Establishing the Quality Unit and Quality System

Management Introduction

What, Why and Why Now

- Smart science, smart business, smart ethics
  - Ensure that product design cost-effectively delivers on the target product profile
- Compliance with Federal Regulations
  - Ensure appropriate safety, identity, strength, purity and quality
- Add value to and protect value of company assets
  - Investors / partners need to be comfortable that all registration enabling information is defendable
    - Data supporting going into man
    - Data in man
  - Regulators need assurance of data integrity for all regulatory submissions
  - Avoid rework, delay, clinical hold, approval issues

How FDA Works

- The FDA can not be present at all times so Quality Unit is their surrogate
  - Independence of QA and management support required
- Requires industry to run by procedures
  - If not performed according to procedure, investigation must be conducted
- Equipment, processes, and test methods must work same way every time
  - Requires qualification and validation
  - Changes must be controlled
- People must be qualified and trained to do their jobs
- Everything must be documented
  - Allows review of documents during inspections to verify how work was conducted
- Overarching Philosophy is that Quality should be built into the product
  - Testing alone cannot be relied on to ensure product quality.

Phase Appropriate Application

R&D / Preclinical	Phase I	Phase II	Phase III	Commercial
GDP, GLP, Early GMPs & GCP			Full GMP	
TPP	Target range	→	Locked for registration	
Process	Safe, repeatable supply Basic process knowledge	→	Robust, well understood, Scale & failure modes managed	
Specs	Broad but safe	→	Tight and controlled	
Stability	Consistent dosing	→	Shelf life	
Methods	Qualified	→	Validated	
Equipment	Calibrated	→	Qualified	
Quality System	More general, selective SOPs Narrower scope under SOPs	→	More detailed and specific SOPs Broader scope under SOPs	

As you gather product and process knowledge through experience

Management Implications

- Consistently follow the right SOPs, leverage vendor quality system detail but remember that the sponsor owns the outcome
- Its all about Documentation
  - Activities & Outcomes
  - Changes
  - Approvals
- Management Responsibility
  - Quality Policy
  - Quality Planning
  - Resource Management
  - Internal Communication
  - Management Review
  - Oversight of Outsourced Activities

Pharmaceutical Quality System

- Applies and is developed throughout the product lifecycle
  - Pharmaceutical Development
  - Technology Transfer
  - Manufacturing
  - Product Discontinuation
- FDA Objectives
  - Achieve Product Realization
  - Establish and Maintain a State of Control
  - Facilitate Continual Improvement
  - Enablers
  - Knowledge Management
  - Quality Risk Management

What Do GLP and GMP Cover?

GLP

in vivo and *in vitro* Testing

- "… for conducting nonclinical laboratory studies that support…applications for research or marketing permits for products regulated by FDA…"
- In vivo or in vitro experiments in which test articles are studied prospectively in test systems under laboratory conditions to determine their safety.
- Does not include studies……to determine physical or chemical characteristics of a test article.

GMP

Development and Manufacture

- Methods, facilities, controls for, the manufacture, processing, packing, or holding of a drug to assure safety, identity and strength and meets the quality and purity that it purports to …possess
- …contain the minimum current good manufacturing practices for preparation of drug products for administration to humans and animals.
- Nothing is "manufactured under GLP". Material for GLP studies can be either non-GMP or GMP depending on manufacturing strategy.

Required Elements of the System

- Process Performance
- Product Quality Monitoring
- Corrective and Preventive Action (CAPA)
- Change Management
- Management Review

Quality System scope and specificity will evolve as the company progresses through development

GLP and GMP System Elements

Common Elements Documented Test Procedures, Standards/Chemicals, Lab Records Training, Equipment Qualification & Calibration	
GLP Unique Elements	**GMP Unique Elements**

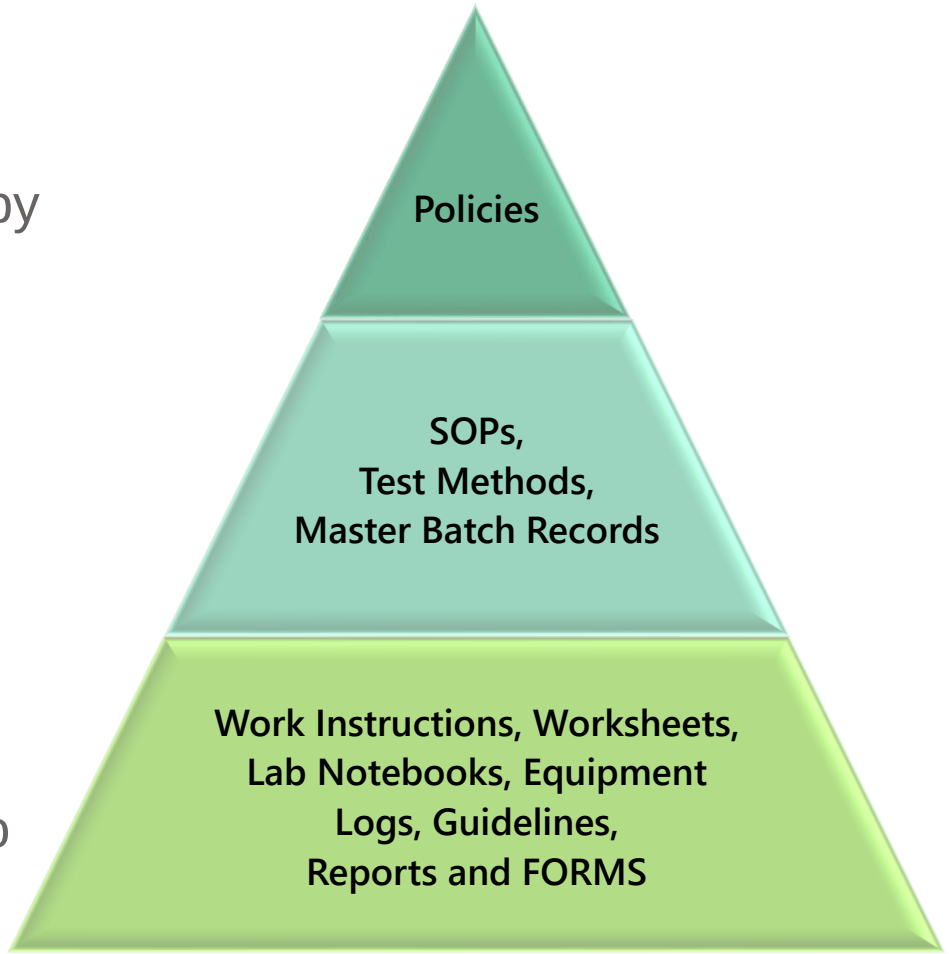
• Study Related:
  • Designated Study Director
  • Master Schedule
  • Study Protocols & sign-off
  • In-process / in-study Inspection
	• Product-related:
	  • Manufacture
	  • Processing
	  • Packing
	  • Testing of Product Quality
	  • Holding
	  • Preparation for administration

Key Initial Elements to Implement

Priority	Core SOPs
Core to Set up the System	• Quality Unit Responsibilities
	• Document Control - Creation, Format, Approval and Issuance of Modifications, Control & Distribution of Controlled Documents
	• Change Control
	• Management & Employee Quality Responsibilities
	• Good Documentation
	• Training
Core to Set up Vendors	• Contractors - Approval of GXP Contractors & Consultants
	• Auditing
	• Content, Generation and Maintenance of Quality Agreements
Core to Execute with Vendors	• Development and Control of Specifications & Stability
	• Batch Disposition - i.e. Review, Approval and Disposition of Clinical Materials
	• Deviations
	• Non-conforming Material - Material Review Board
	• Corrective and Preventive Actions
Follow-On	• Other areas to be controlled by Policy rather than SOP • Clinical specific SOPs • Assembly of a Quality Manual • Additional Phase-appropriate additions and revisions as needed

Document Links for Quality System

- Policy document describes the “what” and “general how” and may or may not be supported by additional procedures.
- SOPs, describe the “how” by outlining the steps to ensure control
- Work sheets, lab notebooks, equipment logs, etc., are documents for real time data to be entered.



Quality Manual for the Quality System

- As the SOPs are developed, we will assemble the Quality Manual
  - Quality Policy
  - Scope of Quality System
  - Process maps and flow charts to show sequences, linkages and interdependencies of processes in Quality System
  - Management responsibilities
- As you review the SOPs don't worry, they can and will be revised / updated
  - The system and SOPs will evolve as the company progresses through the phases of development

Thanks!

Management commitment and focus on the Quality System helps reduce risk and progress the programs!

We hope this was helpful!

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