Standard Operating Procedure REF

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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** |
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| **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) or similar categories• Useful 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** |
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| **FDA cGMP Regulations** (Finished Pharmaceuticals) | *21 CFR Part 211 – Current Good Manufacturing Practice* – eCFR website: ([eCFR](https://www.ecfr.gov/current/title-21/chapter-I/subchapter-C/part-211?utm_source=chatgpt.com" \o "21 CFR Part 211 -- Current Good Manufacturing Practice for ... - 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, Sept 2006): ([U.S. Food and Drug Administration](https://www.fda.gov/regulatory-information/search-fda-guidance-documents/quality-systems-approach-pharmaceutical-current-good-manufacturing-practice-regulations?utm_source=chatgpt.com)) | “FDA Guidance: Quality Systems Approach to Pharmaceutical CGMP Regulations.” |
| **ICH Q10 Pharmaceutical Quality System** | ICH Q10 Guideline PDF: ([ICH Database](https://database.ich.org/sites/default/files/Q10%20Guideline.pdf?utm_source=chatgpt.com)) | “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](https://www.fda.gov/drugs/pharmaceutical-quality-resources/current-good-manufacturing-practice-cgmp-regulations?utm_source=chatgpt.com)) | “FDA CGMP Regulations Portal – Parts 210, 211, 212.” |
| **ISO 9001 Quality Management** | ISO 9001:2015 Standard page: ([ISO](https://www.iso.org/standard/62085.html?utm_source=chatgpt.com)) | “ISO 9001:2015 — Quality Management Systems — Requirements.” |
| **ISO Quality Principles** | ISO Quality Management Principles PDF: ([ISO](https://www.iso.org/iso/pub100080.pdf?utm_source=chatgpt.com)) | “ISO Quality Management Principles (ISO pub 100080).” |
| **GAMP 5 (Good Automated Manufacturing Practice)** | ISPE GAMP 5 Guide 2nd Ed summary page: ([ISPE](https://ispe.org/publications/guidance-documents/gamp-5-guide-2nd-edition?utm_source=chatgpt.com)) | “ISPE GAMP 5 Guide, 2 nd Edition (2022).” |
| **GAMP Records & Data Integrity** | ISPE GAMP Guide – Records & Data Integrity: ([ISPE](https://ispe.org/publications/guidance-documents/gamp-records-pharmaceutical-data-integrity?utm_source=chatgpt.com)) | “ISPE GAMP Guide: Records & Data Integrity (2021).” |
| **Virginia CCA Regulations (Statutory Authority)** | VA Code — Cannabis Control Authority board powers: ([Virginia Law](https://law.lis.virginia.gov/authorities/cannabis-control-authority-virginia/?utm_source=chatgpt.com)) | “Virginia Cannabis Control Authority enabling statute (Va. Code).” |
| **Virginia CCA Official Website / Policy Docs** | Cannabis Control Authority homepage: ([Virginia Cannabis Control Authority](https://cca.virginia.gov/?utm_source=chatgpt.com)) | “Virginia Cannabis Control Authority, official resources.” |

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| Version | Date | Change Description | Approved By |
|  |  | Aligned with updated Quality Manual QM-VA-001 and Master Batch Record SOP. | [Name / Title] |