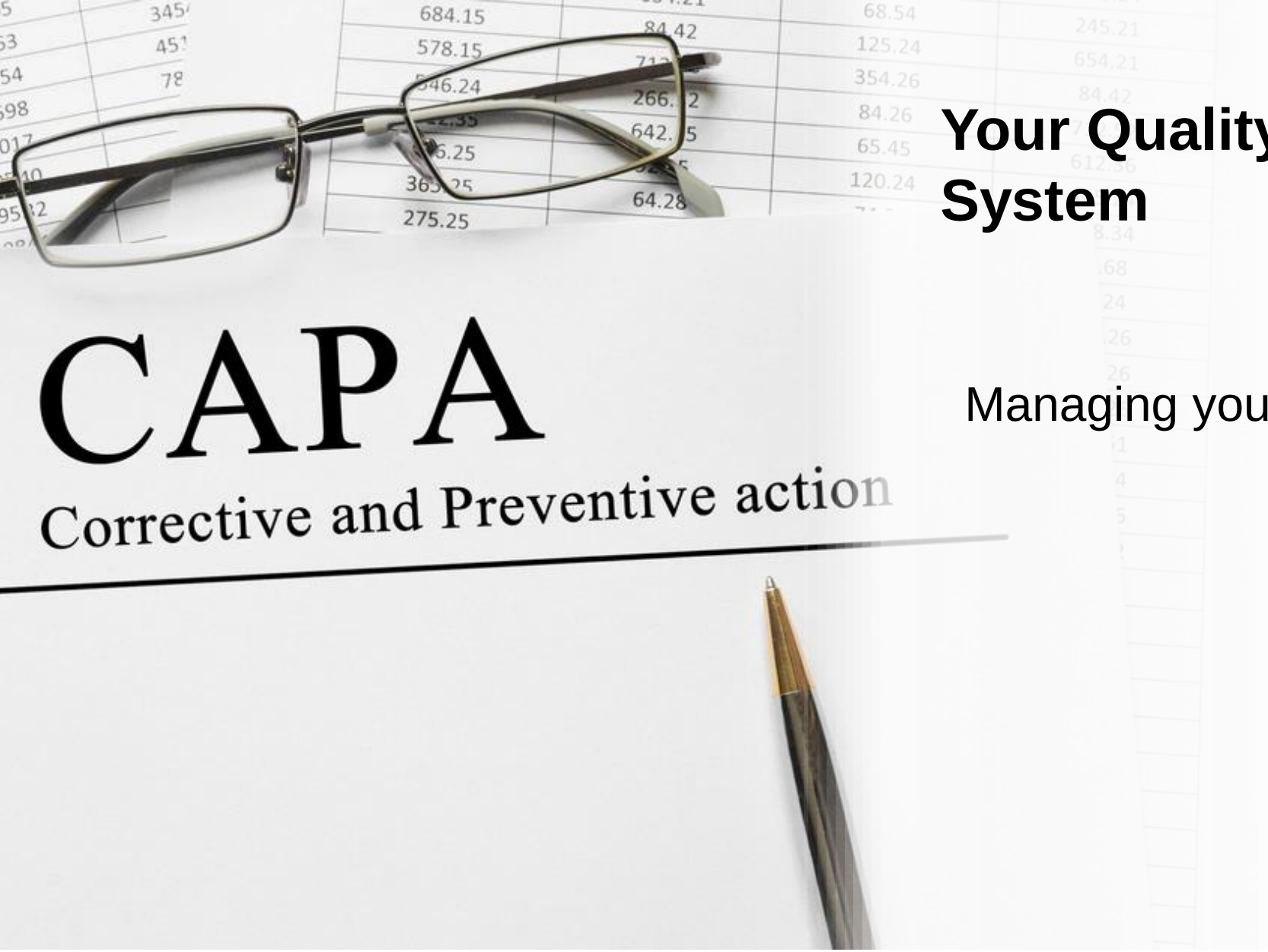


Your Quality Management System

Managing your CAPAs

SeerPharma®
CONFIDENCE IN COMPLIANCE

Topics

- Design & Development of a Quality System
- Quality System Integration
- CAPA, Investigation & Root Cause Analysis
- Language

Design & Development of a Quality System

Design & Development of a Quality System

- Quality System Planning
- Document Hierarchy – target the user
- Management Responsibility

Quality System Planning

- What are the Quality System Elements required for the company?
- How do we make the documentation suitable for the user?
- Who is responsible for what?
- How are they interrelated?
- Nomenclature
- How do we manage all of the documents?

Quality System Planning (cont.)

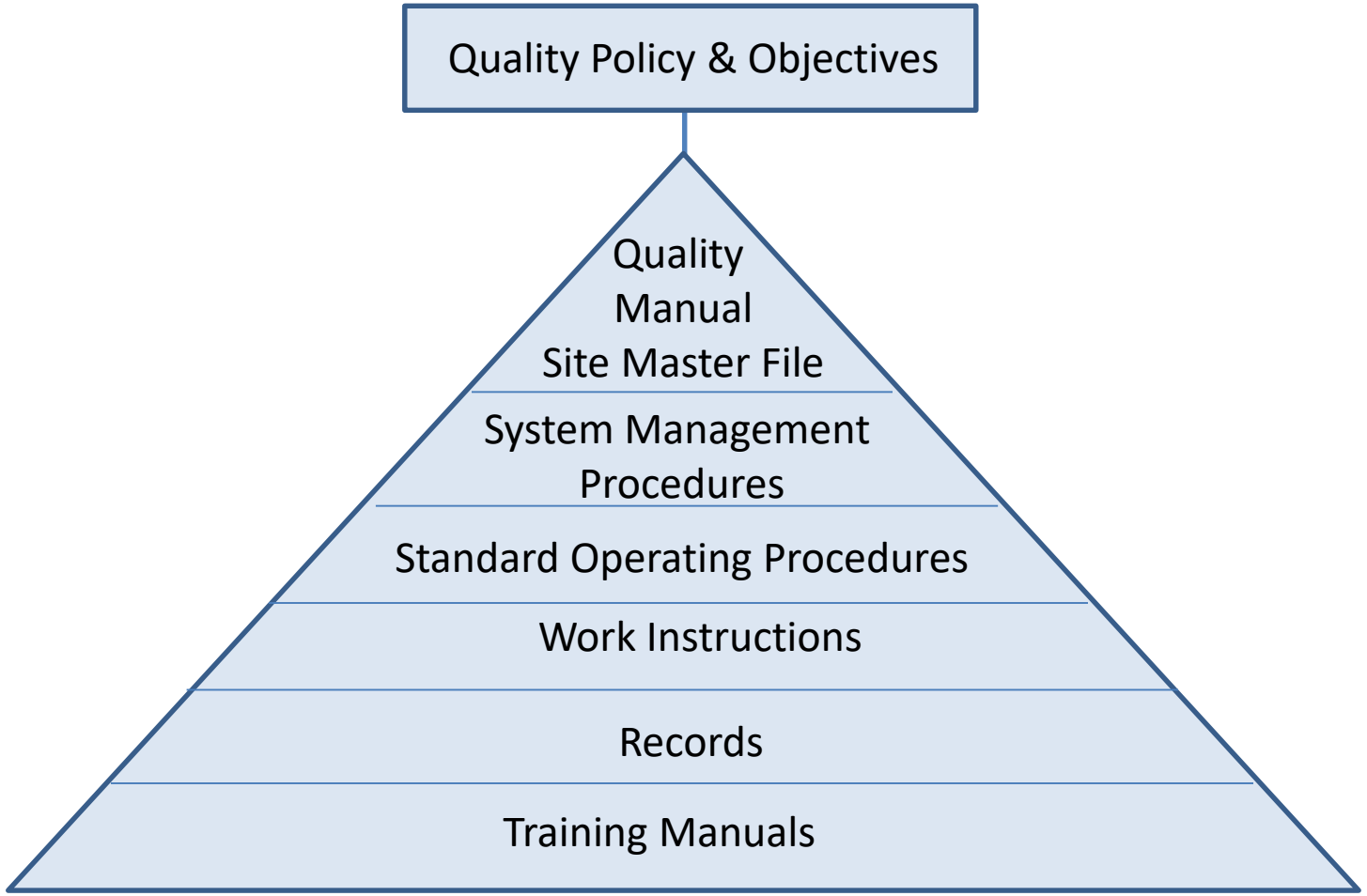
Typical Quality System Elements

Management Responsibility	Product Identification and Traceability	Change Control
Personnel & Training	Materials Management	Corrective & Preventive Action
GMP Contracts/Technical Agreements	Purchasing	Quality Control
Facility Management	Process Control	Control Of Non-conforming Product
Equipment Management	Validation	Audits
Document Management	Product Labelling and Packaging	Periodic Quality Reviews
Records Management	Distribution Management and Control	Risk Management

Quality System Planning (cont.)
Typical Quality System Elements

Management Responsibility	Product Identification and Traceability	Change Control
Personnel & Training	Materials Management	Corrective & Preventive Action
GMP Contracts/Technical Agreements	Purchasing	Quality Control
Facility Management	Process Control	Control Of Non-conforming Product
Equipment Management	Validation	**Audits**
Document Management	Product Labelling and Packaging	Periodic Quality Reviews
Records Management	Distribution Management and Control	Risk Management

Document Hierarchy



SeerPharma®
CONFIDENCE IN COMPLIANCE

Document Hierarchy (cont.)

System Element	Policy Documents	System Document Name	SOP	WI	Records and Other
Management Responsibility	POL 01-01: Quality Policy and Objectives	SOP 01-01: Management Responsibility SMF 01-01: Site Master File	N/A	N/A	JD 01-01 - 06: Job Descriptions REG 01-01: Organization Chart REG 01-02: Responsibility Matrix Minutes of Management Review Meetings Traceability Matrix

Traceability Matrix

ISO 13485 Reference	Quality System Element / SOP/ Policy Reference
4. Quality Management System 4.1 General Requirements 4.2 Documentation Requirements 4.2.1 General 4.2.2 Quality Manual 4.2.3 Medical Device File 4.2.4 Control of Documents 4.2.5 Control of Records	
5 Management Responsibility 5.1 Management Commitment 5.2 Customer Focus 5.3 Quality Policy 5.4 Planning 5.4.1 Quality Objectives 5.4.2 Quality Management System Planning 5.5 Responsibility, authority and communication 5.5.1 Responsibility & Authority 5.5.2 Management representative 5.5.3 Internal communication 5.6 Management Review 5.6.1 General 5.6.2 Review Input 5.6.3 Review output	

Management Responsibility

- **Principle 1**
  - Quality is everybody's job.
- **Principle 2**
  - Because quality is everybody's job, it is in danger of becoming nobody's responsibility.

Management Responsibility (cont.)

- Key Responsibilities Need to be assigned for each QSE:
  - R = Total Responsibility. Authorises the system and authorised to change it as required. This responsibility should not be shared.
  - V = verification Responsibility – responsible for verifying the system is working, ie audit the system.
  - I = Implementation responsibility. Responsible for implementing the system. This responsibility may be shared.

Responsibility Matrix

System Element	QA Manager	Production Manager	Operations Manager	Director
Quality Management	V	I	I	R
Personnel & Training	V	I	R	I
GMP Contracts	R	I	V	I
Facility Management	V	I	R	I
Equipment Management	V	I	R	I
Document Management	R	I	V	I
Product Identification and Traceability	V	I	R	I
Quality Records	R	I	V	I
Materials Management	V	I	R	I
Purchasing	V	I	R	I
Process Control	V	I	R	I
Validation	R	I	V	I

What's Wrong With This?

System Element	QA Manager	Production Manager	Operations Manager	Director
Quality Management	V	I	I	R
Personnel & Training	R/V	I	I	I
GMP Contracts	R/V	I	I	I
Facility Management	R/V	I	I	I
Equipment Management	R/V	I	I	I
Document Management	R/V	I	I	I
Product Identification and Traceability	R/V	I	I	I
Quality Records	R/V	I	I	I
Materials Management	R/V	I	I	I
Purchasing	R/V	I	I	I
Process Control	R/V	I	I	I
Validation	R/V	I	I	I

And What's Wrong With This?

System Element	QA Manager	Production Manager	Operations Manager	Director
Quality Management	V	I	I	R
Personnel & Training	R/V	I	R	I
GMP Contracts	R/V	I	I	I
Facility Management	R	I	R/V	I
Equipment Management	V	R	R	I
Document Management	R/V	I	I	I
Product Identification and Traceability	R/V	I	I	I
Quality Records	R/V	I	I	I
Materials Management	V	R	R	I
Purchasing	R/V	I	I	I
Process Control	R/V	I	I	I
Validation	R/V	I	I	I

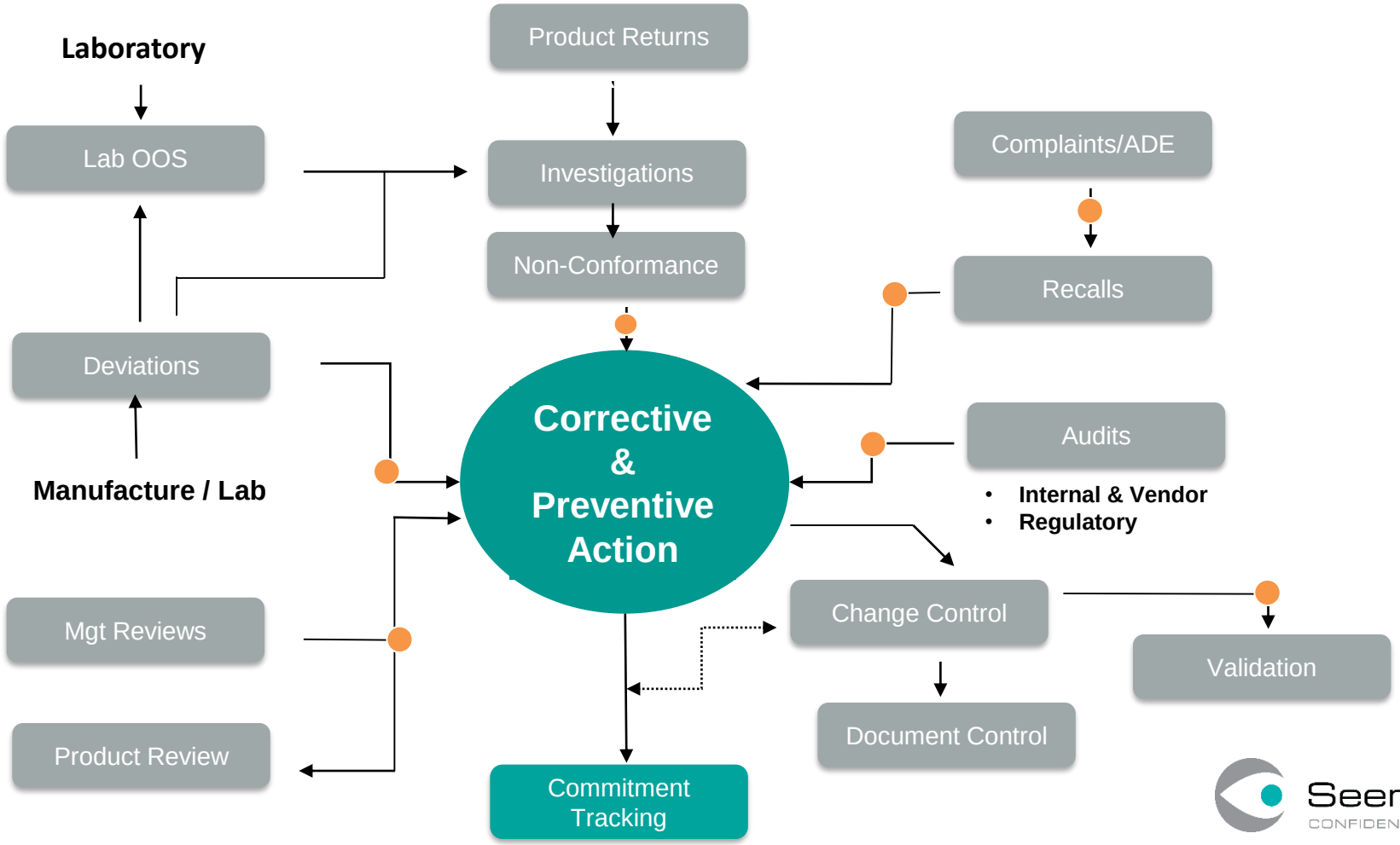
Quality System Integration

Quality System Integration

- Each QSE cannot stand alone like a silo. It must be integrated with other systems.
- Let’s look at CAPA – many elements of the Quality System point directly to it.

Quality System Integration (cont.)

Indicates risk assessment should be utilised as a “gate” to escalation



SeerPharma®
CONFIDENCE IN COMPLIANCE

Qualifying CAPAs
Some Useful Questions to Ask ?

Question ?	Answer Yes	Answer No
Can the problem be handled locally at department level	Probably not a CAPA	Probably a CAPA
Is the problem really a symptom	Add to existing information - no CAPA unless significant risk	If significant risk raise a CAPA
Is there a high compliance risk	Raise a CAPA	Raise CAPA only if occurs frequently
Is there a high product/ patient risk	Raise a CAPA	Raise CAPA only if occurs frequently
Is the problem likely to re-occur	Raise CAPA only if not tolerable	Raise CAPA only if high risk

CAPA, Investigation & Root Cause Analysis

Deviation, CAPA and Risk

Deviation used to be a reporting system

"1.4 A Pharmaceutical Quality System appropriate for the manufacture of medicinal products should ensure that:

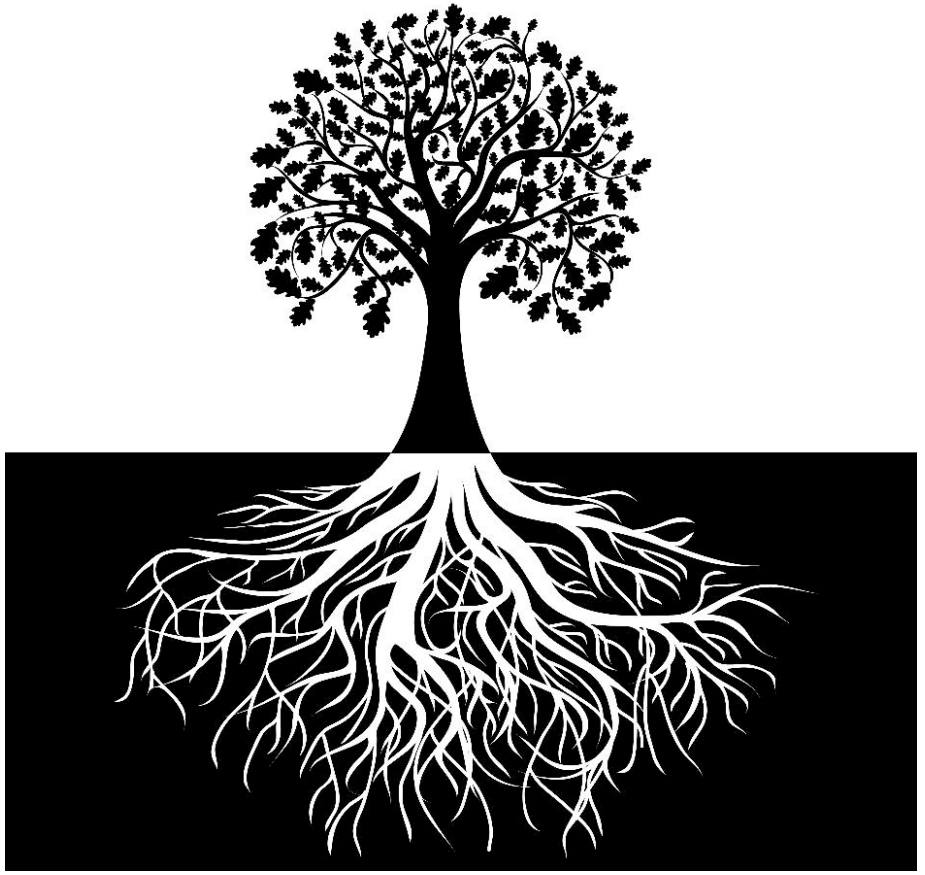
> (xiv) An appropriate level of root cause analysis should be applied during the investigation of deviations, suspected product defects and other problems…… Appropriate corrective actions and/or preventive actions (CAPAs) should be identified and taken in response to investigations. The effectiveness of such actions should be monitored and assessed, in line with Quality Risk Management principles"

The Language of Problem Solving

- **CAPA (Corrective Action / Preventive Action) –** CAPA is a GxP regulatory **concept** that focuses on investigating, understanding, and correcting discrepancies in an attempt to prevent their recurrence.
- **Failure Investigation -** the process of gathering information and investigating the attributes of a particular failure and identifying potential causes of failure.
- **Root Cause Analysis –** a systematic process of analysing potential causes of failure to identify the true causes of a particular undesirable event.

CAPA and Root Cause Analysis (RCA)

- While CAPA is central to the Quality System, Root Cause Analysis is central to the CAPA system.



Important CAPA Definitions

Correction:

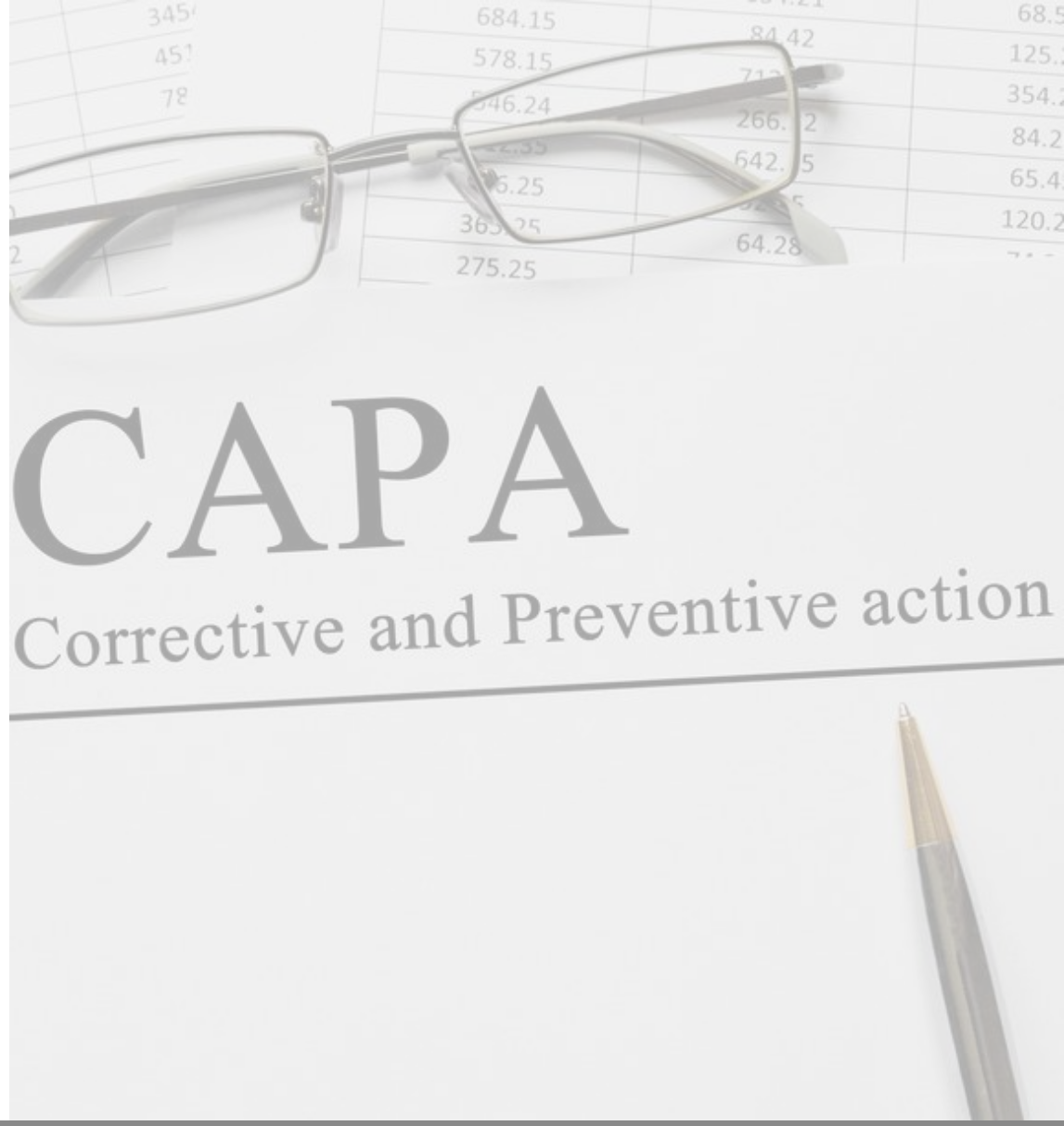
- Action to correct (or contain) a non-conformity or other undesirable situation

Corrective Action:

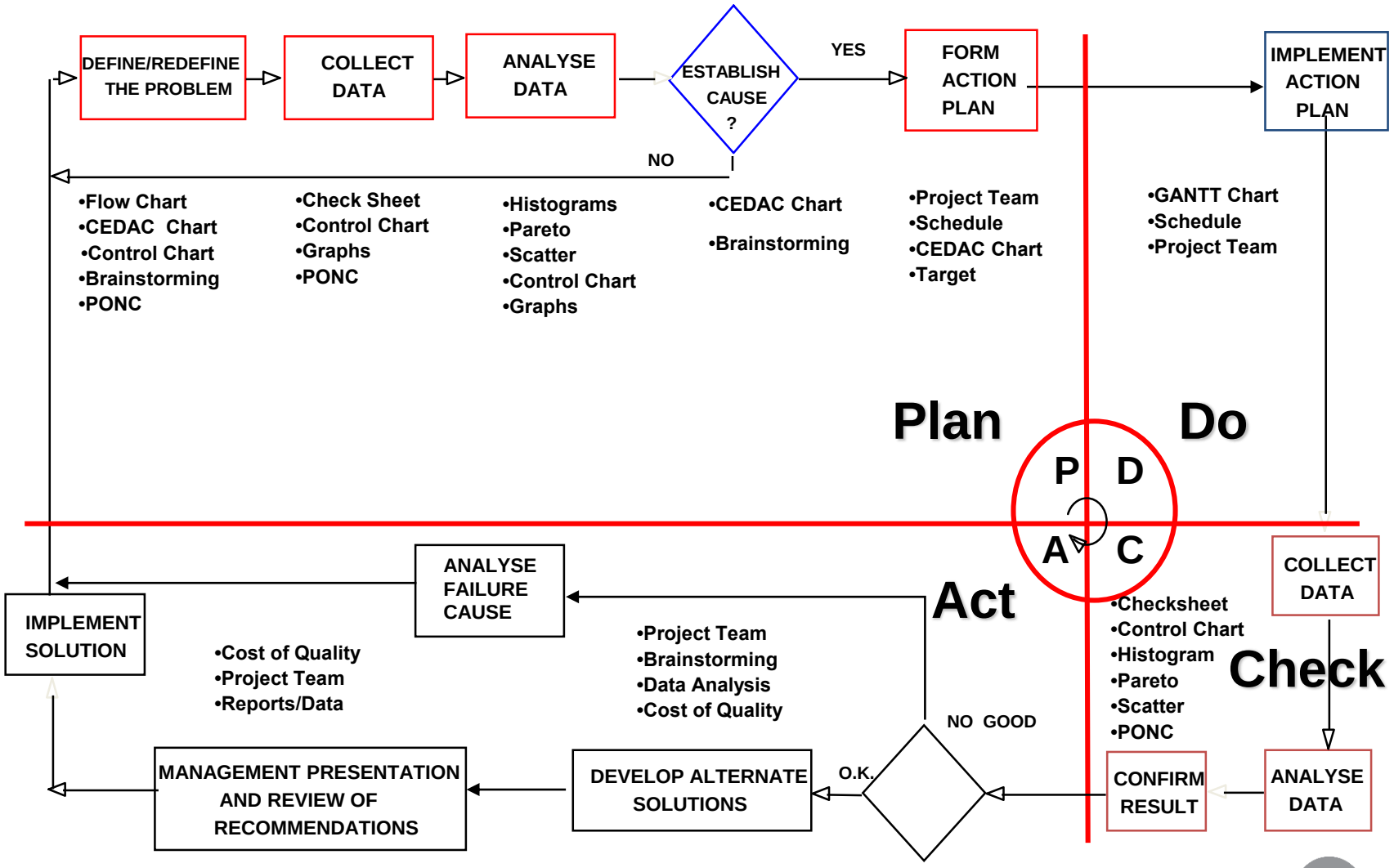
- Action to eliminate the cause of a detected non-conformity or other undesirable situation

Preventive Action:

- Action to eliminate the cause of a potential non-conformity or other undesirable potential situation



Problem Solving/RCA



Describing the Problem: “The Fax”

You transmitted an important "FAX" to your boss while you were interstate last week. You are relying heavily on this reaching him that day because if it does not, vital information regarding supply of components to the plant will not reach him and will disrupt production.

When you return to the plant the next week, you are heavily criticised for not checking its arrival.

The boss received the FAX two days late. A new employee, misreading the document, thought it was for you and placed it with the rest of your mail.

Prepare a brief statement describing the problem.

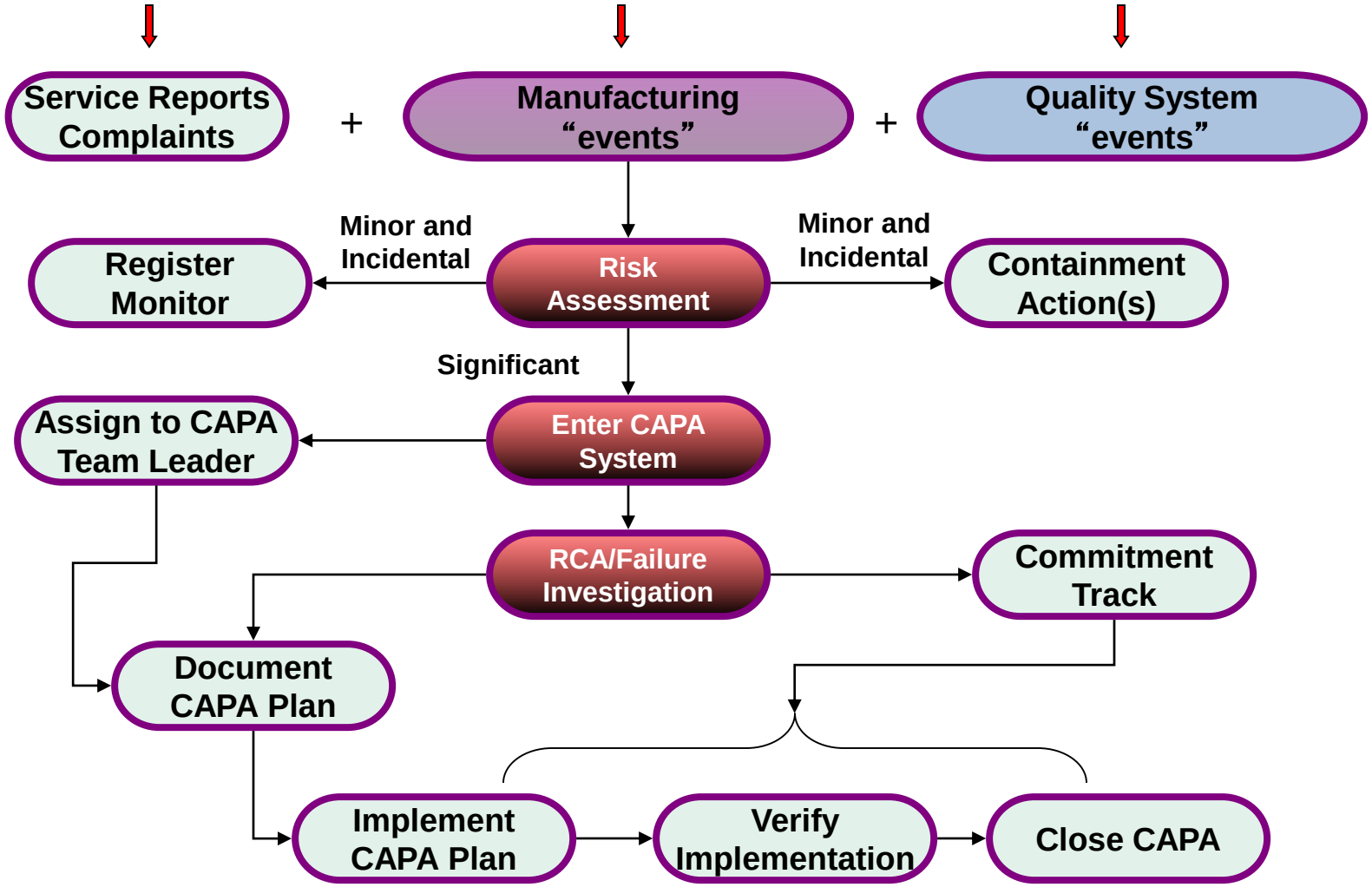
Problem Statements?

Problem Statements	Problem Statement	Solution	Cause
Inadequate communications			
Training inadequate			
Didn’t follow up			
Need a fax procedure			
Should have phoned.			
The boss didn’t get the fax			
The MRP system is inadequate			
Production disrupted			

Problem Statements?

Problem Statements	Problem Statement	Solution	Cause
Inadequate communications			X
Training inadequate			X
Didn’t follow up			X
Need a fax procedure		X	
Should have phoned.		X	
The boss didn’t get the fax	X		
The MRP system is inadequate			X
Production disrupted	X		

CAPA Management Process



CAPA Management

- How many CAPAs should I have?
- I just implemented my CAPA System and I now have 130 CAPAs!

10 Top Reasons for Deficient Failure Investigations

- Various independent groups involved: No unified ownership
- Company investigator lacked proper expertise or training
- Other higher priority work takes precedence over investigation
- Investigators do not have authority to seek information from others
- The investigation SOP is not used/followed
- Insufficient time or resources given to conduct or complete work
- Investigator identifies problem but no corrective action plans
- Problem never identified because “tough” questions are not asked
- No follow through to correct problem and prevent recurrence
- Investigators write what they think managers want to hear.

Language

The Confusing (English) Language of GMP

In the beginning there was:

- Shall (universally used by the FDA in their CFRs – a legal requirement)
- Should (a requirement but alternates that provide same QA are acceptable)
- May (no restrictions)

Then (for Australia) the Australian regulator said that wherever you read “should” in the PIC/S code, it means “must”.

Comparisons of Codes
Appearance Rate of Instructional Modal (Helping) Verbs

Code	“Must”	“Shall”	“Should”	“May”
PIC/S PE 009-13	29	1	418	32
PIC/S PE 009-8	26	0	358	24
TGA 1990	15	0	602	102
FDA CFR Part 211	4	301	1	27

Language – Pet Hates

- **Interchanging terminology/Nomenclature**
  - Deviation
  - Investigation
  - Non-conformance
  - Non-compliance
  - Non-conforming Product
  - Incident
  - Corrective Action
  - Complaints

Some companies inappropriately, have one process to manage all these.

Wrap-up

- Clause 1.3 PIC/S of the Code says Management are responsible for providing tools.
  - Quality System Planning - Matrices
  - Document Hierarchy – Matrices
  - Management Responsibility - RACI
  - Integration – Process Mapping
  - Language