QUALITY MANAGEMENT SYSTEM

FROM THEORIES TO PHARMACY PRACTICE

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Scope of Discussion

Part 1
1. What is Quality Management System? Definition / History

Part 2
2. What are the benefits / advantages of having a QMS?

Part 3
3. What are the current PFDA Regulations?

Part 4
4. Applications to various Pharmacy Practice
   - Industry (R&D, Manufacturing, Importer, Distributor); Clinical Trials/ Studies; Retailing (Drugstores, Hospital, Industrial Pharmacy)

Part 5
5. How should you get started?
   - Building your QMS
   - Structured QMS Documentation
   - QMS Documentation Hierarchy
   - Three Core Values in Implementing QMS
   - Verifying your QMS Implementation

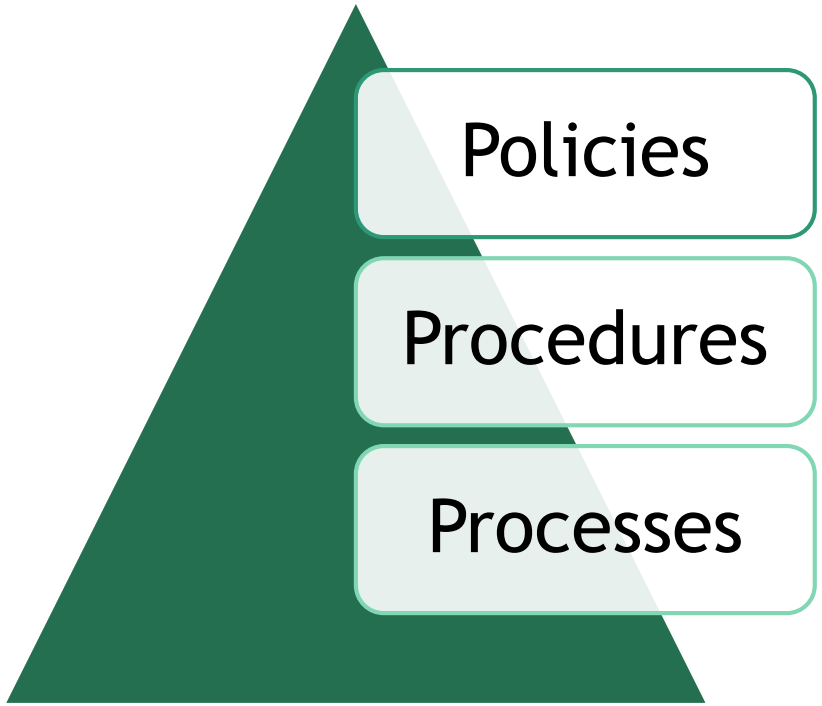
Part 6
6. Conclusions

Part 1

Introduction: Quality Management System (QMS)

- What is QMS?

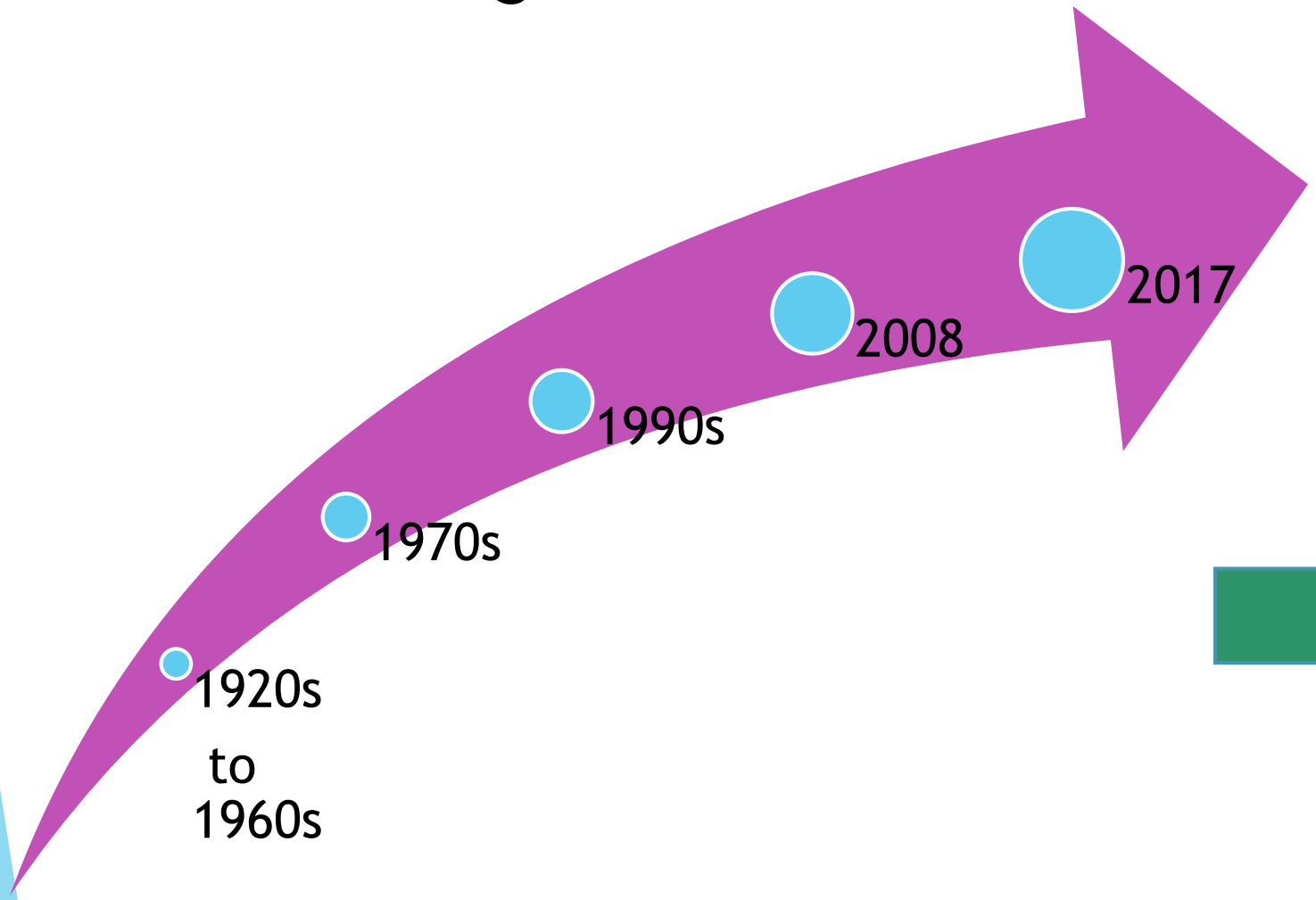
  QMS is a structured collection of policies, processes, documented procedures and records and their associated responsibilities.



Part 1

Introduction: Quality Management System (QMS)

Historical Background:



EXCELLENT QUALITY PRODUCT OR SERVICE

Part 2

What are the benefits of QMS?

- Simplify
- Clarify
- Control

Part 2

What are the benefits of QMS?

Simplify

- Structured and written policies, processes and procedures
- Opportunities to review and help the organization become more competitive
- Improved communication within the organization
- Structured approaches in correcting defects, mistakes or deviations
  - CAPA are consistently undertaken based on priority and risk
  - CAPA process ensures higher risk problems and issues are promptly and properly dealt with
- Improved complaint handling results to better customer satisfaction

Part 2

What are the benefits of QMS?

Clarify

- QMS clarifies roles and responsibilities
- QMS helps understand the internal processes and how these processes link together
- Employees understand where their contribution fits in the big picture
- QMS will drive consistency in the various processes, as well as, continuous improvement

Part 2

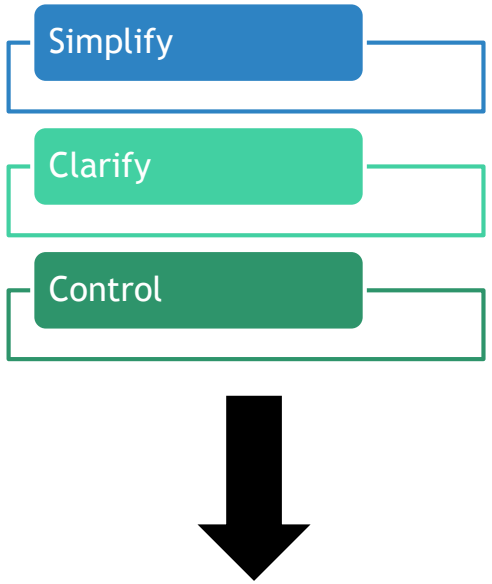
What are the benefits of QMS?

Control

- Control processes for better effectiveness and to increase efficiency
- Measure, monitor and encourage continuous improvement in quality and productivity which will become part of the organization culture
- Involvement of top management
  - Regular measurement, training and reporting to executive management of critical indicators

Part 2

What are the benefits of QMS?



- Better quality of products and services
- Lesser waste of resources (time and materials)
- Improved customer satisfaction
- Improved profitability and improved bottom line

Part 3

Regulatory Requirements

AO 2012-0008 (dated Jun 25, 2012) Adoption and implementation of the Pharmaceutical Inspection Cooperation Scheme (PIC/S) Guides for the Good Manufacturing Practice (GMP) for Medicinal Products (effectivity date: July, 2013)

- **PIC/S Guide to GMP (PE 009-13, 1 January, 2017)**

AO 2013-0027 Adoption & Implementation of the WHO Annex 5 on GDP & Annex 9 on GSP for Pharmaceutical Products, issued Oct. 2, 2013 (effective Oct. 17, 2014)

- Annex 5 - WHO Good Distribution Practices for Pharmaceutical Products WHO Technical Report Series, No. 957, 2010
- Annex 9 - WHO Good Storage Practices for Pharmaceutical Products WHO Technical Report Series, No. 908, 2003

AO 2014-0034 (dated Oct. 13, 2014) Rules and Regulations on the Licensing of Establishments in the Manufacturer, Conduct of Clinical Trial, Distribution, Importation, Exportation, and Retailing of Drug Products

Part 3

Regulatory Requirements

AO 2013-0027 Adoption & Implementation of the WHO Annex 5 on GDP & Annex 9 on GSP for Pharmaceutical Products, issued Oct. 2, 2013 (effective Oct. 17, 2014)

- Annex 5 - WHO Good Distribution Practices for Pharmaceutical Products WHO Technical Report Series, No. 957, 2010
- Annex 9 - WHO Good Storage Practices for Pharmaceutical Products WHO Technical Report Series, No. 908, 2003

Specific Objective

To use the WHO Guide to GDP and GSP as the standard in assessing GDP and GSP compliance of drug establishments and retailers.

Scope:

This order shall apply to FDA and Drug Establishments and Retailers.

Definition of Terms:

"Retailer" means any establishment which sells or offers to sell any health product directly to the general public.

Part 3

Regulatory Requirements

AO 2013-0027 Adoption & Implementation of the WHO Annex 5 on GDP & Annex 9 on GSP for Pharmaceutical Products, issued Oct. 2, 2013 (effective Oct. 17, 2014)

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Chapter 6 (Annex 5) Quality Management

1. There should be a documented quality policy describing the overall intentions and policies of the distributor regarding quality, as formally expressed and authorized by management.
2. Quality Management should include:
   - An appropriate infrastructure or "quality system" is in place
   - Systematic actions
   - Cover the main principles of quality assurance
   - Defined shared responsibility for the quality and safety of products
   - Authorized procurement and release procedures
   - Traceability of products
   - Authorized SOPs for all administrative and technical operations

Part 3

Regulatory Requirements

AO 2014-0034 (dated Oct. 13, 2014) Rules and Regulations on the Licensing of Establishments in the Manufacturer, Conduct of Clinical Trial, Distribution, Importation, Exportation, and Retailing of Drug Products

Specific Objectives

To establish rules and regulations in the licensing of drug establishments to align with the recently promulgated laws and regulations;

To ensure compliance of establishments to FDA and international standards and requirements of the following, but not limited to, GMP, GDP, GSP, and Good Clinical Practice.

Scope:

This order shall apply to establishments in the country, including local government units, government owned and controlled operations other government offices and instrumentalities engaged in the manufacture, distribution, importation, exportation, sale, offer for sale and transfer of drug product. This shall also apply to Contract Research Organizations (CROs) and/or Sponsors engaged in the conduct of clinical trials.

Definition of Terms:

"Clinical Trial" refers to any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamics effects of an investigational product (s)…. With the object of ascertaining its safety and/or efficacy.

Part 3

Regulatory Requirements

AO 2012-0008 (dated Jun 25, 2012) Adoption and implementation of the Pharmaceutical Inspection Cooperation Scheme (PIC/S) Guides for the Good Manufacturing Practice (GMP) for Medicinal Products (effectivity date: July, 2013)

Specific Objective

To use the PIC/S Guide as the standard in assessing GMP compliance of drug establishments.

Scope:

This order shall apply to FDA and Drug Establishments.

Definition of Terms:

"Drug Establishment" refers to drug manufacturers/ repackers, drug importers, drug distributors, drug wholesaler or drug exporter and entities belonging to definition of establishment.

"Establishment" means a sole proprietorship, a partnership, a corporation, an institution, an association, or an organization engaged in the manufacture, importation, exportation, sale, offer for sale, distribution, donation, transfer, use, testing, promotion, advertising, or sponsorship of health products including the facilities and installation needed for its activities.

Part 3

PIC/S GMP (2009 vs 2017)

AO 2012-0008 (dated Jun 25, 2012) Adoption and implementation of the Pharmaceutical Inspection Cooperation Scheme (PIC/S) Guides for the Good Manufacturing Practice (GMP) for Medicinal Products (effectivity date: July, 2013)

	PE-009-13	PE-009-09
Date effective	January, 2017	Sept., 2009
Chapter 1 - Title	Pharmaceutical Quality System	Quality Management
Sections:	Principle	Principle
	Pharmaceutical Quality System	Quality Assurance
	Good Manufacturing Practice	Good Manufacturing Practice
	Quality Control	Quality Control
	Product Quality Review	Product Quality Review
	Quality Risk Management	Quality Risk Management

Part 3

Scope of PIC/S GMP

(PIC/S Guide to GMP (PE 009-13, 1 January, 20

AO 2012-0008 (dated Jun 25, 2012) Adoption and implementation of the Pharmaceutical Inspection Cooperation Scheme (PIC/S) Guides for the Good Manufacturing Practice (GMP) for Medicinal Products (effectivity date: July, 2013)

Part 3

Pharmaceutical Quality System

- PIC/S Guide to GMP (PE 009-13, 1 January, 2017)

PHARMACEUTICAL QUALITY SYSTEM

Principle:

Quality objective:

- Ensure that medicinal products are fit for intended use
- Comply with the requirements of the MA
- Do not put patients at risk due to inadequate safety, quality or efficacy.

Responsibility of:

Senior management with the participation and commitment of everyone: its employees, suppliers and distributors

Part 3

Pharmaceutical Quality System

- PIC/S Guide to GMP (PE 009-13, 1 January, 2017)

How to achieve the PQS objectives:

- There must be a comprehensively designed and correctly implemented PQS incorporating GMP and QRM
- Should be fully documented and its effectiveness monitored
- Adequately resourced with competent personnel
- Suitable and sufficient premises, equipment and facilities

Part 3

Pharmaceutical Quality System

- PIC/S Guide to GMP (PE 009-13, 1 January, 2017)

1.1 Quality Management is -

- It is a wide-ranging concept, which covers all matters, which individually or collectively influence the quality of a product.
- It is the sum total of the organized arrangements made with the objective of ensuring that medicinal products are the quality required for their intended use.
- Quality Management therefore incorporates Good Manufacturing Practice.

Part 3

Pharmaceutical Quality System

- PIC/S Guide to GMP (PE 009-13, 1 January, 2017)

1.2 GMP applies -

- To the lifecycle stages from the manufacturer of investigational products, technology transfer, commercial manufacturing through product discontinuation.

Part 3

Pharmaceutical Quality System

- PIC/S Guide to GMP (PE 009-13, 1 January, 2017)

1.3 When developing your own PQS -

- Consider the size and complexity of the company's activities.
- The design of the system should incorporate appropriate risk management principles including the use of appropriate tools.
- Ensure that the effectiveness of the system is demonstrated.

Part 3

Pharmaceutical Quality System

- PIC/S Guide to GMP (PE 009-13, 1 January, 2017)

1.4 PQS requirements appropriate for the manufacture of medicinal products.

Part 3

Pharmaceutical Quality System

- PIC/S Guide to GMP (PE 009-13, 1 January, 2017)

1.5 Responsibility of senior management:

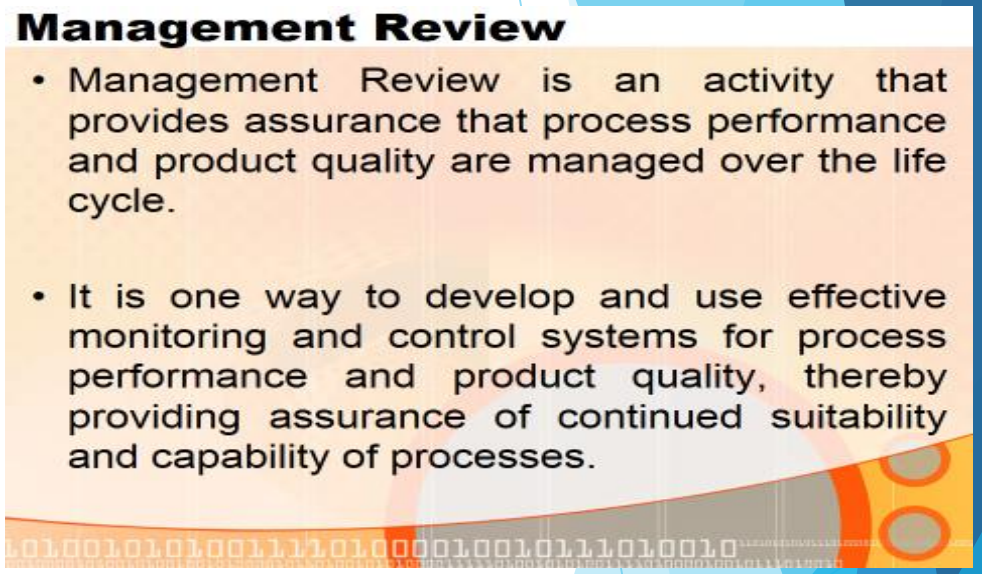
1. Ensure an effective PQS is in place,
2. Adequately resourced and that roles, responsibilities, and authorities are defined,
3. PQS is communicated and implemented throughout the organization

Part 3

Pharmaceutical Quality System

- PIC/S Guide to GMP (PE 009-13, 1 January, 2017)

1.6 Management Review



- MR should be periodic
- Involvement of senior management
- On the operation of the PQS

- Purpose: to identify opportunities for continual improvement of products, processes and the system itself

Part 3

Pharmaceutical Quality System

- PIC/S Guide to GMP (PE 009-13, 1 January, 2017)

1.7 PQS should be defined and documented.

- Quality Manual or equivalent documentation should be established. It should contain a description of the QMS including management responsibilities.

Part 3

Pharmaceutical Quality System

- PIC/S Guide to GMP (PE 009-13, 1 January, 2017)

1.8 GMP as part of QMS (covering the 11 requirements)

1.9 Quality Control as part of GMP (covering the 8 requirements)

1.10 to 1.11 Product Quality Review (covering the 12 requirements)

1.12 Quality Risk Management

QRM is a systematic process for the assessment, control, communication and review of risks to the quality of the medicinal product. It can be applied both proactively and restrospectively.

1.13 The principles of QRM are that:

a. **The evaluation of the risk to quality is based on scientific knowledge, experience with the process and ultimately links to the protection of the patient;**

b. **The level of effort, formality and documentation of the QRM processes is commensurate with the level of risk.**

Part 4

Applications to Various Pharmacy Practice

AO 2014-0034 (dated Oct. 13, 2014) Rules and Regulations on the Licensing of Establishments in the Manufacturer, Conduct of Clinical Trial, Distribution, Importation, Exportation, and Retailing of Drug Products

- Industry
  - R&D and Manufacturer
  - Repacker
  - Importer / Trader
  - Distributor
- Contract Research Organization (CRO)
- Retailing (Community Drugstore/ Hospital / Institutional/ RONPD*)

*RONPD – Retail Outlet for Non-Prescription Drugs includes drug establishment such as supermarket, convenient store and other similar establishment authorized to sell only identified Over-The-Counter (OTC) and household remedy products directly to the general public on a retail basis). Also reclassified by FDA as RONPD are the Boticas ng Barangay.

Part 4

Applications and Practice

SCOPE OF PIC/S GMP	R&D/MFG/ REPACKER	IMPORTER / TRADER	DISTRIBU-TOR	CRO	RETAILING
PHARMACEUTICAL QUALITY SYSTEM	✓	✓	✓	✓	✓
PERSONNEL	✓	✓	✓	✓	✓
PREMISES & EQUIPMENT	✓	✓	✓	✓	✓
DOCUMENTATION	✓	✓	✓	✓	✓
PRODUCTION	✓	x	x	x	x
QUALITY CONTROL	✓	✓	✓	✓	✓
OUTSOURCED ACTIVITIES	✓	✓	✓	✓	✓
COMPLAINTS & RECALLS	✓	✓	✓	✓	✓
SELF INSPECTION	✓	✓	✓	✓	✓

Legend: ✓ Applicable x Not Applicable

Part 4

Applications and Practice

SCOPE OF PHARMACEUTICAL QUALITY SYSTEM (PQS)	R&D/MFG/ REPACKER	IMPORTER / TRADER	DISTRIBU-TOR	CRO	RETAILING
Principle - Drugs are fit for use - Comply with MA/LTO requirements - Do not put patients at risk	✓	✓	✓	✓	✓
Requirements:					
1. Quality Management in place - influence product quality	✓	✓	✓	✓	✓
2. GMP applies to the lifecycle of the product	✓	✓	✓	✓	✓
3. Size & complexity - fit for purpose	✓	✓	✓	✓	✓
4. PQS for the manufacture of drug product	✓	*x*	*x*	*x*	*x*

Legend: ✓ Applicable *x* Not Applicable

Part 4

Applications and Practice

SCOPE OF PHARMACEUTICAL QUALITY SYSTEM (PQS)	R&D/MFG/ REPACKER	IMPORTER / TRADER	DISTRIBU-TOR	CRO	RETAILING
5. Role of Senior Management – as ultimate responsible	✓	✓	✓	✓	✓
6. Periodic Management Review	✓	✓	✓	✓	✓
7. PQS defined and documented, e.g. Quality Manual	✓	✓	✓	✓	✓
8. GMP as part of Quality Management	✓ all	✓ iii to xi	✓ iii to xi	✓ iii to xi	✓ iii to xi
9. Quality Control as part of GMP	✓	x	x	x	x
10. Product Quality Review – conduct & evaluate results	✓ all	✓ iv to xii, except vii, ix, xi	✓ Iv, v, viii, xi, xii	x	x
11. Quality Risk Management – apply QRM where possible	✓	✓	✓	✓	✓

Part 4

Applications and Practice

	R&D/MFG/ REPACKER	IMPORTER / TRADER	DISTRIBU-TOR	CRO	RETAILING	ACADEME (CP)
Category of activity	Goods producing	Service	Service	Service	Service	Service
Activity/ "Product"	Manufacture quality drugs	Sell quality drugs	Deliver quality drugs	Execute quality study	Dispense quality drugs	Provide high quality education
Applicable GXP/ *Accreditation	GMP, GLP, GSP, GDP	GMP, GSP, GDP	GMP, GSP, GDP	GCP, GSP, GDP	GPP, GSP, GDP, GMP	*PAASCU
Sample processes	Manufacturing Packaging Testing Warehousing Product Complaints, Recalls, Investigations, Annual Product Review, Management Rev, Internal Quality Audit, Auditing of suppliers	Warehousing Quality oversight to TPC; APR, MR, IQA, Product Complaints, Recalls, Investigations, Auditing	Receiving of stocks; Warehousing; Distribution; Quality Oversight to Third Party Contractors, MR, IQA, Product Recall, Complaints, Investigations	Receiving of stocks; Warehousing; Distribution; Quality Oversight to TPC, MR, IQA, Product Recall, Complaints, Investigations	Receiving of stocks; Warehousing; Dispensing; MR, IQA, Product Recall, Complaints, Investigations	Management Review, Internal Audit, Complaints, Investigations And other relevant processes of its operations

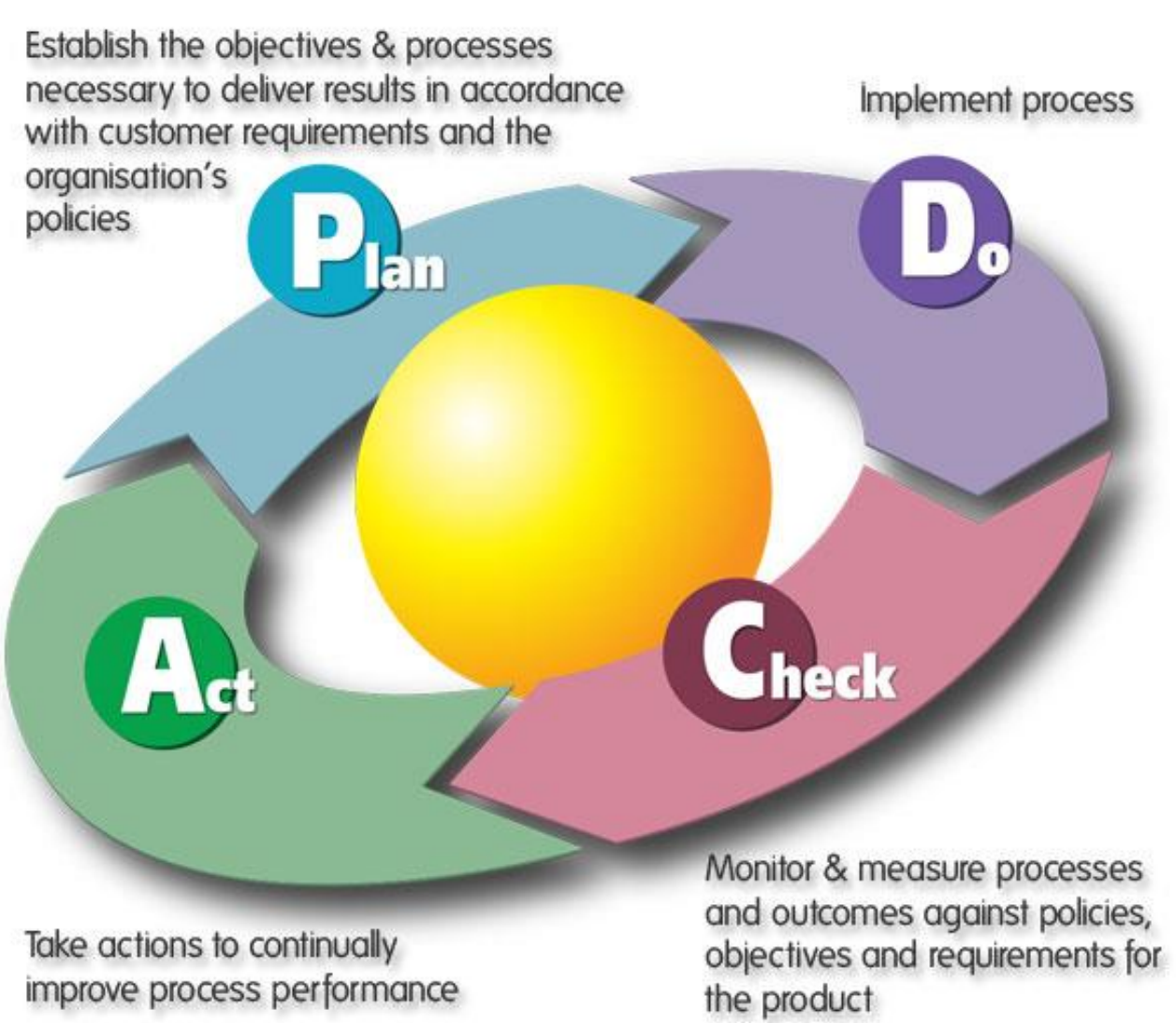
*Goods producing industry - industry which creates some kind of tangible object; ex. manufacturing, agriculture, construction
Service industry - include everything else; ex. banking, communications, wholesale and retail trade, all professional services

Part 4

Applications and Practice

The PDCA Cycle – the process approach

QUALITY
RISK
MANAGEMENT



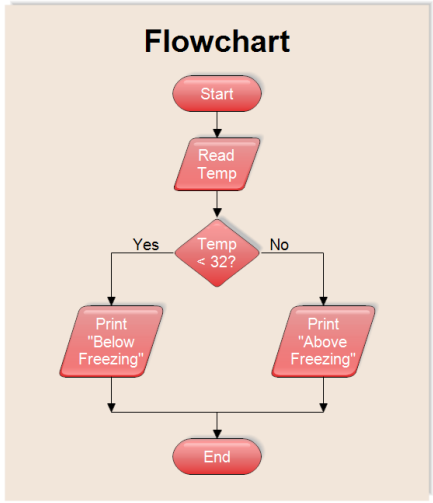
Part 4 Applications and Practice

Process Approach

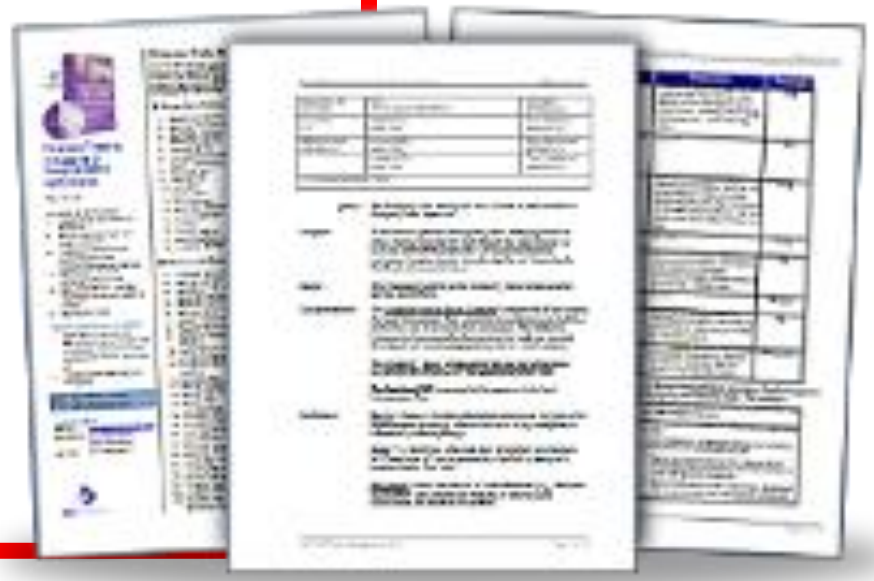
Is there a standard way of describing a process?

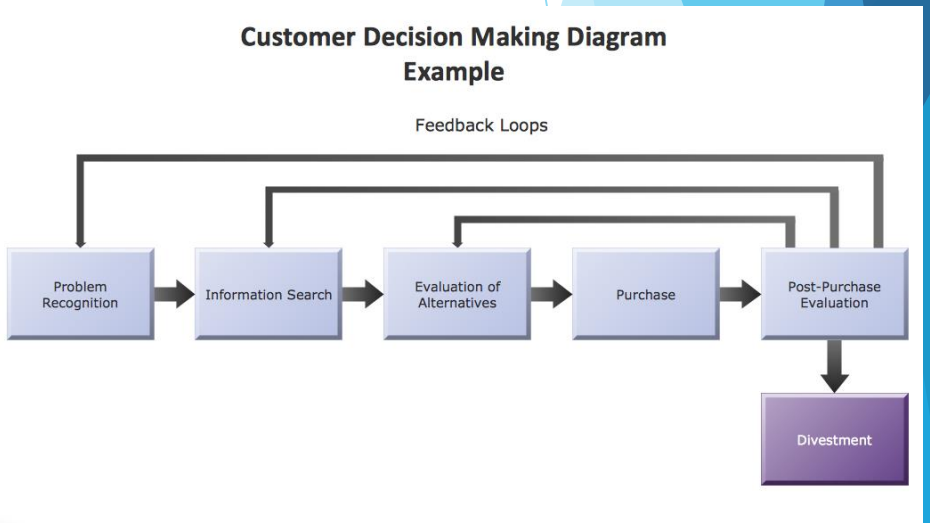
There is no standard way to describe a process.

- Flowchart
- Block diagram
- Responsibility matrix
- Written procedures
- pictures



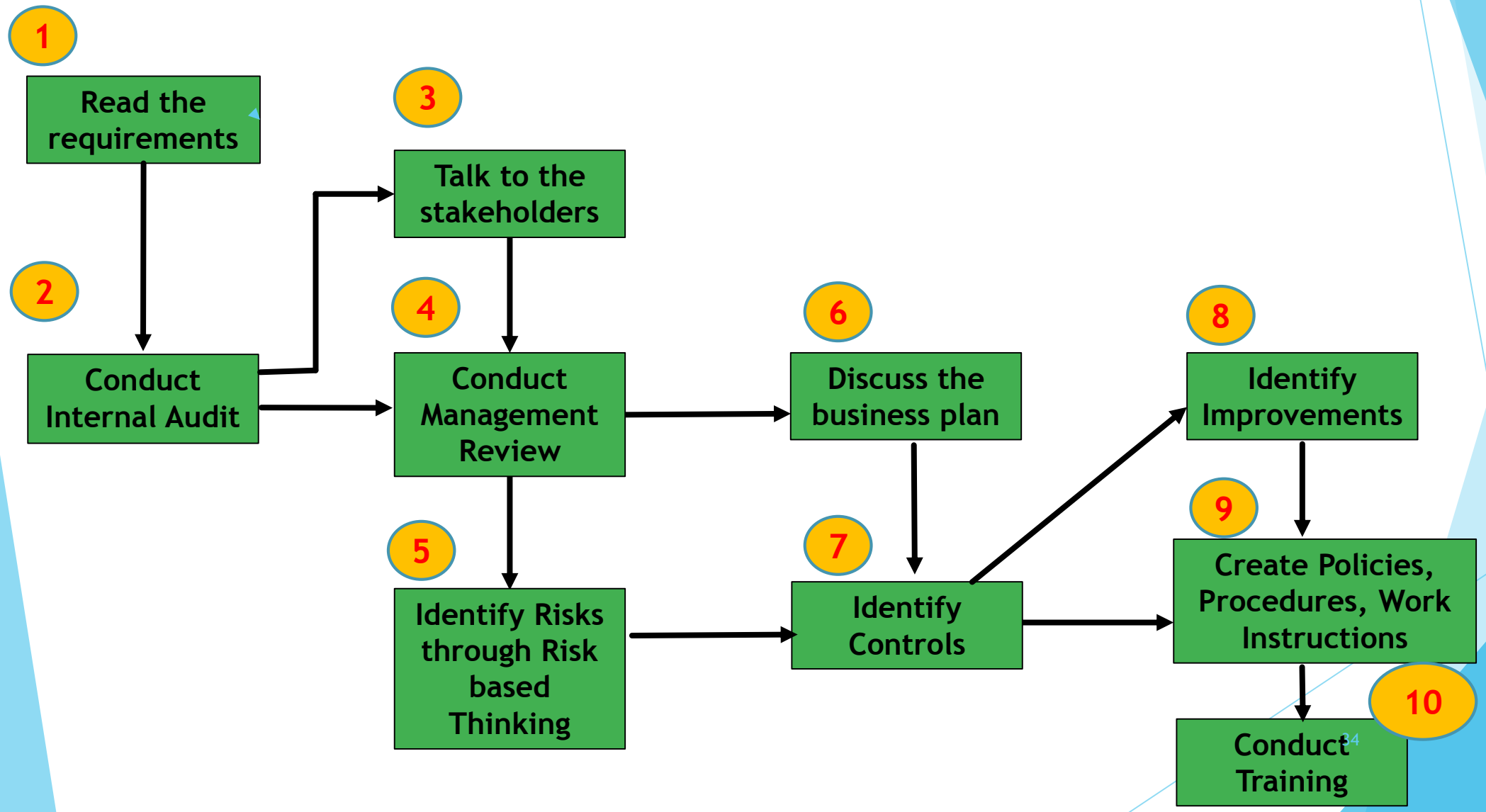
Responsibility Assignment Matrix		Person or Role/Department:				
KEY:	R – RESPONSIBLE A – ACCOUNTABLE C – CONSULTED I – INFORMED	Project Manager	Team Leaders	Project Members	Project Admin Support Office	Steering Committee
Code	Issue / Date:					
	Approved by:					
	Activity / Task Name					
100	Design phase	RA	R	I		C
200	Planning Project	A	R	I		C
300	Booking Contractors	A	C	I	R	C
400	Production	A	C	R		I
500	Cost Control	R	C	I	I	C
600	Ensuring Quality & Standards	A	R	R	R	C





Part 5

How should you get started? - Building your QMS



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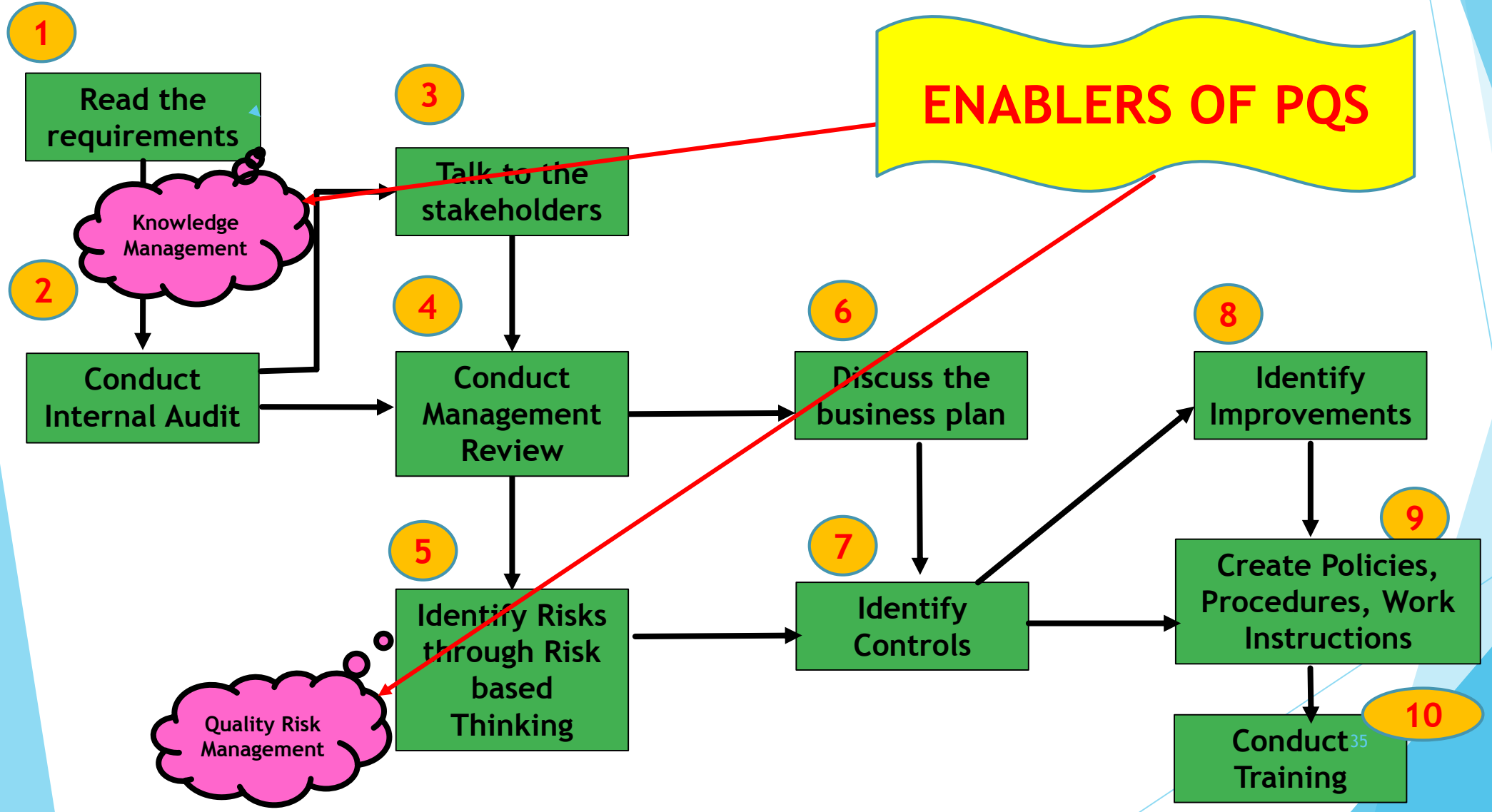

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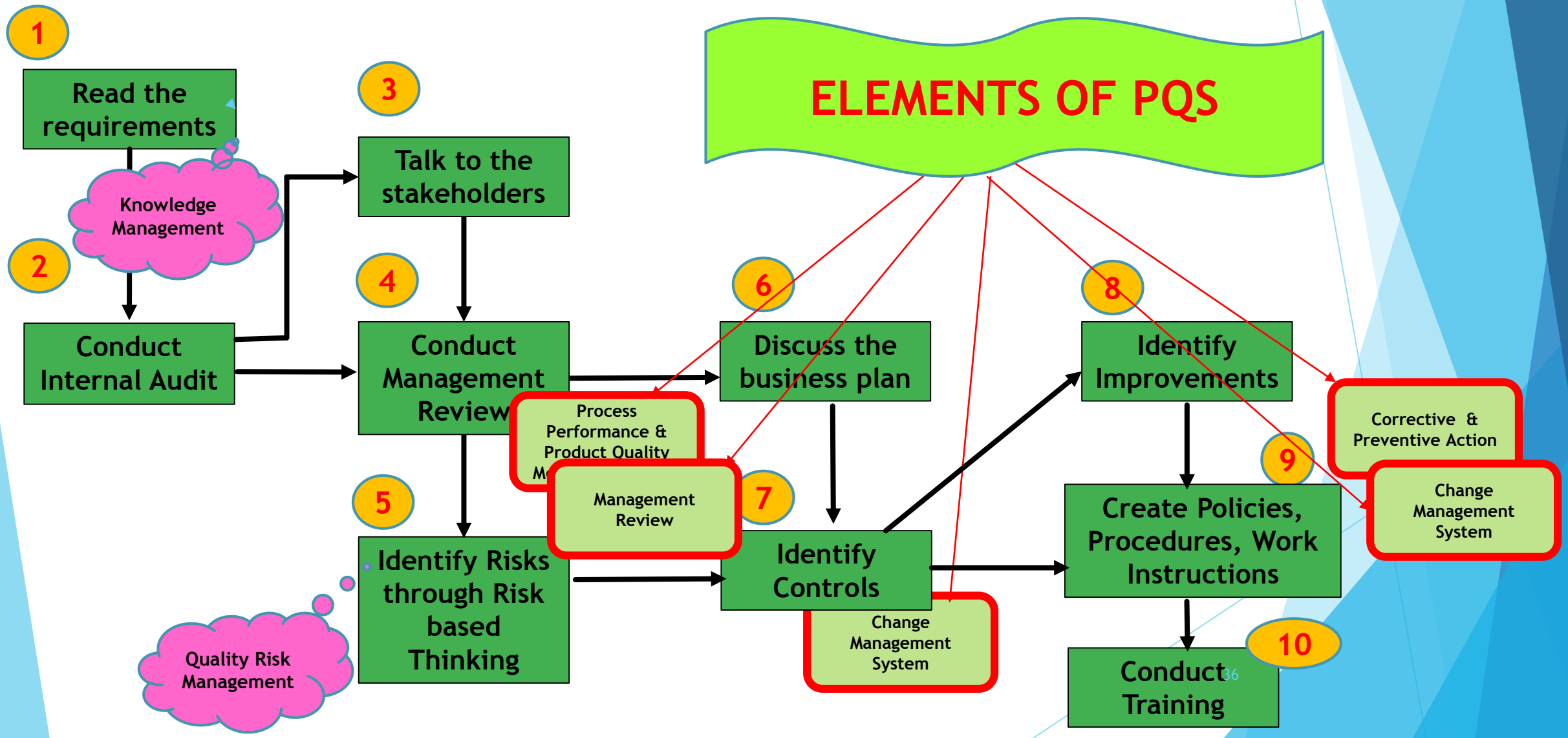

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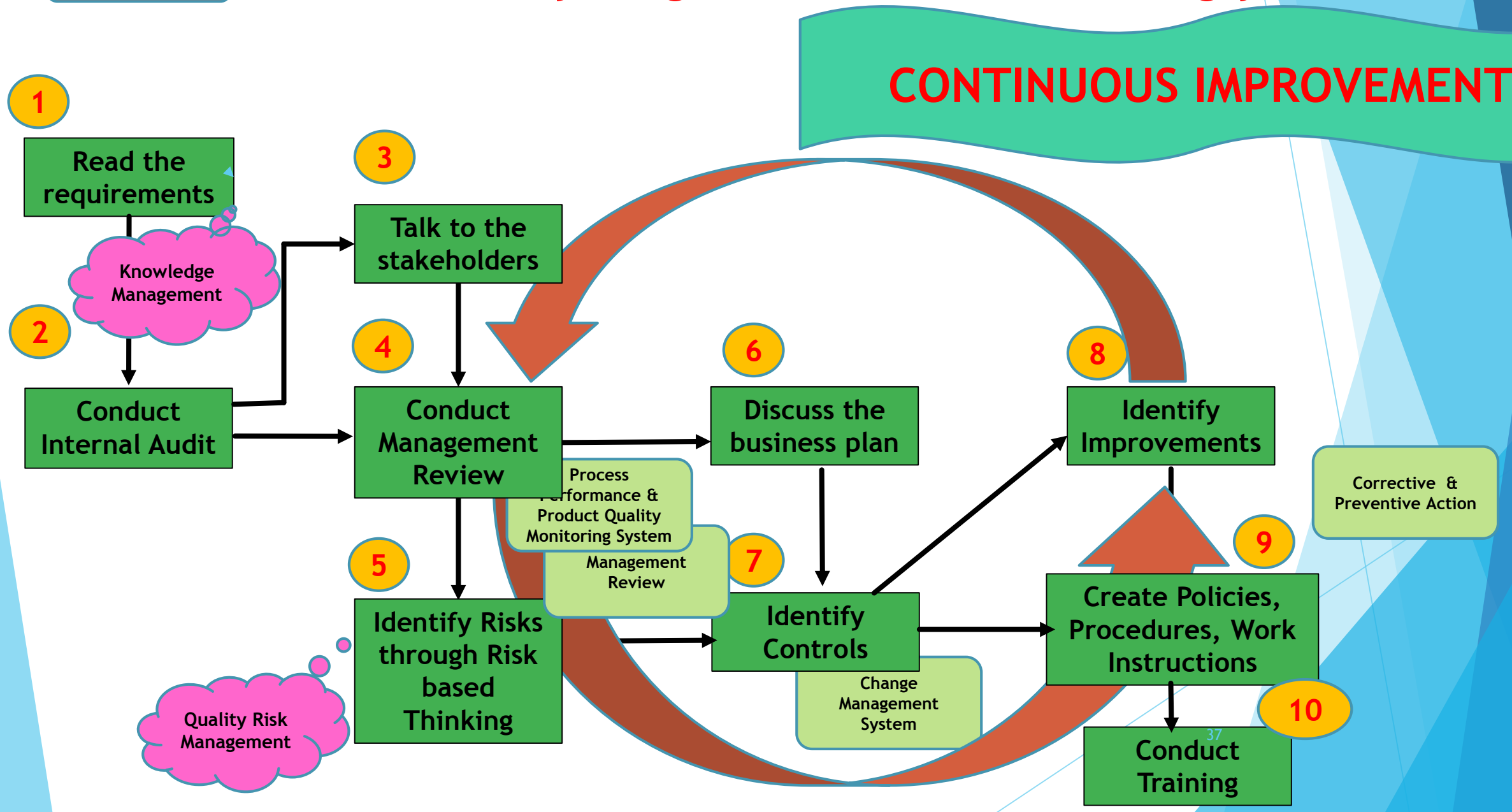

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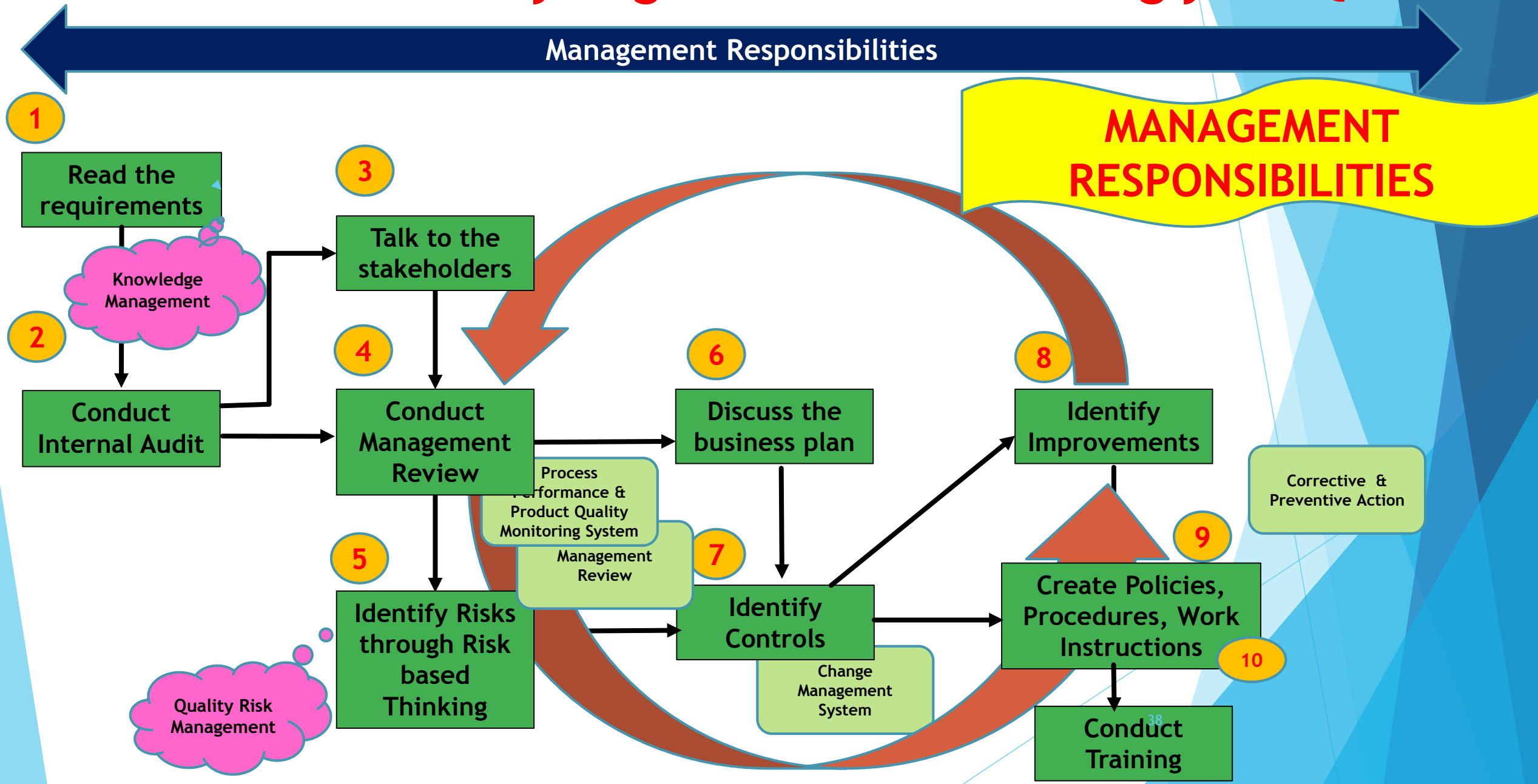


Part 5

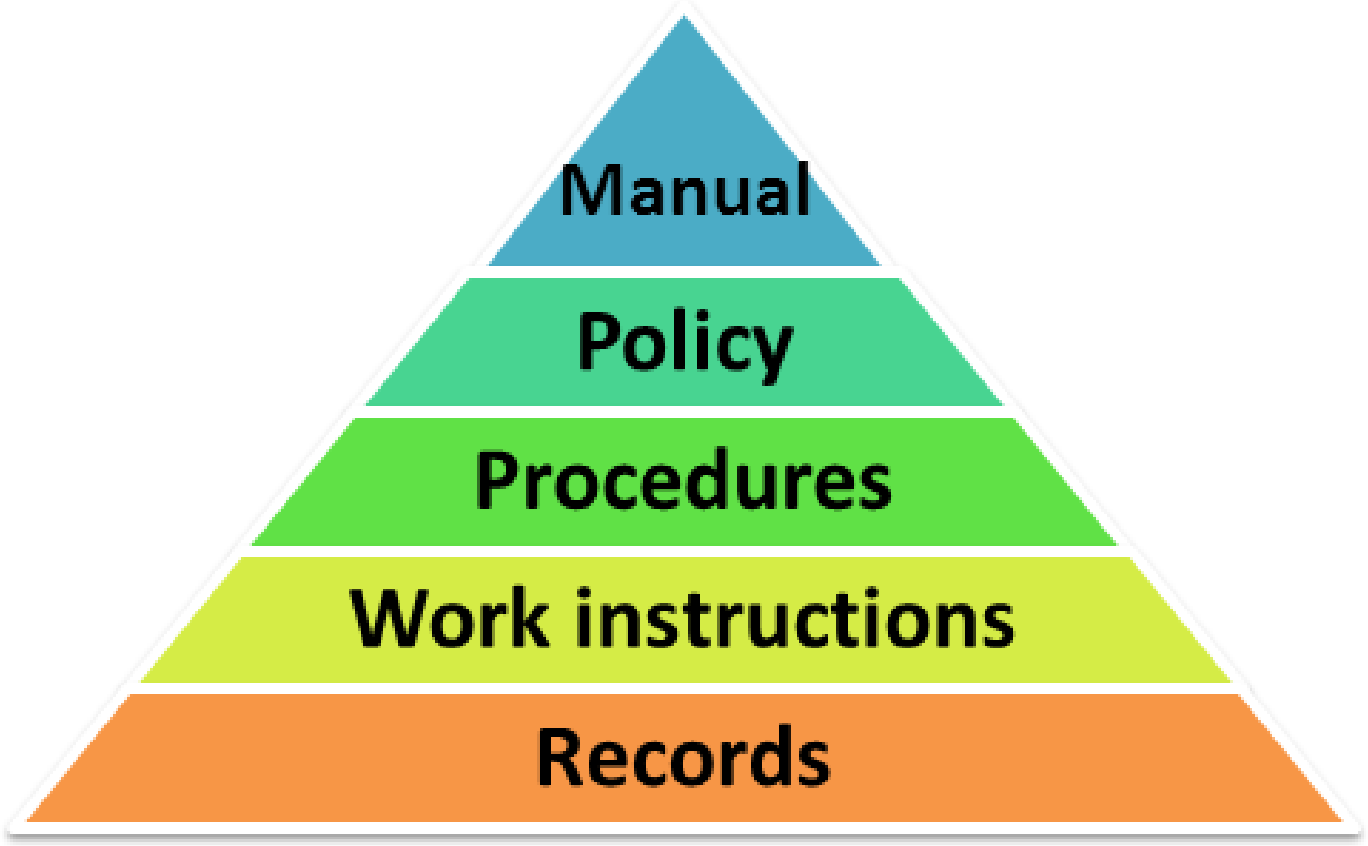
Structured PQS Documentation

FIT FOR PURPOSE QMS

- FOCUS ON EFFICIENCY
- CREATE PROCESSES & DOCUMENTS
- STRUCTURED & CONSISTENT
- APPROPRIATE & PROPORTIONATE
- PRAGMATIC & CLEAR
- LINK TO REAL PRACTICES
- INTEGRATED INTO DAILY WORK

Part 5

Structured PQS Documentation



PQS should be defined and documented.

Part 5

Three core values in implementing PQS:

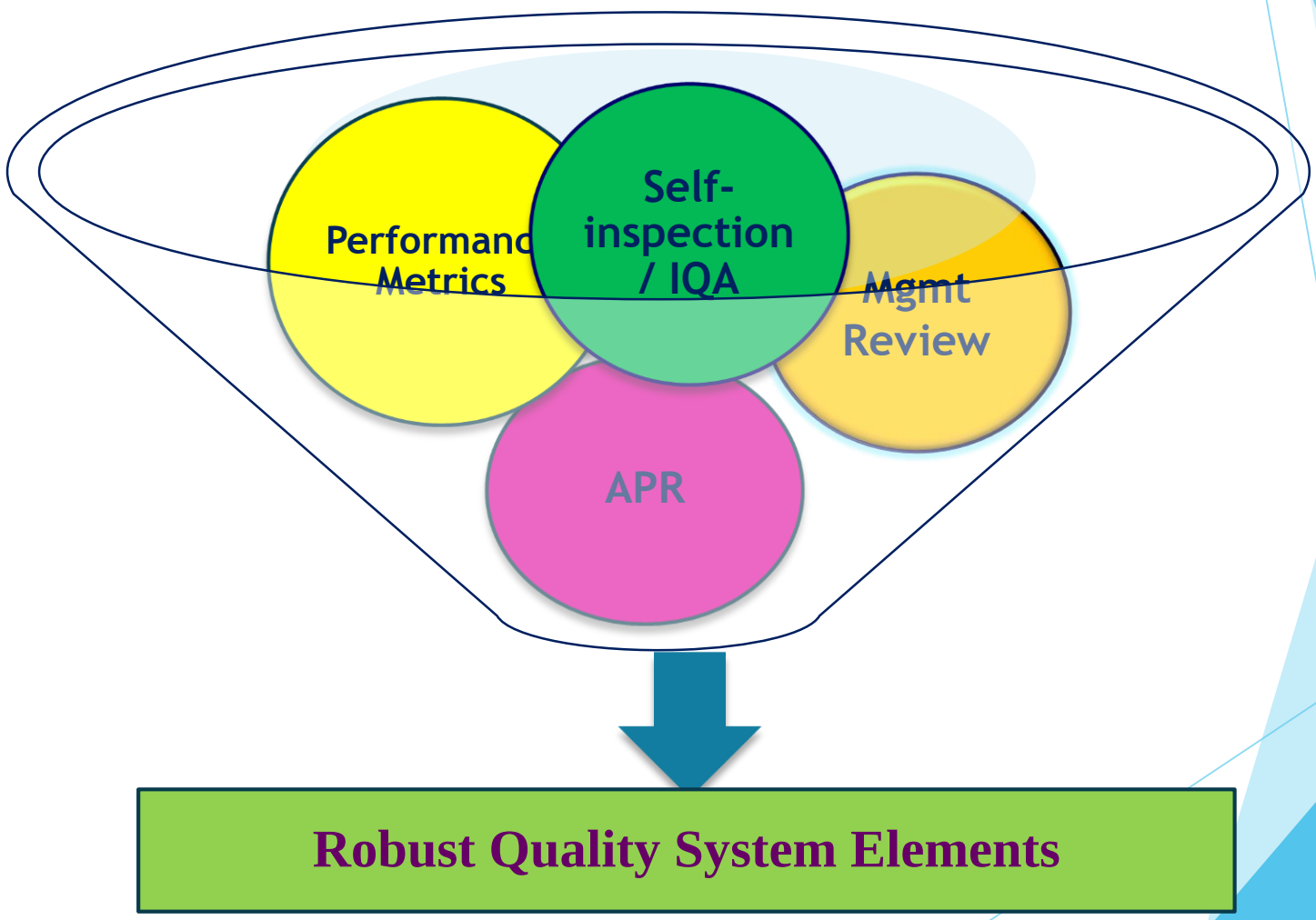
Make it matter: PQSS should improve results and this should matter to your customers.

Make it work: The PQS should fit the way you do business and should work for your company.

Make it last: Your PQS should drive long term improvements that last the test of time.

Part 5

Verifying your PQS implementation



Part 6

Conclusions:

1. QMS should not be an add-on, but a way of normally doing business in a regulated industry.
2. To implement PQS effectively:
   - Know and understand the correct interpretation of the regulations and requirements
   - Use enablers like Knowledge Management & Quality Risk Management
   - Put systems in place to implement the four elements which serve as the major pillars of the PQS: (Process Performance and Product Quality Monitoring System, CAPA system, Change Management System and Management Review)
   - Look for opportunities to continually improve
   - Management take full responsibility on the effective implementation of the PQS
     - Provide adequate resources (manpower and other resources)
     - Provide adequate training and poor communication

Part 6

Conclusions:

3. A list of SOPs has never been a QMS!
4. PQS goes beyond GMPs with a ISO approach.
5. QMS is applicable to all types of organizations, thus not limited to manufacturing operations but is also applicable to the service industry.
6. Advantages of QMS:
    a. Organized processes
    b. Improved the efficiency of the processes
    c. Continuous improvement

Part 6

Conclusions:

7. Basic Rules in formulating your PQS:

- "Keep it Simple" This means that processes, documents, records should fit your business. Bigger is not necessarily better. So fit for purpose.

- "Adding Business Value". QMS should help you serve your customers better, with fewer disruptions and greater efficiency, and provide an outstanding return-on-investment.

- "Never Do Anything Just to Please the regulator". When the focus is primarily on just plain compliance, your opportunity to achieve real improvement can be lost.

Part 6

Conclusions:

8. Staying in compliance means:

- Management demonstrating through their actions, decisions and interest
- Good GMP training program to ensure knowledge and awareness
- Appropriate staff numbers in all areas
- Continually appraise systems (product review, internal audit and management review)
- Measure (performance metrics)
- Everyone taking responsibility

Fostering a Quality Culture

- Enhanced process stability drives productivity and performance
- Prevention reduces compliance risks & costs
- Lesser complaints & investigations
- Improved rate of survival & growth

References:

- AO 2012-0008 (dated Jun 25, 2012) Adoption and implementation of the Pharmaceutical Inspection Cooperation Scheme (PIC/S) Guides for the Good Manufacturing Practice (GMP) for Medicinal Products (effectivity date: July, 2013)

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Thank You

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