Real-World Strategies for Conducting Successful Root Cause Analysis

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Agenda

- Introduction
- Warm-up exercises
  - Hydraulic Fluid
- Definitions
- Root Cause Analysis and Methodologies
- Case Study
- Examples
- Q&A

Introduction

- Your speaker
- Why Root Cause Analysis is important

Who is George Bernstein?

- Principal with Double Dragon Consulting
- Ph.D. in Chemical Engineering
- 20+ years of Pharma experience
- Wide range of experience:
  - Quality Systems Development and Remediation
  - GMP, GCP, GLP, GPP
  - Training
  - Project/Program Management
  - Facility Construction and Commissioning
  - Root Cause Analysis
  - Business Process Re-engineering
- Our websites: www.consultmai.com
  www.doubledragonconsulting.com

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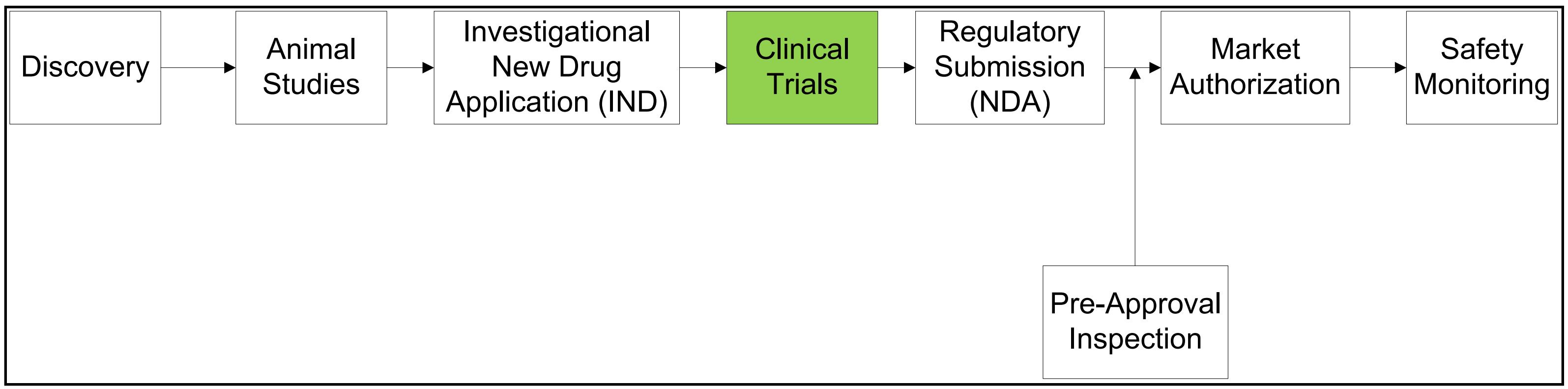
Introduction – Why RCA is Important



Warm-up Exercises

- Hydraulic Fluid

Hydraulic Fluid

This is an actual event that involves:

1. Automatic Elevator Co. of Durham
2. Duke University Hospital System (DUHS)
3. Cardinal Health
4. DUHS Staff
5. 3,650 Patients

Automatic Elevator

- Hired by DUHS in September 2004 to repair an elevator
- Repair required replacement of hydraulic fluid
- Mechanics found empty buckets and used them to hold the used hydraulic fluid
- The buckets used to contain detergent used by DUHS to clean surgical instruments
- Buckets now containing used hydraulic fluid were left by Automatic Elevator at the hospital

Cardinal Health

- Buckets of hydraulic fluid were found and returned to DUHS central stores
- From central stores the hydraulic fluid was returned to Cardinal Health's distribution warehouse
- Cardinal Health later distributed the hydraulic fluid to two of DUHS regional hospitals – Durham Regional Hospital and Duke Health Raleigh Hospital

DUHS Staff

- The hydraulic fluid was used by hospital staff to wash surgical instruments, prior to sterilization
- The hydraulic fluid was used for a period of 2 months

Which one is the hydraulic fluid?

DUHS Staff

- The hydraulic fluid occasionally left the instruments feeling slightly oily

  "It is not uncommon for instruments to feel slick, as a lubricant is added during the normal cleaning process to prevent rust and ensure the instruments work smoothly during surgery."

- Approximately 3,650 patients were affected.

The Question

Who was responsible?

Who was Responsible?

- Automatic Elevator?
- Cardinal Health?
- DUHS staff?
- Surgical nurses?
- Surgeons?

Whose Fault was It?

Everyone is responsible

Deviations and Root Cause

- Definitions
- Motivation

Definitions

Continuous Improvement

- Activities (typically corrective or preventive) taken to increase the ability of a process to fulfill quality/regulatory objectives

Deviation

- Results when a written procedure is not followed or an unexpected result is obtained
  ➔ All deviations must be recorded and impact evaluated and justified

Root Cause

- In terms of cause and effect, Root Cause is the fundamental reason(s) for the failure of a procedure which, when resolved, prevents a recurrence of the problem.
  ➔ Data collection and analysis are usually necessary to determine the root cause, and therefore guide decisions about the corrective and preventive actions needed for improvement.

CAPA

- Corrective Action(s) – action(s) taken to correct or fix a failed procedure
- Preventive Action(s) – action(s) taken to prevent similar issues from occurring in the future

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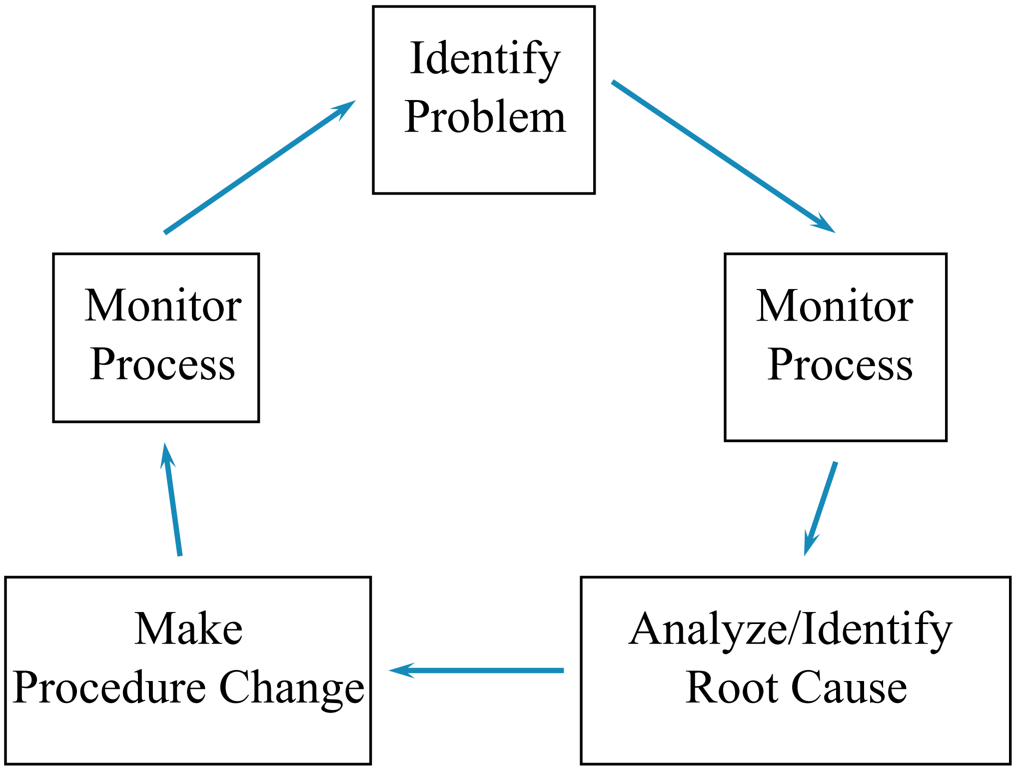
The Closed Loop Process Model



Motivation

- Compliance Risk
- 483 Observations
- Potential for product recall
- Target for FDA audits
    - Exposes many aspects of a site's quality systems
- Makes good business sense

Root Cause Analysis

- Categories
- Methods
- Data Collection and Analysis

Categories

Materials
- Defective raw material
- Wrong type for job
- Lack of raw material

Manpower
- Inadequate capability / resources
- Lack of Knowledge
- Lack of skill
- Stress
- Improper motivation

Machine / Equipment
- Incorrect tool selection
- Poor maintenance or design
- Poor equipment or tool placement
- Defective equipment or tool

Environment
- Orderly workplace
- Job design or layout of work
- Surfaces poorly maintained
- Physical demands of the task
- Forces of nature

Management
- No or poor management involvement
- Inattention to task
- Task hazards not guarded properly
- Other (horseplay, inattention....)
- Stress demands
- Lack of Process
- Lack of Communication

Methods
- No or poor procedures
- Practices are not the same as written procedures
- Poor communication

Management system
- Training or education lacking
- Poor employee involvement
- Poor recognition of hazard
- Previously identified hazards were not eliminated

From Management Oversight Risk Tree approach classification

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Root Cause

What is the root cause of the hydraulic fluid mishap?

- Hint: the root cause is not always training.

Hydraulic Fluid Root Cause

- Management
  - Inadequate supervision of outside contractors

Role of the Investigator

- In order to conduct an effective deviation investigation, the deviation investigator must have:
  - Good investigation skills
  - Excellent facilitation skills
  - Good documentation/reporting skills
  - Good working relationship with production workers in order to identify, fix, and prevent reoccurrence
  - Good technical writing skills
  - Good knowledge of the process(es) within the scope of the investigation
  - A good understanding of quality systems

3 Popular RCA Methods

- 5 Whys

  The technique was originally developed by Sakichi Toyoda and was later used within Toyota Motor Corporation during the evolution of their manufacturing methodologies. It is a critical component of problem solving training delivered as part of the induction into the Toyoda Production System.

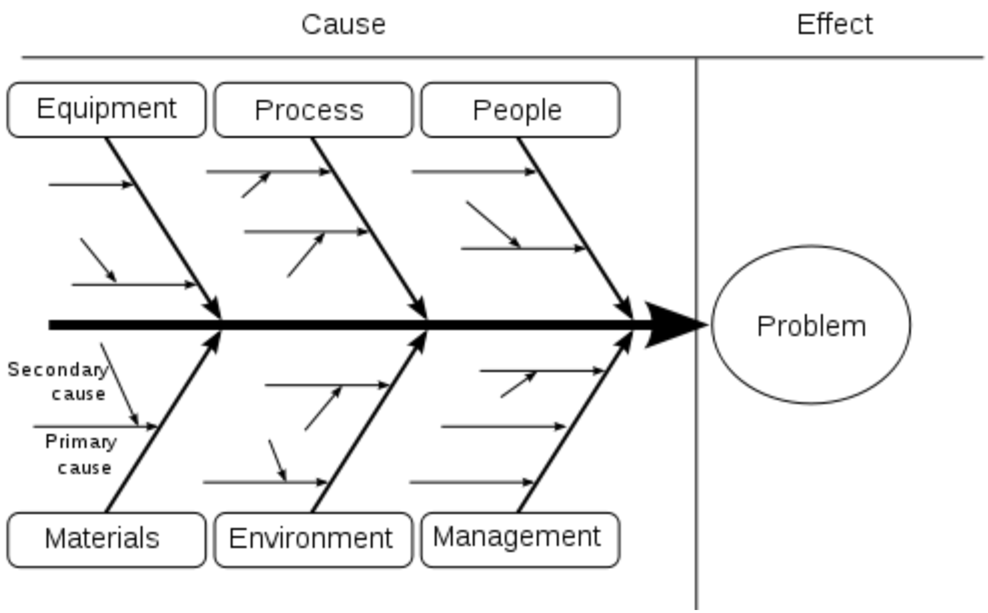
- Ishikawa Diagram

  Ishikawa diagrams (also known as the fishbone diagram or cause-and-effect diagram) were proposed by Ishikawa in the 1960s.Cause-and-effect diagrams can reveal key relationships among various variables, and the possible causes provide additional insight into process behavior.

- Failure Mode and Effects Analysis (FMEA)

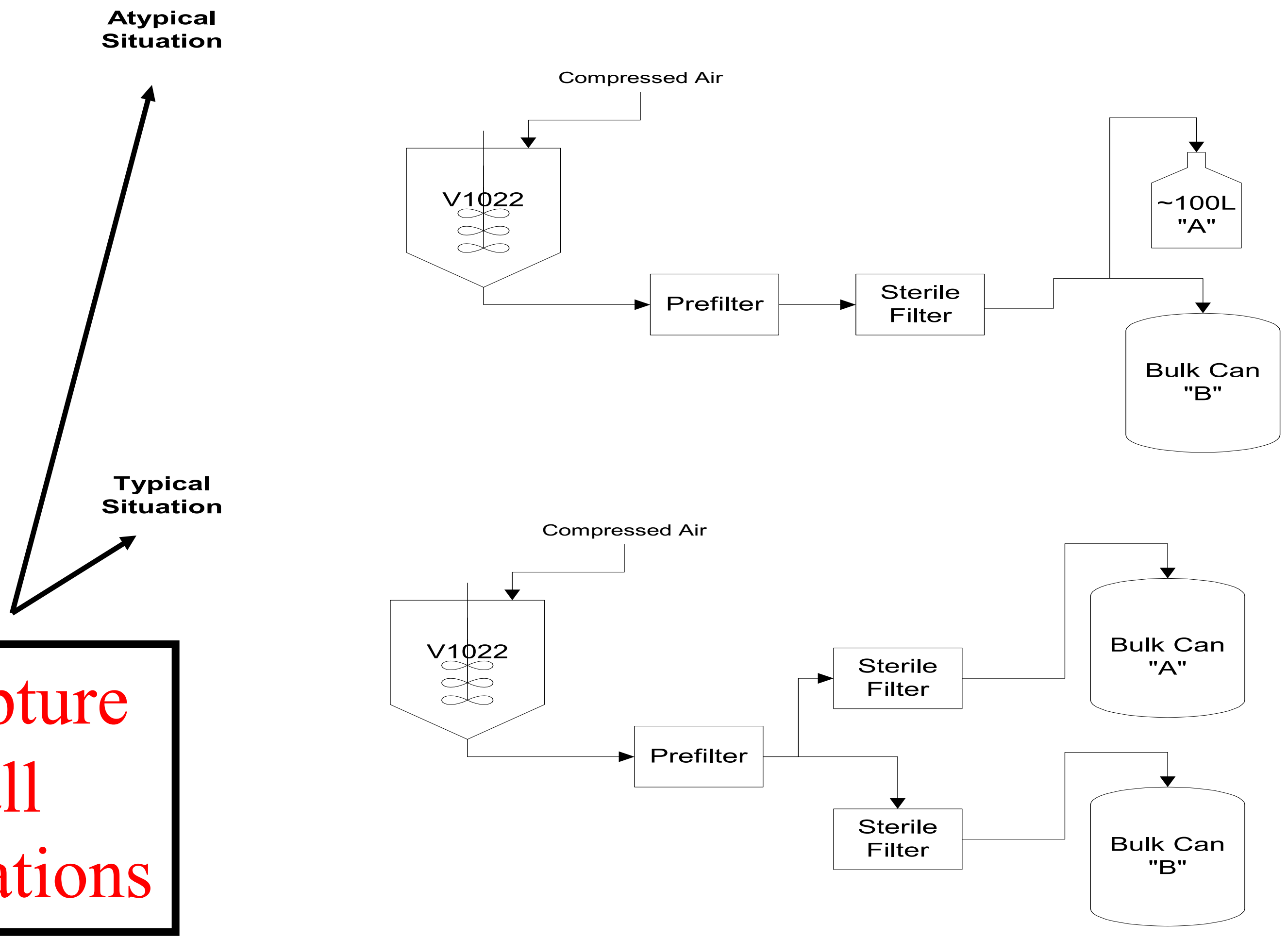
  is a procedure for analysis and classification of potential failure modes by the severity and likelihood of the failures. A successful FMEA activity helps a team to identify potential failure modes based on past experience with similar products or processes.

Fishbone Diagram



- **People**: Anyone involved with the process
- **Methods**: How the process is performed and the specific requirements for doing it, such as policies, procedures, rules, regulations and laws
- **Machines:** Any equipment, computers, tools etc. required to accomplish the job
- **Materials**: Raw materials, parts, pens, paper, etc. used to produce the final product
- **Measurements**: Data generated from the process that are used to evaluate its quality
- **Environment:** The conditions, such as location, time, temperature, and culture in which the process operates

Process Flow Diagram - Equipment



Capture all situations

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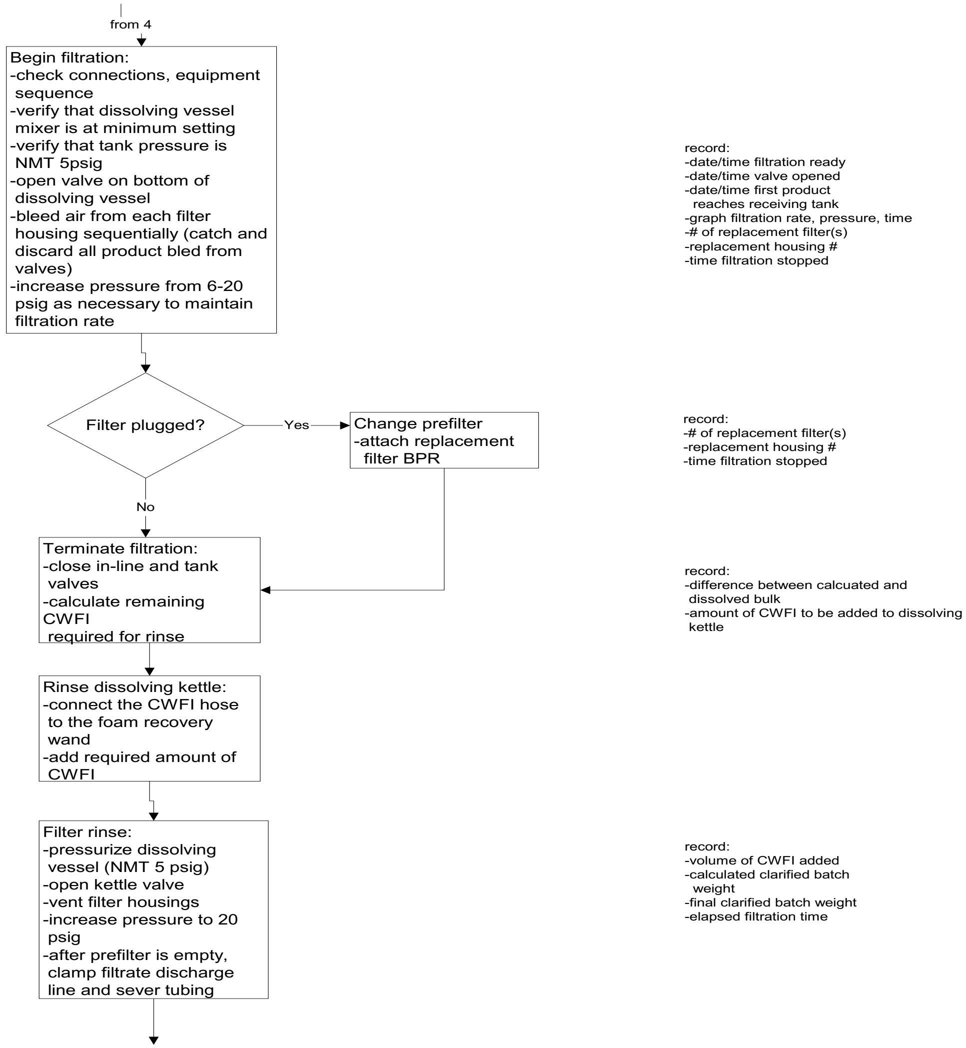
Process Flow Diagram - Process



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FMEA

- Useful for development of processes / procedures to ensure minimal likelihood of failures (risk management)
- Involves completing a worksheet where each step is evaluated in terms of the risk of failure
- Risk severity is calculated as the product of :
  - Severity of failure
  - Likelihood of occurrence of failure
  - How difficult it is to detect failure

FMEA

Item / Function / process step	Potential failure mode	Potential effects of failure	S (severity rating	Potential Cause	O (occurrence rating)	Current controls	D (detection rating)	RPN (risk priority number) = S x O x D
Fill tub	Overflow	Property damage	8	Level sensor failure	2	Manual observa tion	5	80

1. Identify all process steps
2. Completed worksheet for each item / function / process step
3. Calculate RPN (Risk Priority Number) for each entry
4. Entries with highest RPN are given the highest priority for corrective action:
   - Try to eliminate the failure mode if possible
   - Minimize the severity of the failure
   - Reduce the occurrence of the failure mode
   - Improve failure detection

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Data Collection and Analysis

Data collection.

80%

Analysis

20%

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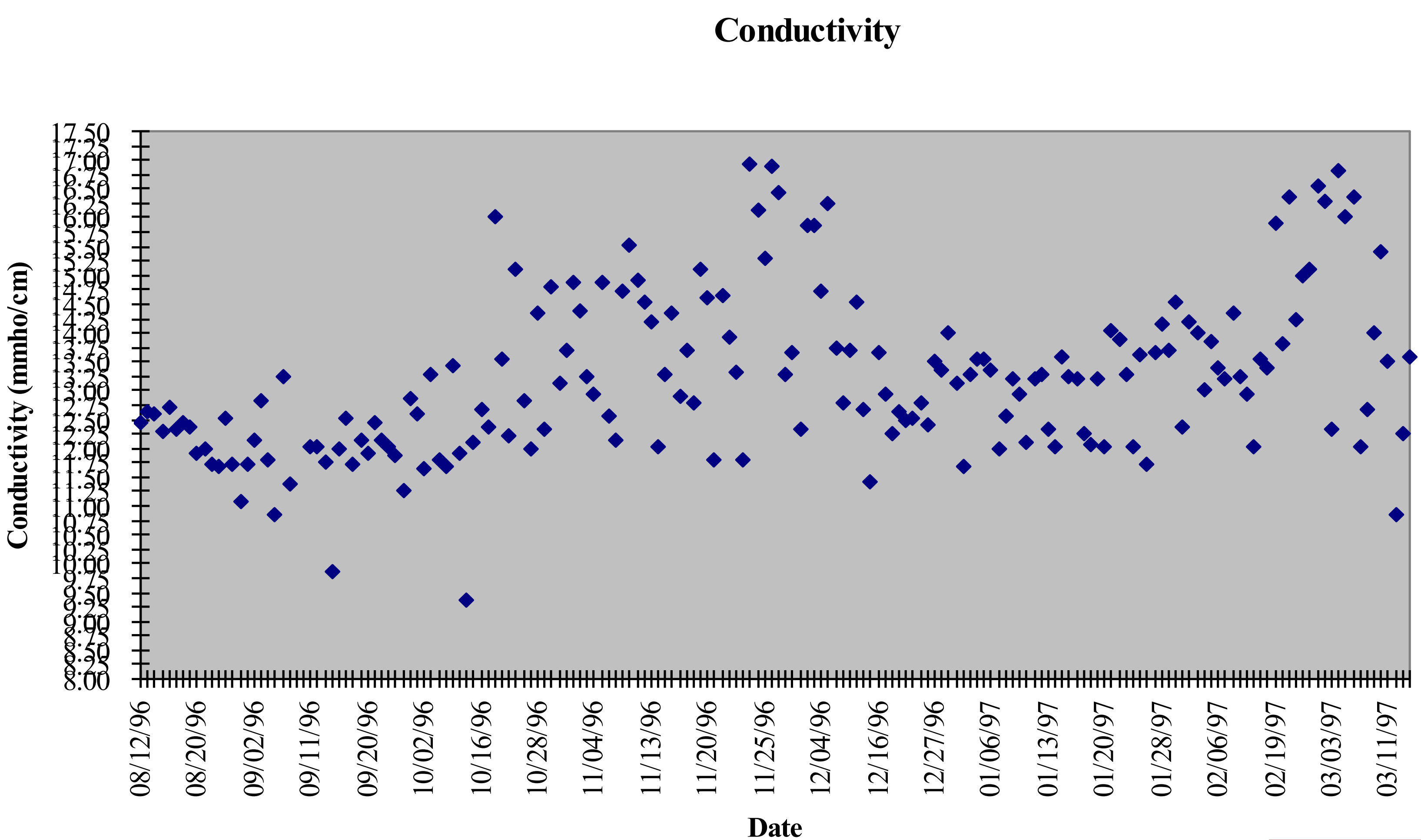
Example Run Chart - Raw Materials



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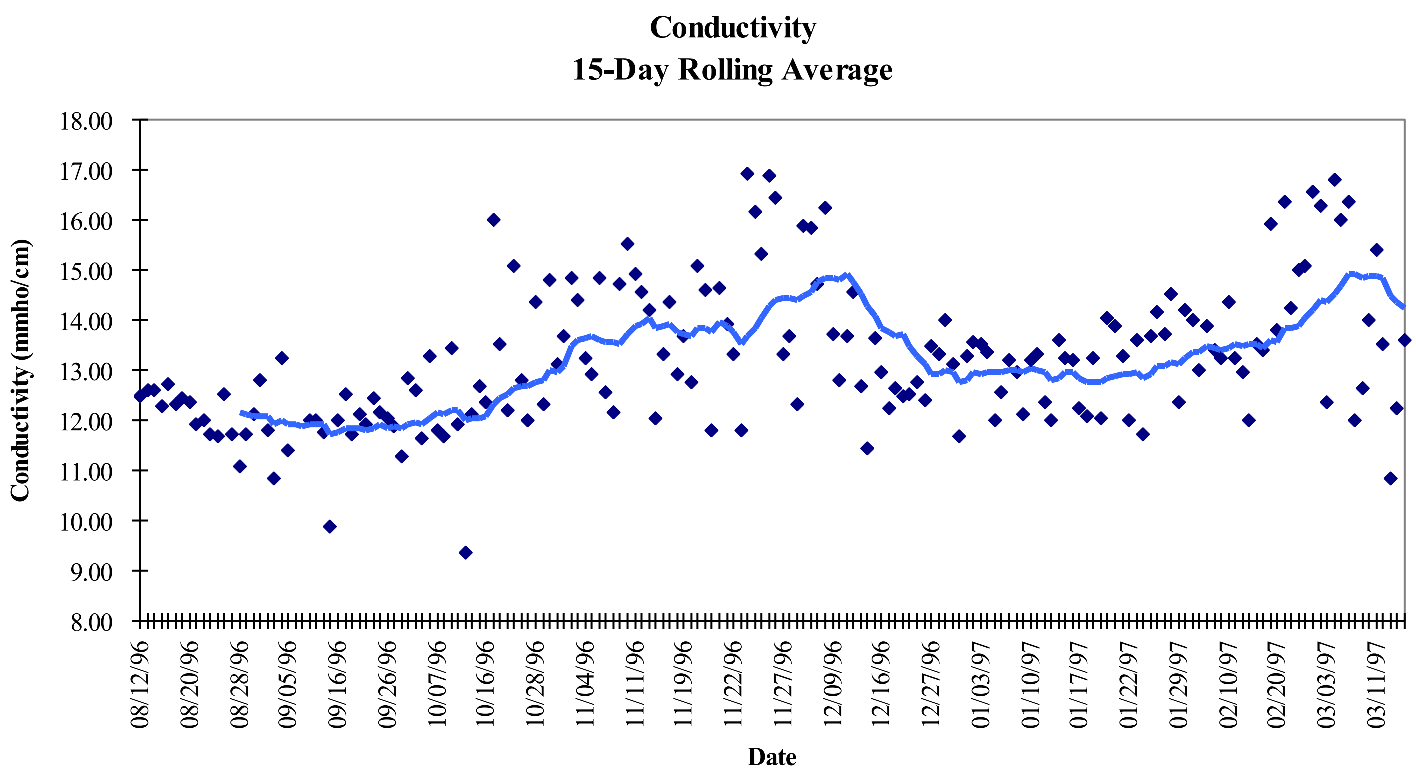
Example Run Chart - Raw Materials



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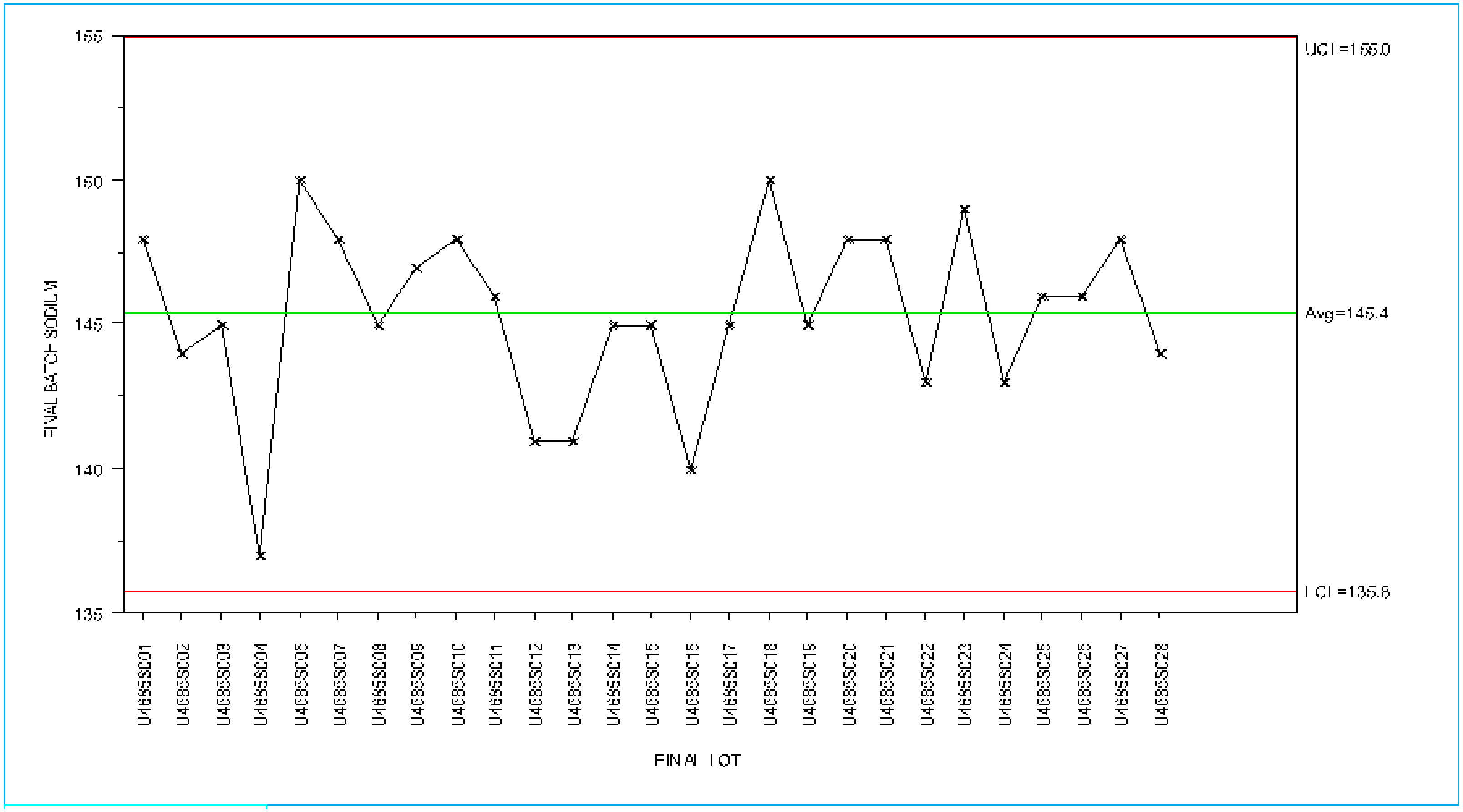
Example - Run Chart



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Methods - Tips

1. To be effective, **RCA must be performed systematically,** usually as part of an investigation, with conclusions and root causes identified backed up by documented evidence. Usually a **team effort** is required.
2. There may be more than one root cause for an event or a problem, the difficult part is demonstrating the persistence and sustaining the effort required to develop them. The purpose of identifying all solutions to a problem is to **prevent recurrence at lowest cost in the simplest way.** If there are alternatives that are equally effective, then the simplest or lowest cost approach is preferred.
3. Root causes identified depend on the way in which the **problem or event is defined**. Effective problem statements and event descriptions (as failures, for example) are helpful, or even required.
4. To be effective the analysis should **establish a sequence of events or timeline** to understand the relationships between contributory (causal) factors, root cause(s) and the defined problem or event to prevent in the future.
5. Root cause analysis can help to transform a reactive culture (that reacts to problems) into a forward-looking culture that solves problems before they occur or escalate. More importantly, it reduces the frequency of problems occurring over time within the environment where the RCA process is used.
6. RCA is a **threat to many cultures** and environments. Threats to cultures often meet with resistance. There may be other forms of management support required to achieve RCA effectiveness and success. For example, a "non-punitory" policy towards problem identifiers may be required.
7. Use peer review as an effective method to improve the quality of investigations.

Examples and Applications

- Problem #1 – Endotoxin excursions during tunnel sterilizer validation
- Problem #2 – Weights out of cal
- Problem #3 – Wrong filter

Problem #1 – Tunnel Sterilizer

- Problem Statement

  Results of residual endotoxin testing associated with qualification of depyrogenation tunnel showed that 2 out of 10 treated vials did not meet the acceptance criteria of at least a 3-log reduction of the endotoxin spike. All endotoxin results met acceptance criteria when the protocol was repeated.
- Approach

  Identify potential causes
  - Temperature
  - Vial dwell time
  - Over-spiking*
  - Contaminated vials*
  - Test lab error
  - Contamination during handling and shipping
- Conclusion
  - Historically, finished product endotoxin excursions are rare
  - Excursions during depyrogenation tunnel have not been observed
  - Likely that this is a single and isolated occurrence.

⇒ Inference

Problem #2 – Weights out of Cal

- Problem Statement

  Weight set used for daily weigh scale suitability check was outside of as-found acceptance range, probably due to mis-handling by operators.

- Approach
  - Evaluate the difference between accepted and as found values to determine if difference is significant

- Conclusion
  - Difference between accepted and as found values is less than the precision of the scale
  - The weight set used for daily suitability check is not appropriate for the weigh scale (Class E1 – accurate to 0.001 mg vs. Class 4 – accurate to 0.1 g)

➡ Seek out SME

Problem #3 – Wrong Filter

- Problem Statement
  The wrong part number filter was used during soy bean oil filtration

- Approach
  - Compare specifications of filter used with specifications of filter used during process validation.
  - [Compare filter used to filter specified in terms of filter characteristics]

- Conclusion
  - Specifications of filters was different (bacterial clearance and loading characteristics) [Could not find validation documentation for filtration step]
  - Reject soy bean oil – cost of investigation is greater than value of the material.

➡ Know costs

In Summary

Regarding Root Cause Analysis, remember:

- Training isn't always the root cause
- Look at trending to see if a repeating problem – maybe you didn't identify the root cause or implement the appropriate preventive action.

Questions?

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