

Implementing a Holistic Approach to your Quality Management System

Steven R. Cagle
V.P. of Marketing & Product Development
Sparta Systems, Inc.

Agenda

- **Session Objectives**
- **Quality Management System Overview**
- **Traditional Challenges**
- **Re-defining CAPA**
- **Implementing a Quality Management Software Solution**
- **Conclusion**
- **Q&A**

Discuss critical components of an effective Quality Management System (QMS), challenges with current systems, and solutions to overcome these challenges by implementing a holistic Quality Management Software solution.

General Introduction

- ✦ 8.5.2 Corrective Action – Corrective actions shall be appropriate to the effects of the nonconformities encountered. A documented procedure shall be established to define requirements for
 - a) reviewing nonconformities (including customer complaints)
 - b) determining the cause of nonconformities
 - c) evaluating the need for action to ensure that nonconformities to not recur
 - d) determining and implementing action needed, including, if appropriate, updating documentation
 - e) recording of the results of any investigation and of action taken, and
 - f) reviewing the corrective action taken and its effectiveness

- 8.5.3 Preventive action – The organization shall determine action to eliminate the causes of potential nonconformities in order to prevent their occurrence. Preventive actions shall be appropriate to the effects of the potential problems.
- It is also determine potential nonconformities and their causes
 - a) evaluating the need for action to prevent occurrence of nonconformities
 - b) determining and implementing action needed
 - c) recording of the results of any investigations and of action taken, and
 - d) reviewing preventive action taken and its effectiveness

Quality Regulation 21 CFR 820.100

➤ U.S. Food and Drug Administration's regulation governing medical device manufacturers quality systems:

- (a) Each manufacturer shall establish and maintain procedures for implementing corrective and preventive action:
 - (1) analyzing processes, work operations, concessions, quality audit reports, quality records, service records, complaints, returned products, and other sources of quality data to identify existing and potential causes of nonconforming product, or other quality problems
 - (2) investigating the cause of nonconformities relating to product, processes, and the quality system
 - (3) identifying the actions needed to correct and prevent recurrence of nonconforming product and other quality problems
 - (4) verifying or validating the corrective and preventive action
 - (5) Implementing and recording changes in methods and procedures needed to correct and prevent identified quality problems
 - (6) Ensuring that information related to quality problems or nonconforming product is disseminated to those directly responsible for assuring the quality of such product or the prevention of such problems; and
 - (7) Submitting relevant information on identified quality problems, as well as corrective and preventive actions, for management review

Quality Regulation 21 CFR 211.22

- ✚ **Very similar is the U.S. FDA's regulation for pharmaceutical manufacturers 21 CFR Part 211.22 (Quality Control Unit)...**
 - ▶ responsibilities of a quality control unit...to assure that no errors have occurred or, if errors have occurred, that they have been fully investigated.
 - ▶ The quality control unit shall have the responsibility for approving or rejecting all procedures or specifications impacting on the identity, strength, quality, and purity of the drug product
- ✚ **...and in Part 211.92 (Production Record Review)**
 - ▶ Any unexplained discrepancy...or the failure of a batch or any of its components to meet any of its specifications shall be thoroughly investigated...The investigation shall extend to other batches of the same drug product and other drug products that may have been associated with the specific failure or discrepancy. A written record of the investigation shall be made and shall include the conclusions and follow-up.

Quotes from Current FDA Warning Letters

- ✦ Each manufacturer shall establish **procedures for quality audits** and conduct such audits to assure that the **quality system is in compliance** with the established quality system requirements and to determine the **effectiveness of the quality system** . Quality audits shall be conducted by individuals who do not have direct responsibility for the matters and shall be taken when necessary. A report of the results of each quality audit, and reaudit(s) where taken, shall be made and such reports shall be reviewed by **management having responsibility** for the matters audited. The dates and results of quality audits and reaudits shall be documented as required by 21 CFR 820.22 . internal quality audits conducted by your firm failed to verify that the quality system was effective in fulfilling quality system objectives (FDA 483, Item #2).

Quotes from Current FDA Warning Letters

- ✦ Your firm fails to implement and maintain corrective and preventive action (CAPA) procedures that include requirements for **analyzing processes, work operations, concessions, quality audit reports, quality records, service records, complaints, returned product, and other sources of quality data to identify existing and potential causes of nonconforming product**, or other quality problems as required by 21 CFR 820.100(a)(1).
- ✦ Your firm fails to establish and implement corrective and preventive action (CAPA) procedures that include **requirements for identifying the action(s) needed** to correct and prevent recurrence of non-conforming product and other quality problems as required by 21 CFR 820.100(a)(3)
- ✦ All activities required by 21 CFR 820.100 must be verified or validated to ensure that such **action is effective and does not adversely affect** finished devices, and the results of these activities shall be documented as required by 21 CFR 820.100(a)(4) and (b). Your firm's CAPA procedures fail to document how analysis is done and fails to require verification/validation that CAPA does not adversely affect finished devices (FDA 483, Item #8).

Preamble

- ▶ Having regard to the Treaty establishing the European Community, All manufacturers should operate an effective quality management system of their manufacturing operations, which requires the implementation of a pharmaceutical quality assurance system.

Article 13 - Complaints

- ▶ Any complaint concerning a defect shall be recorded and investigated by the manufacturer...

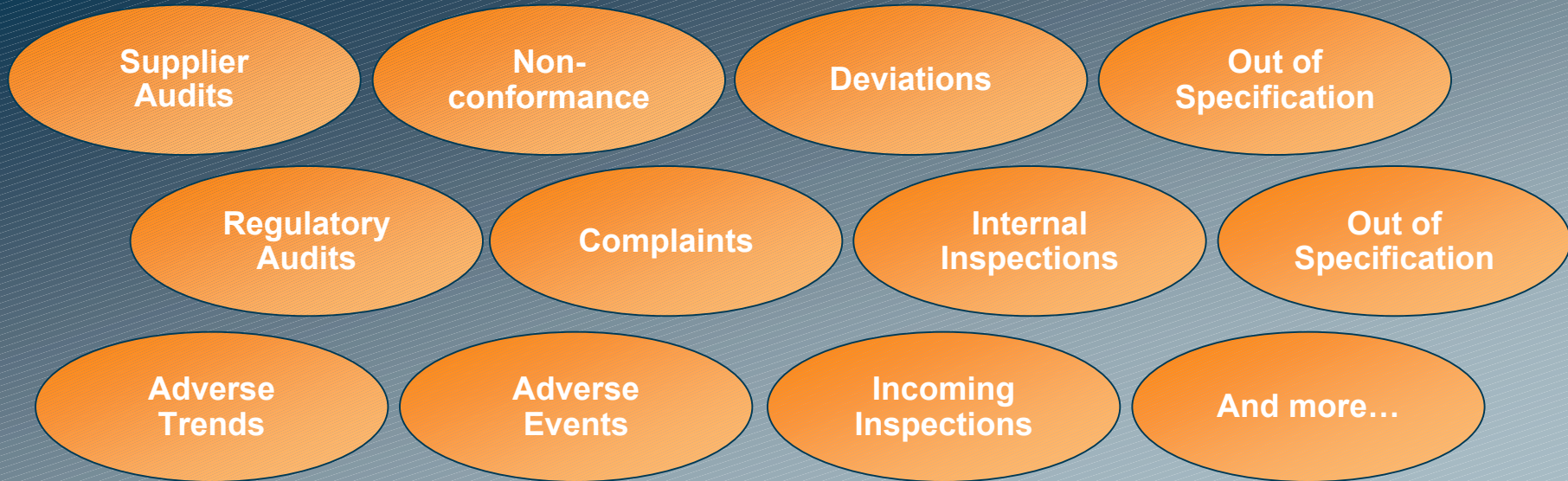
Article 14 - Inspections

- ▶ The manufacturer shall conduct repeated self-inspections...in order to monitor the implementation and respect of good manufacturing practice and to propose any necessary corrective measures. Records shall be maintained of such self-inspections and any corrective action subsequently taken.

**CAPA is much more than just
“corrective actions” and
“preventive actions”.**

**Any opportunity to improve quality
in your organization is a CAPA!**

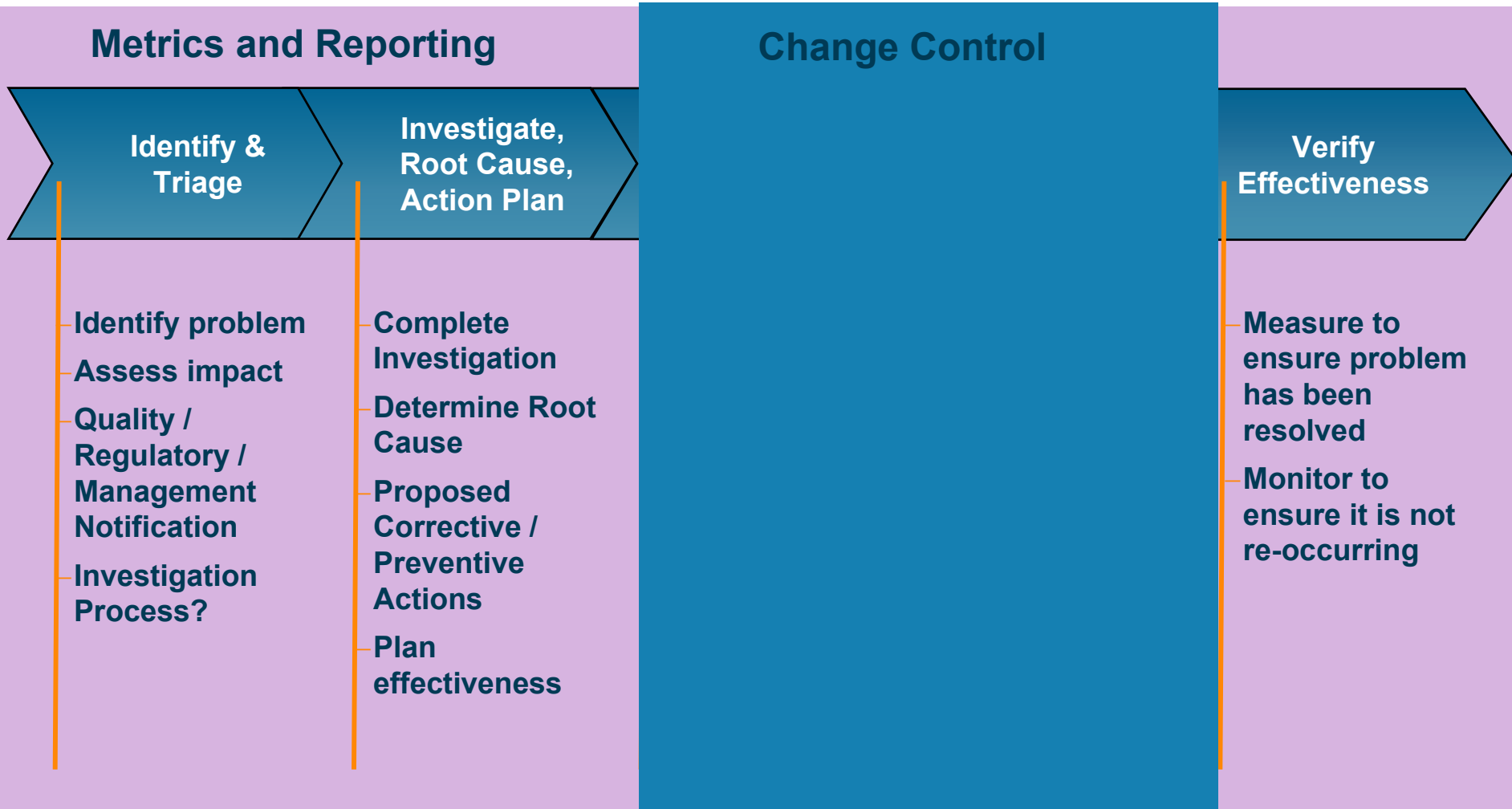
Holistic QMS Defines CAPA Sources



- **Numerous source areas for CAPA**
- **Scope of “problems” that drive CAPAs go beyond nonconforming product**
- **Any process that affects product quality is included**

CAPA Process – best practices

- **Regardless of where the problem originates, or what type it is, it must follow a process**



Addressing QMS Challenges

Typical QMS Challenges

➤ Challenges in Problem Identification

- ▶ Missing view of the big picture
- ▶ Lack of ownership and accountability
- ▶ Inability to link related problems
- ▶ Insufficient tools for trending and analysis



Problem
Identification

➤ Challenges in Investigation

- ▶ Quality of investigations is poor
 - Missing & incomplete information
 - Inability to easily review similar past investigations
- ▶ Inconsistent investigation process & Root Cause
- ▶ Not determining root cause
- ▶ Past due investigations, not being closed, get lost



Identify &
Investigate
Root Cause

➤ Challenges in Planning

- ▶ Vague root cause analysis
- ▶ Confusion over what is “corrective” and what is “preventive” action
- ▶ Inability to relate corrective actions to source problems
- ▶ Lack of integration to Change Control System



Create
Action Plan

Typical QMS Challenges (cont.)

⚡ Challenges in Review & Approval

- ▶ Not sure who needs to approve
- ▶ Approvals in serial, not parallel
- ▶ Approval process takes long time
- ▶ Lack of key stakeholder input

Review &
Approve Plan

⚡ Challenges in Implementation

- ▶ No way to track issues through workflow
- ▶ Lack of visibility to open items
- ▶ Lack of visibility to related items
- ▶ Changes to plan mid-stream
- ▶ Compliance risk

Implement
Actions

⚡ Challenges in Effectiveness

- ▶ Easy to “forget” to measure effectiveness
- ▶ Difficult to gather necessary metrics
- ▶ No means to generate metrics
- ▶ Inability to measure effectiveness does not give us any assurance if we are addressing the root cause of the problems

Verify
Effectiveness

Holistic Approach to Quality Management

- Globalize (harmonize) around a common philosophy and approach to CAPA and source Events
- Obtain full compliance with cGxPs, as well as regulatory & customer expectations
- Use quality metrics as a basis for continuous improvements
 - ▶ Trending – Problem Analysis
 - ▶ Thorough Investigations and Root Cause Analysis
 - ▶ Ensuring CAPA effectiveness
 - ▶ Bring attention to risk areas to prevent problems

Implement a centralized Quality Management System:

- Manages all inputs and outputs as well as the actual actions
- Scalable to be deployed on a global basis
- Functionality / Flexibility to meet business requirements

Re-defining CAPA

➤ Definitions

- ▶ Standardize definitions across the organization
- ▶ Terms like “deviation”, “event”, “nonconformance”, “correction”, “corrective action”, “preventive action”, “discrepancy” must be consistent for each operating unit
- ▶ The same term should have the same meaning everywhere, and drive the same process
- ▶ CAPA sources include: Complaints, Audits Observations, Trends can feed CAPA

➤ Determine, scope identification & impact of new system

- ▶ Where does the process need to change?
- ▶ Who will the system affect?
- ▶ What existing policies may change?
- ▶ Understand the difference between the “what” and the “who”

Define the Inputs & Process

Record the Event

- **Capture all related data of any event regardless of the type**
 - ▶ Source
 - ▶ Date & Time of Event
 - ▶ Type
 - ▶ Description
 - ▶ Department
- **For issues surrounding Events, utilize a quality evaluation:**
 - ▶ Quality Event only
 - ▶ Quality Event + CAPA
 - ▶ Quality Event + Investigation + CAPA + Change Control
- **Log observations / trends to implement pro-active changes**

✦ Assign Investigator

- ▶ Use “Push” or “Pull” concept
- ▶ Assess impact, consider decision tree approach

✦ Create Investigation Plan

- ▶ Use Parent-Child concepts – track each investigation “task”
- ▶ Use Investigation Templates

✦ Track & Complete Investigations

- ▶ Use workflow, due dates and reminders
- ▶ Escalation of past due investigations
- ▶ Search & Reporting
- ▶ User Dashboards

✦ Analyze Root Cause

- ▶ Structure Root cause Analysis Tree
- ▶ Use Root Cause to Drive CAPA process

CAPA Plan & Approval

- **Review currently in progress CAPAs**
- **Create CAPAs and link to root cause**
 - ▶ If multiple CAPAs identify which ones resolve which root cause?
 - ▶ Which actions must be closed to close the deviation?
- **Create an Effectiveness Plan at this time**
- **Determine Approvers**
 - ▶ Use pre-set approver functions if possible
- **Route Investigation & CAPA plan for approval**
 - ▶ Email alerts, reminders
 - ▶ Dashboards
- **Obtain Approval**
 - ▶ Ability to reject to various previous workflow states

Implementing CAPA & Effectiveness

- ✚ **Each CAPA record should have its own record and workflow**
- ✚ **Use Parent-child relationships to break up the process into “smaller bites”**
 - ▶ Action Item Tracking
- ✚ **Track completion and verification of each CAPA**
 - ▶ Use workflow, due dates and reminders
 - ▶ Escalation of past due investigations
 - ▶ Search & Reporting
 - ▶ User Dashboards
- ✚ **Measure effectiveness according to the plan -> evidence that root cause has been eliminated**

Important QMS Requirements

High Level Requirements

Defining the Requirements

Centralized database

Handles all process areas - modular

Workflow driven

Proactive user notification and escalation

Action items management

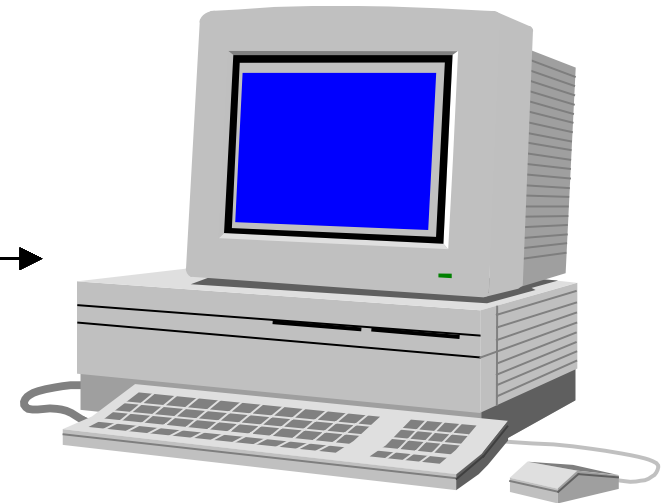
Querying & Reporting

Elaborate security by user-group

Management reports

Performance Metrics & Trending

Part 11 Compliance



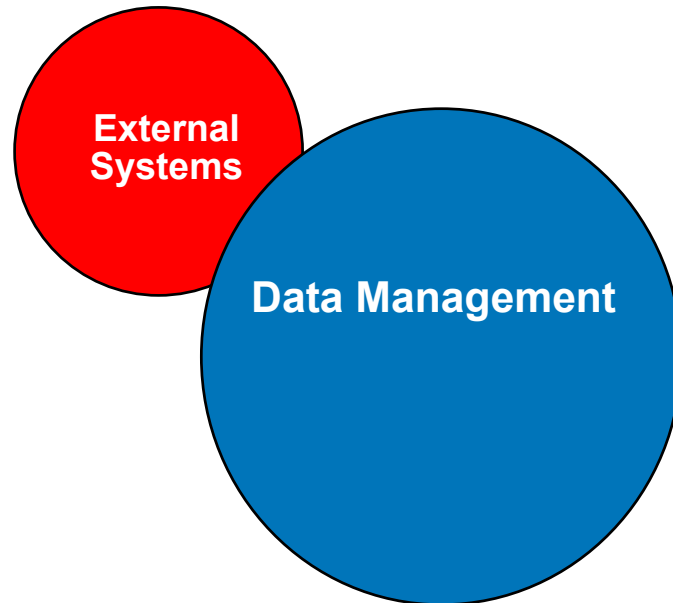
Management of all Data

➤ **Modular approach to handling all source areas but maintains individual requirement**

- ▶ Multiple “Record Types” to handle all process areas
- ▶ Ability to create user defined fields
- ▶ Configurable data entry forms
- ▶ Validation and business rules

➤ **Integration to external systems**

- ▶ E.g., Create deviations automatically from ERP
- ▶ E.g., Create OOS Investigation from LIMS
- ▶ Master data (customer, product/item, etc.)

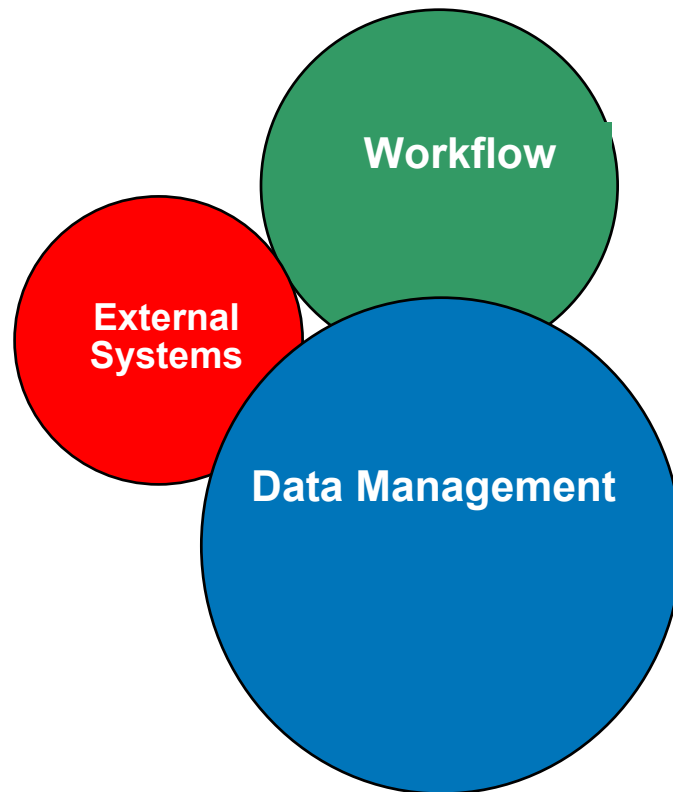


➤ Configurable workflow

- ▶ Automate review and approval process based on meta data
- ▶ Business-rule based workflows
- ▶ Parallel Approvals
- ▶ Process changing activity
- ▶ E-mail notifications

➤ Integrated source areas process to Corrective Action process

- ▶ Parent – child relationships
- ▶ Cross referencing



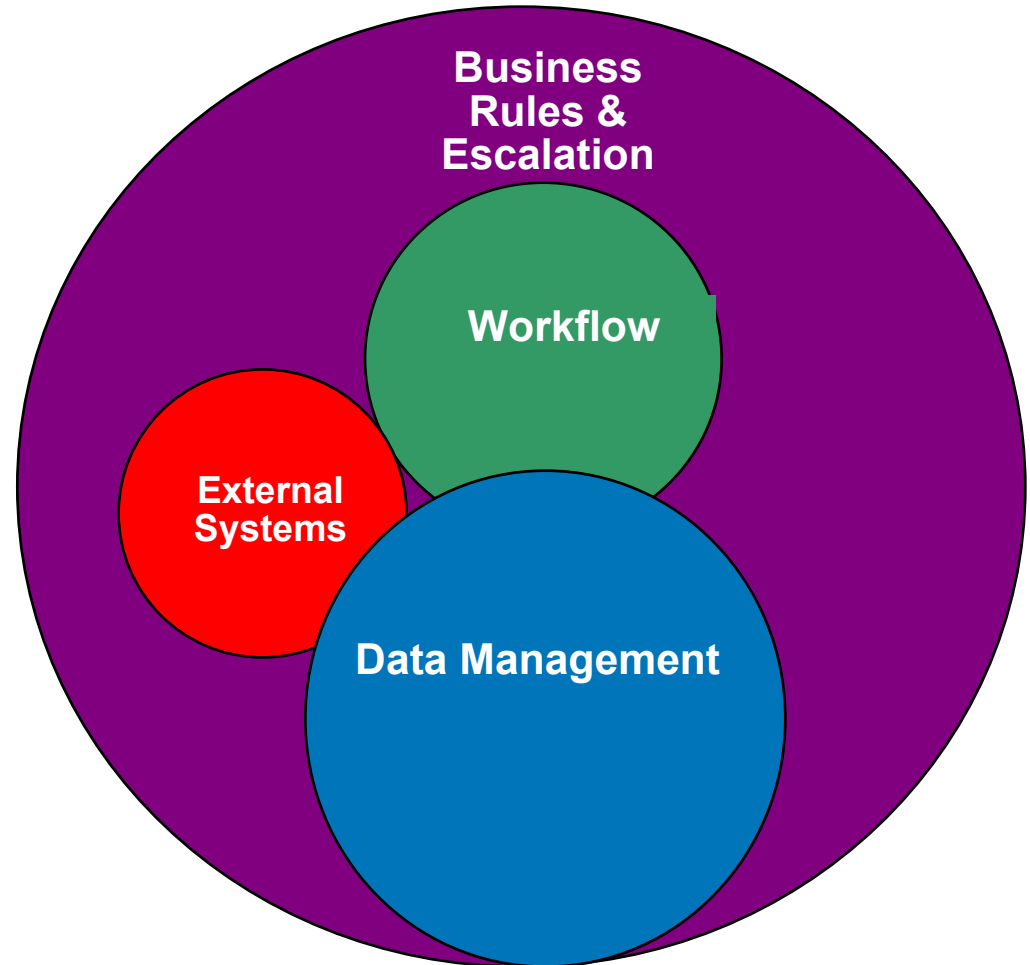
Escalations and Business Rules

Business rules enforcement

- ▶ Date Due, Milestone Dates
- ▶ Automatically assigning investigators, reviewers, approvers
- ▶ Automatically scheduling tasks based on type of Record

Escalation

- ▶ “Reminders” of tasks reaching expected completion date
- ▶ Escalation of CAPA past due



Query, Reporting, Trending

Querying

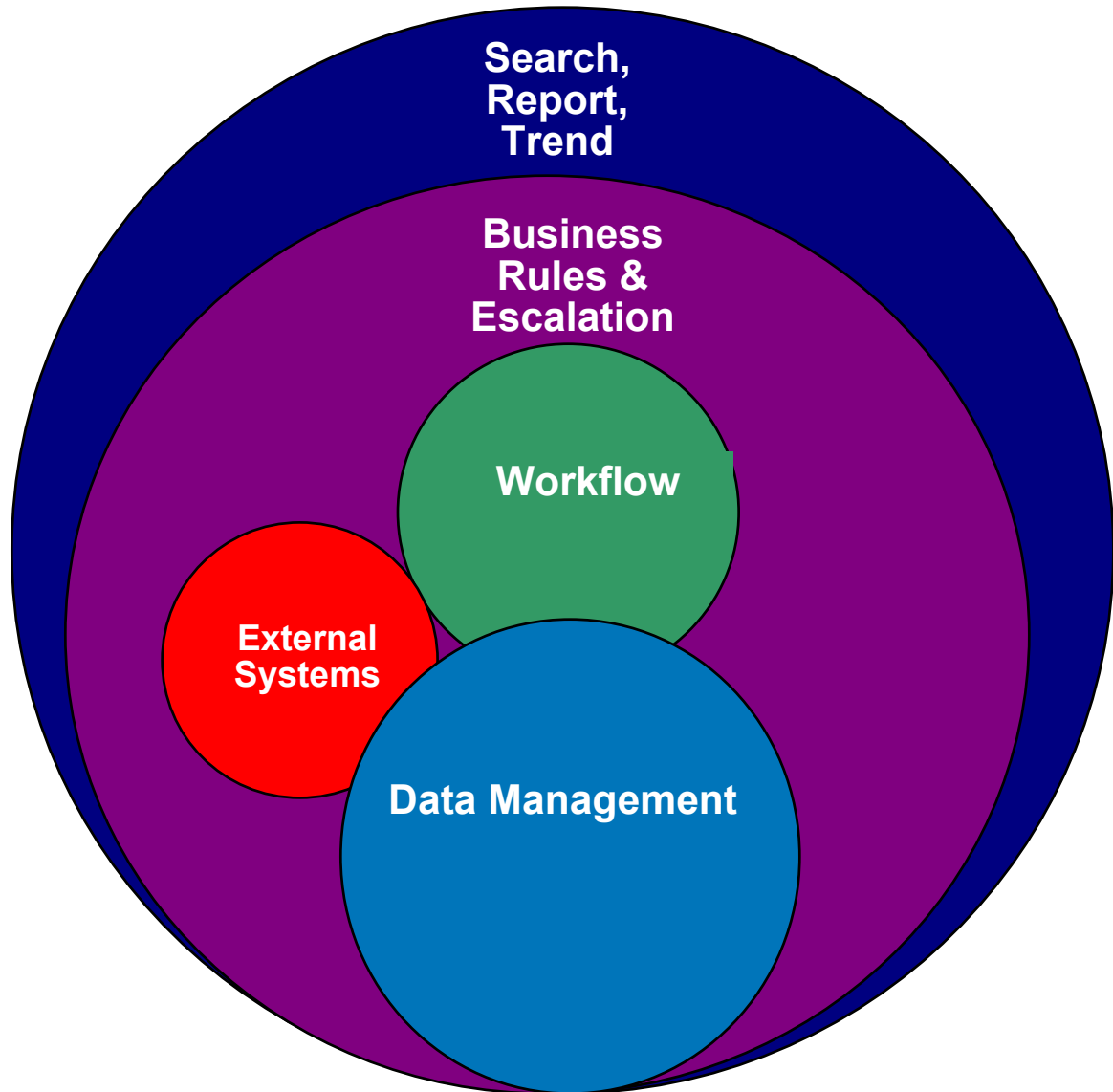
- ▶ Ability to query on all fields
- ▶ Full text / search engine functionality
- ▶ Ability to save searches

Reporting

- ▶ Customizable report format
- ▶ On screen view, print, email, save
- ▶ Status reporting

Trending

- ▶ Across all sites
- ▶ Across all source areas
- ▶ Root cause analysis
- ▶ Identify occurrence rate decrease / increase
- ▶ Ability to detect trends automatically



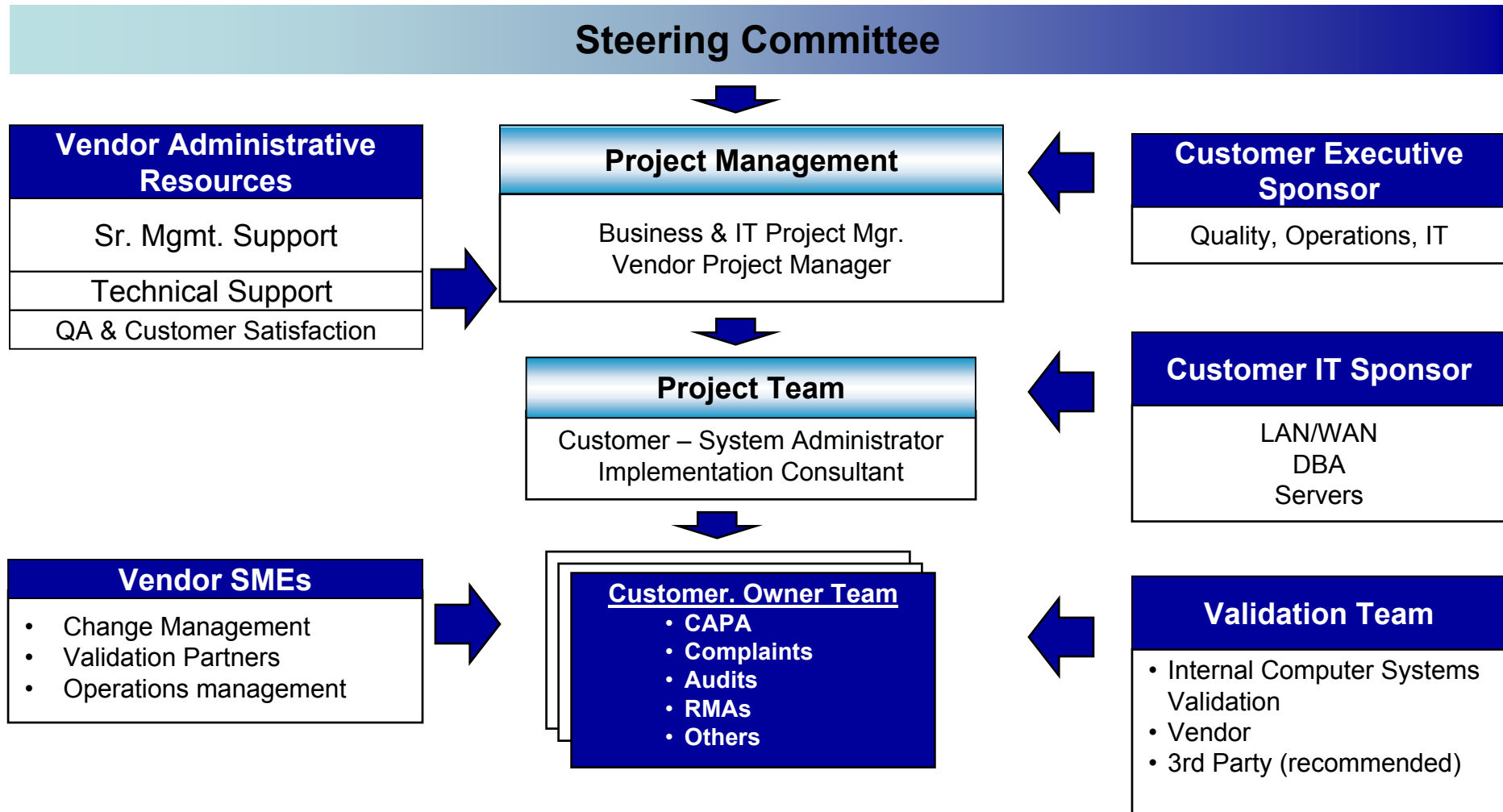
Compliance with Part 11

- Does the system conform with your firm's Part 11 requirements?
- Has the software "passed" the test, i.e., has it gone through FDA audits at another firm?
- Can it be validated?
- How confident are you in the above assessment?

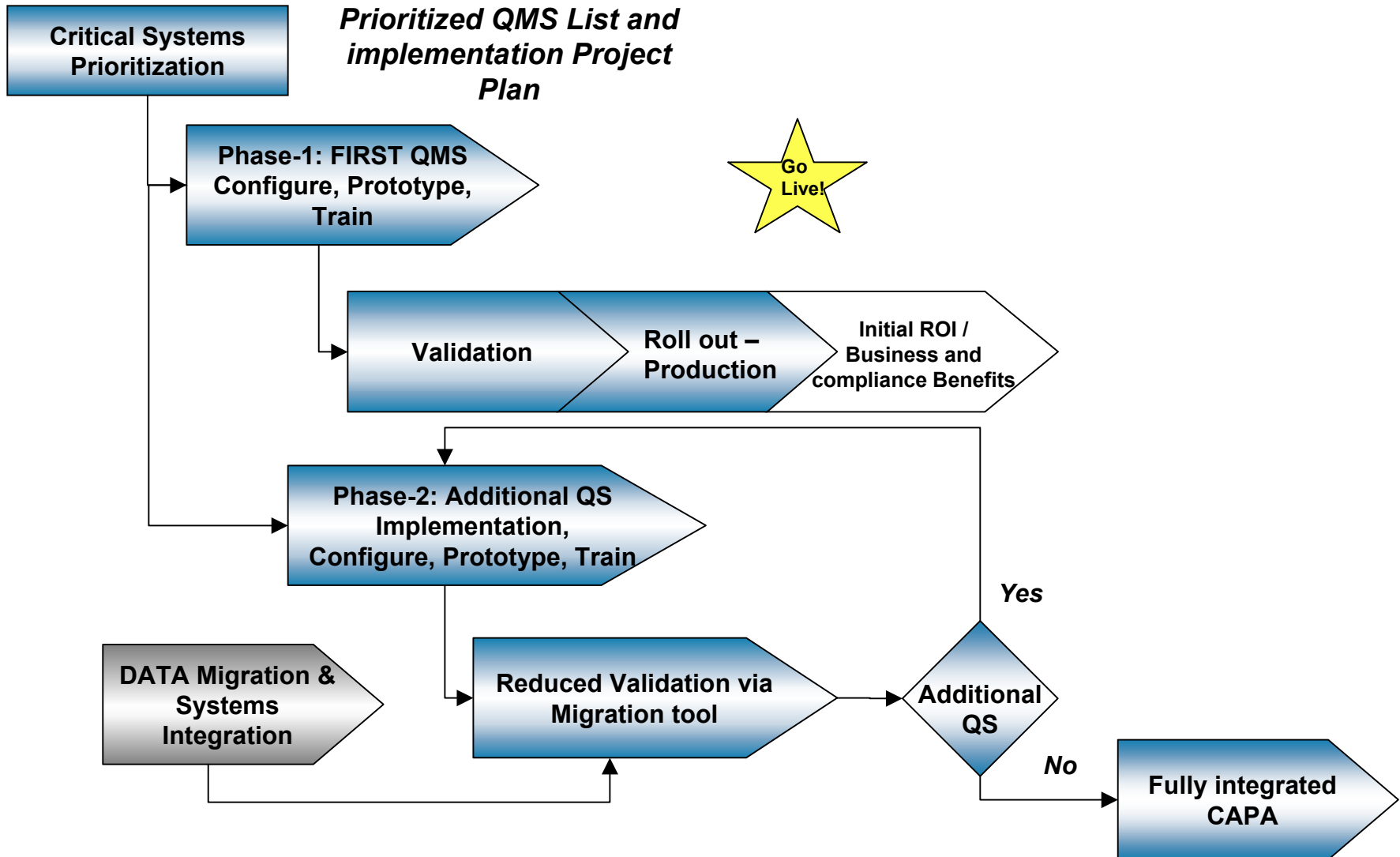
- Full audit trail
- Reporting features
- Configurable security groups
- Complete record of created and modified data
- Enforced workflow sequencing
- Password composition rules
- Electronic Signatures made up of two unique components
- Password aging/expiration
- Cannot re-use previous password
- Account Locking and Admin Notification after failed log-in Attempts
- Session time-out
- Requirement of "reason" for data modification
- Administrator / Configuration Audit Trail

Implement Solution

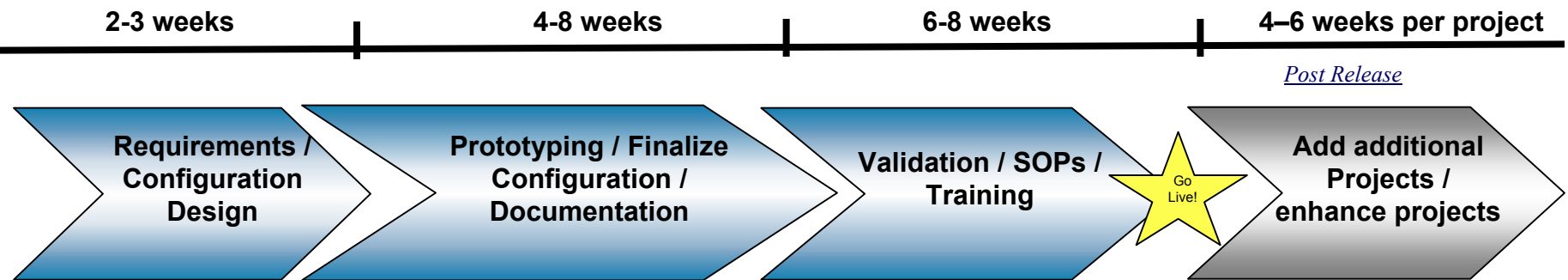
Structured Project Organization



Rapid ROI - Phased Approach



Implementation Schedule



- Product Orientation
- Detailed "As Is" of current processes, organization and systems
- Visioning session for "to-be" concepts
- System Configuration Design
- Installation of Development Environment
- Configure Prototype 1
- Project Team Workshop-1
- Configure Prototype 2

- Project Team Workshop-2
- Finalize Configuration Design
- Reports Customization
- Train on Validation Templates
- Develop Validation Protocols
- Complete setup of integration tools
- Develop User Requirement Definition
- Functional specifications
- Initial validation activities

- Install Production
- Execute and approve IQ
- Execute and approve OQ
- Execute and approve PQ
- Complete validation protocol
- Create Training Materials
- Revise SOPs
- Train Super Users
- Train Users
- Train Help Desk
- Roll out phase

- Support application
- Enhance configuration
- Add additional project areas to support additional needs
- PQ
- Leverage Migrator for reduced validation
- Roll out phase

Conclusion

Conclusion (cont.)

- QMS encompasses the overall process related to events / observations from multiple sources, as well as their investigations, and resolutions
- A “best practices” QMS system requires a single, scalable system, which uses a holistic approach
- Implementing a global QMS system may require your organization to change how it defines CAPA as well as it how it conducts the CAPA process
- Implementing a system can be successfully accomplished by using established software, a harmonized approach, and an organized project structure

