cGMP / CAPA
5 Whys	• Sakichi Toyoda (founder of Toyota Industries)• Formalised inside Toyota Production System (TPS) by Taiichi Ohno, *Toyota Production System: Beyond Large-Scale Production* (English ed. 1988)	• Ohno, T. (1988). *Toyota Production System.* Productivity Press ISBN 0915299143• ISO 9001:2023 §10.2 Non-Conformity & Corrective Action (note on "root-cause analysis techniques")	• Fast, first-pass drill-down to a single root cause• Works well for "human-factor" or single-path problems
Fishbone (Ishikawa) Diagram	• Kaoru Ishikawa, quality-control professor, University of Tokyo (early 1960 s)• English exposure via Ishikawa, *Guide to Quality Control* (JUSE Press, 1976)	• Ishikawa, K. (1986). *Guide to Quality Control* (Quality Resources) ISBN 0873890293• ICH Q10 Annex I (2008): lists cause-and-effect diagrams and 5 Whys as acceptable RCA methods	• Structured brainstorming to display multiple contributing factors under "6 M" (Man, Machine, Methods, Materials, Measurement, Mother Nature)

Tool	Original Developer / First Publication	Key Reference Documents & Standards	Typical Use in cGMP / CAPA
			or similar categories• Use ful when several interacting causes exist

Why These Tools Are Accepted in cGMP / CCA CAPA Systems

1. **Regulatory Guidance**
    - **FDA** and **ICH Q10** both expect "systematic root-cause analysis" for deviations and CAPAs; they do **not** prescribe one method but cite 5 Whys and Ishikawa as recognized techniques.
    - **21 CFR 211.192** (Finished Pharmaceuticals) requires review of "any unexplained discrepancy" and "documentation of the investigation," which industry typically satisfies with an RCA worksheet.
2. **GAMP 5** & **ISO 9001:2023** highlight 5 Whys/Fishbone as suitable problem-solving tools within quality-management frameworks.
3. **Virginia CCA** (like most state cannabis regulators) defers to FDA cGMP expectations and ISO-style QMS elements for deviation handling. Using these well-documented methods demonstrates "industry-standard" diligence.

Links to referenced documents:

Area / Standard	Primary Reference (official URL or document)	Citation for SOP
FDA cGMP Regulations (Finished Pharmaceuticals)	*21 CFR Part 211 – Current Good Manufacturing Practice* – eCFR website: (eCFR)	"21 CFR 211 – Current Good Manufacturing Practice for Finished Pharmaceuticals (eCFR, U.S. FDA)."
FDA Quality-Systems Guidance	*Quality Systems Approach to Pharmaceutical CGMP Regulations* (FDA Guidance,	"FDA Guidance: Quality Systems Approach to Pharmaceutical CGMP Regulations."

Area / Standard	Primary Reference (official URL or document)	Citation for SOP
	Sept 2006): (U.S. Food and Drug Administration)	
ICH Q10 Pharmaceutical Quality System	ICH Q10 Guideline PDF: (ICH Database)	"ICH Q10 Pharmaceutical Quality System, Step 4 (2008)."
21 CFR Parts 210 & 211 Overview	FDA cGMP portal (aggregated parts 210 / 211 / 212): (U.S. Food and Drug Administration)	"FDA CGMP Regulations Portal – Parts 210, 211, 212."
ISO 9001 Quality Management	ISO 9001:2015 Standard page: (ISO)	"ISO 9001:2015 — Quality Management Systems — Requirements."
ISO Quality Principles	ISO Quality Management Principles PDF: (ISO)	"ISO Quality Management Principles (ISO pub 100080)."
GAMP 5 (Good Automated Manufacturing Practice)	ISPE GAMP 5 Guide 2nd Ed summary page: (ISPE)	"ISPE GAMP 5 Guide, 2 nd Edition (2022)."
GAMP Records & Data Integrity	ISPE GAMP Guide – Records & Data Integrity: (ISPE)	"ISPE GAMP Guide: Records & Data Integrity (2021)."
Virginia CCA Regulations (Statutory Authority)	VA Code — Cannabis Control Authority board powers: (Virginia Law)	"Virginia Cannabis Control Authority enabling statute (Va. Code)."
Virginia CCA Official Website / Policy Docs	Cannabis Control Authority homepage: (Virginia Cannabis Control Authority)	"Virginia Cannabis Control Authority, official resources."

Version	Date	Change Description	Approved By
		Aligned with updated Quality Manual QM-VA-001	[Name / Title]

and Master Batch
Record SOP.