



Mount Wachusett
Community College

AQS 110

INTRODUCTION TO METROLOGY

Prepared by Gretchen Ingvason as part of NSF ATE Grant #1304474 –
(National Science Foundation Advanced Technical Education)



Start near. Go far.



mwcc.edu

AQS 110

Introduction to Metrology

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by the National Science Foundation under
Grant No. 1304474



Any opinions, findings, and conclusions or recommendations expressed in this material are those of the author(s) and do not necessarily reflect the views of the National Science Foundation.

COURSE OBJECTIVE

- Identify and apply sampling methods, inspection, measurement and test equipment as fundamental quality control techniques.
- Describe metrology concepts including gage reproducibility and repeatability, calibration and traceability to recognized standards.
- Demonstrate the ability to collect and statistically review data collected and distinguishing the variability and errors associated with inspection, measurement and test equipment.
- Demonstrate the ability to utilize the basic seven quality tools: Pareto chart, flow chart (run chart), check sheets, control charts, cause and effect diagrams, histograms and scatter diagrams.



COURSE OBJECTIVE (cont.)

- Express the principles of validation and qualification as it applies to manufacturing processes.
- Describe the principles of lean manufacturing and six sigma improvement techniques.
- Demonstrate the ability to write and speak effectively through written assignments, lab reports and discussions.

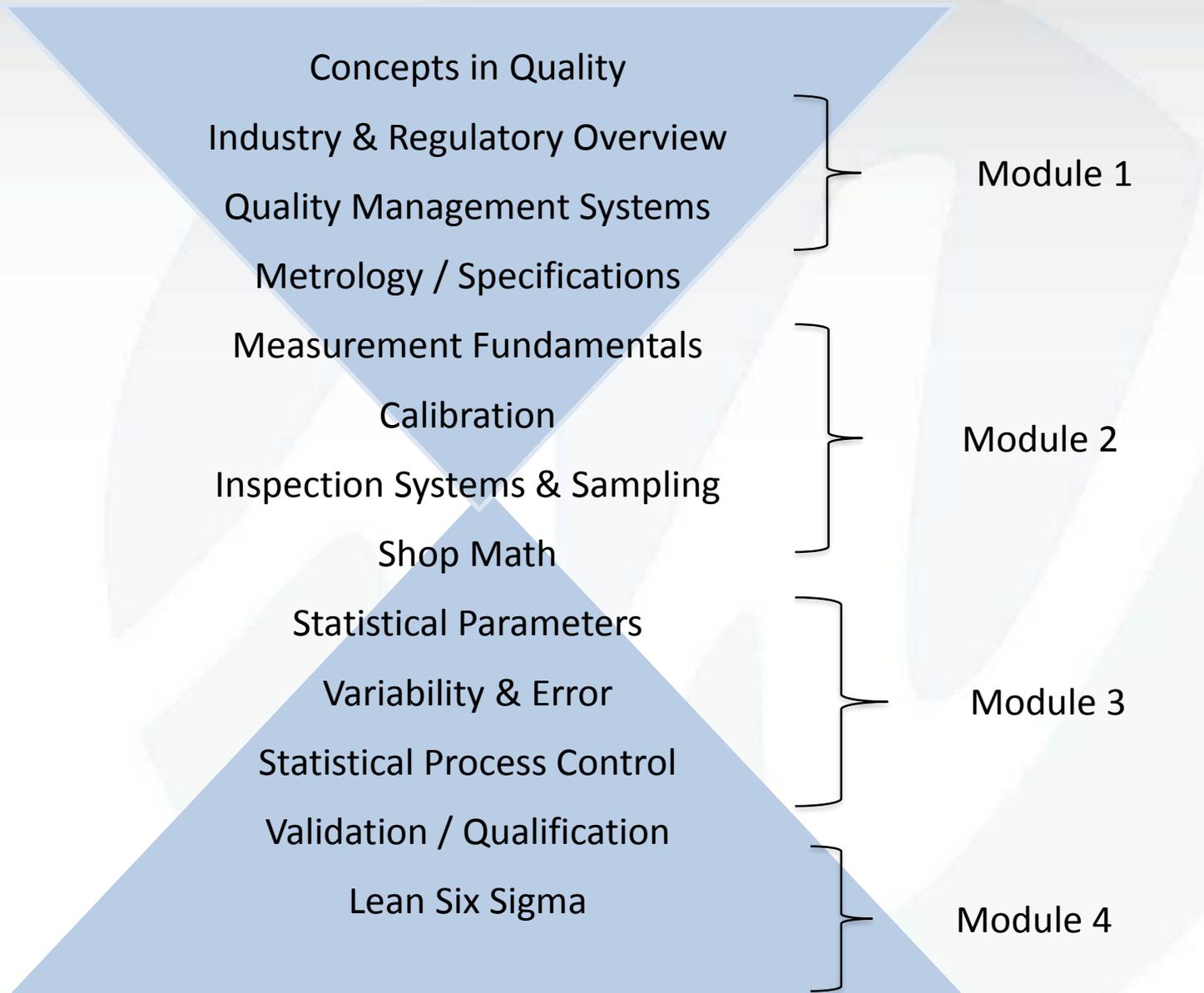


SYLLABUS

Week	Topic	Week	Topic
1	Concepts in Quality Industry and Regulatory Overview	9	Shop Math Statistics Introduction
2	Quality Control & Quality Assurance	10	Statistics (cont.)
3	Metrology / Specifications	11	Variability & Error
4	Measurement Fundamentals	12	Statistical Process Control
5	Measurement Fundamentals (cont.)	13	Validation / Qualification
6	Calibration	14	Lean Six Sigma
7	Calibration (cont.)	15	Final Exam - cumulative
8	Inspection Systems & Sampling		



INTRODUCTION TO METROLOGY



MY BACKGROUND



BLD111120 [RF] © www.visualphotos.com



HOW ABOUT YOU?



- Name
- Hobbies – like to do
- Work history
- Goals – job, college, etc.

Quality Technician – Career Pathways

- Multitude of industries
 - Pharmaceutical, biopharmaceutical, Medical Device, Automotive, Aerospace, Plastics, Food and Beverage, etc.
- ASQ Certifications
 - Certified Technician
 - Certified Quality Inspector
 - Certified Process Analyst
- Entry into Engineering Technology or 4-year degree
- Quality Engineering
- Regulatory Specialist

www.asq.org

VARIOUS INDUSTRIES & SECTORS

- Manufacturing
 - Corporate offices, Plants
 - Controlled Environments
- Service
 - Corporate Offices
 - Field work

MANUFACTURING - Careers

- **Aerospace**
 - Complete vehicles, components
- **BioTechnology**
 - Vaccines, forensics, cosmetics
- **Chemicals**
 - Adhesives, paint, pesticides, soaps
- **Computer & Electronics**
 - Audio/video, components, etc.
- **Fabricated Metal Products**
 - heat treating, engraving, nails,
- **Foods**
 - Animal feed, seasonings, snacks
- **Machinery**
 - Mowers, HVAC, assembly equipment
- **Medical Devices & Supplies**
 - Pacemakers, gurneys, filters
- **Measurement Systems**
 - Gages, Vision Systems, CMM
- **Paper Products**
 - Boxes, gift wrap, diapers
- **Pharmaceuticals**
 - Prescription, over-the-counter
- **Rubber & Plastic Products**
 - Tires, hoses, bags, pipes
- **Transportation & Parts**
 - Cars, trucks, boats, components
- **Various Retail Goods**
 - Toys, clothing, sporting goods

SERVICE INDUSTRY - Careers

- **Construction**
 - Buildings, Infrastructure, roofing
- **Consulting**
 - Management, Scientific, technical
- **Educational**
 - Training, K-12, Secondary
- **Financial & Insurance**
 - Banks, Mortgages, Brokers
- **Government /Public Admin**
 - Judicial, security, fire protection
- **Healthcare**
 - Blood banks, diagnostic labs
- **Information Services**
 - Publishing, archiving
- **Inspection Services**
 - Residential, Power plants, Electrical
- **Retail**
 - Department Stores, Auto Dealers
- **Social Services**
 - Relief Services, Vocational Rehab
- **Scientific / Technical**
 - Testing Services, Engineering Firms

BIOTECHNOLOGY - Careers

- **Agriculture / Aquaculture**
 - Protect animals/crops from disease
 - Growing plants/animals in water
- **Biodefense**
 - Protect air/food/water from pathogenic microorganisms
- **Biofuels**
 - Diesel/ethanol purified from natural sources
- **Biopharmaceuticals**
 - genomics, vaccines
- **Cosmetics**
 - Discover and manufacture components
- **Environmental Monitoring**
 - Lab methods (i.e. microarrays) used to monitor air/water/soil
- **Food Safety**
 - Identify pathogens or chemical additives and their source
 - Track source of meat (illegal/poached)
- **Forensics**
 - Criminal investigations (DNA)
- **Medical Diagnostics**
 - Various tests

www.biotech-careers.org

MODULE 1: QUALITY CONCEPTS

- Quality – What is it?
- Quality Control & Quality Assurance
- Quality Systems Overview



CONCEPTS IN QUALITY

WHAT IS QUALITY

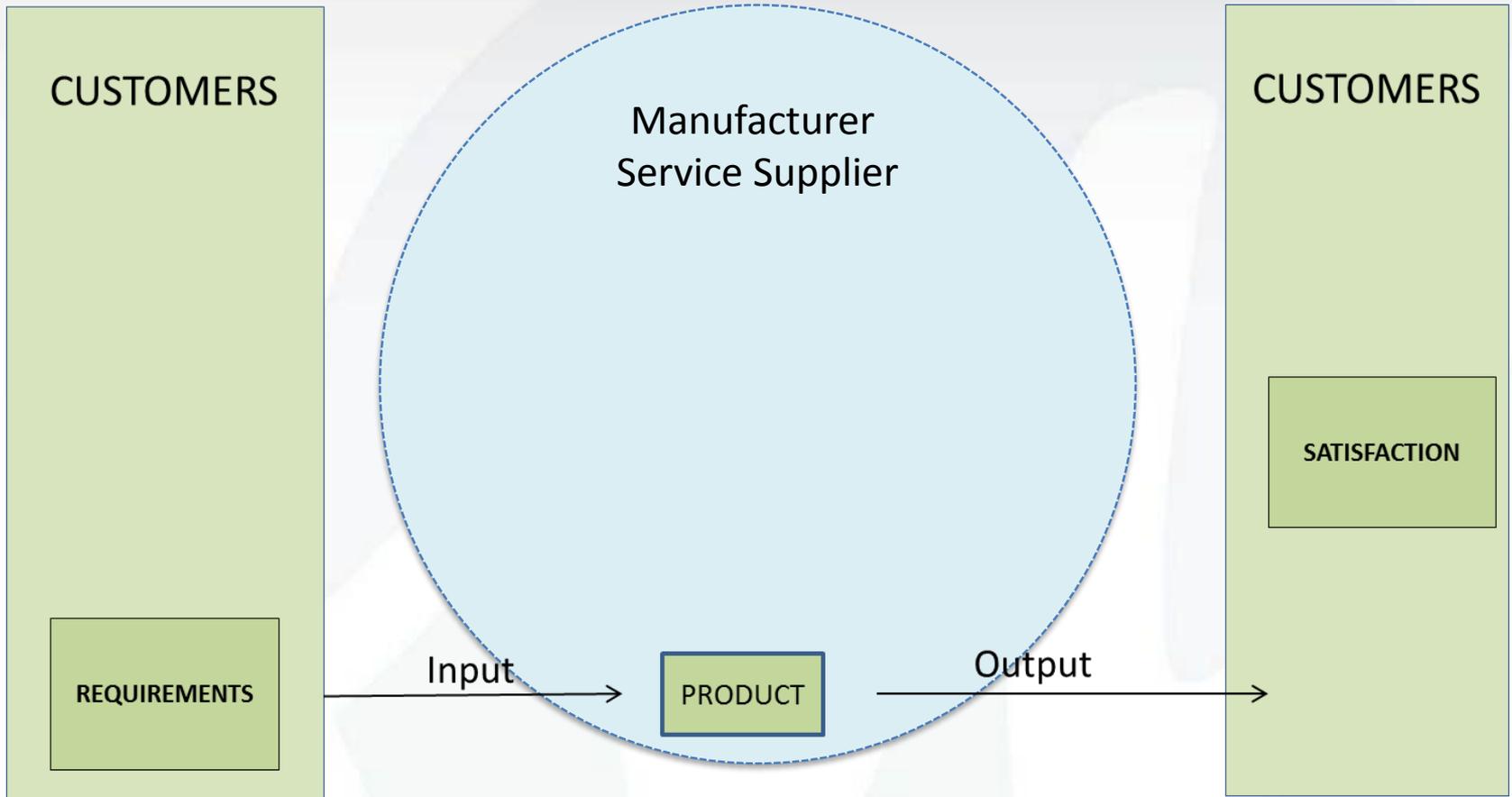
- Merriam-Webster dictionary
qual·i·ty noun \ˈkwä-lə-tē\
 - : how good or bad something is
 - : a characteristic or feature that someone or something has
 - : a high level of value or excellence
- Quality is a relative concept
Quality is a product (or service) with the features and characteristics which determine desirability and can be controlled to meet certain basic requirements.

WHAT IS QUALITY

Quality is a product (or service) with the *features and characteristics* which determine *desirability* and can be *controlled* to *meet certain basic requirements*.

- Who determines desirability of features /characteristics?
- Why are they desirable?
- What are the requirements that can be controlled?
- How is it known if the requirements are met?

Quality is determined by the Customer (end-user) based on THEIR expectation and needs.



ISO9001:2008E Process Model

CUSTOMER vs. SUPPLIER

- Who is the Customer?
 - Internal versus External

Customer vs. Supplier



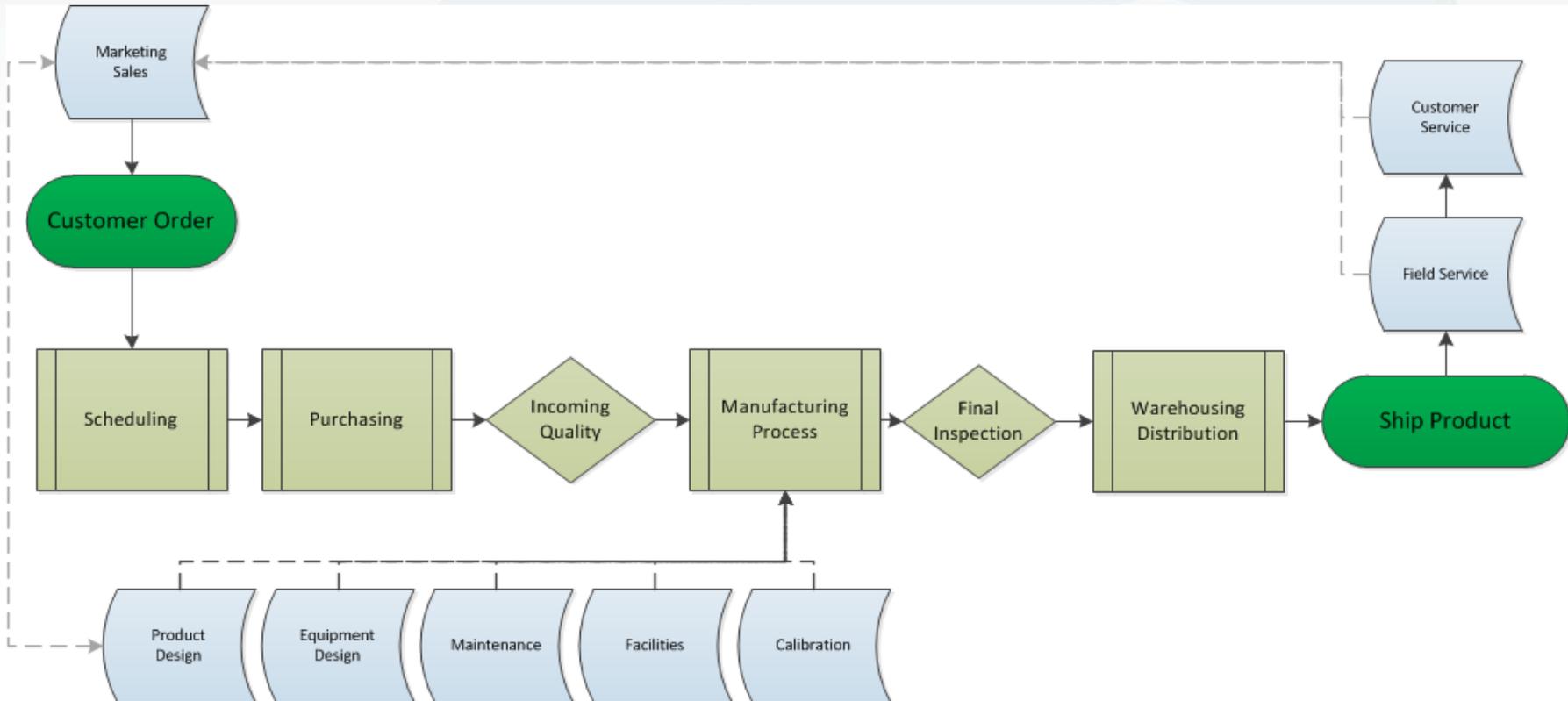
Customer vs. Supplier

- Who is the Customer?
 - User of the material, product, service

Customer vs. Supplier

- Who is the Customer?
 - User of the material, product, service
 - Internal – within the company / department

PROCESS FLOW - MANUFACTURING



Customer vs. Supplier

- Who is the Customer?
 - User of the material, product, service
 - Internal – within the company / department
 - External – outside the company
 - Designer / Assembler
 - End-User

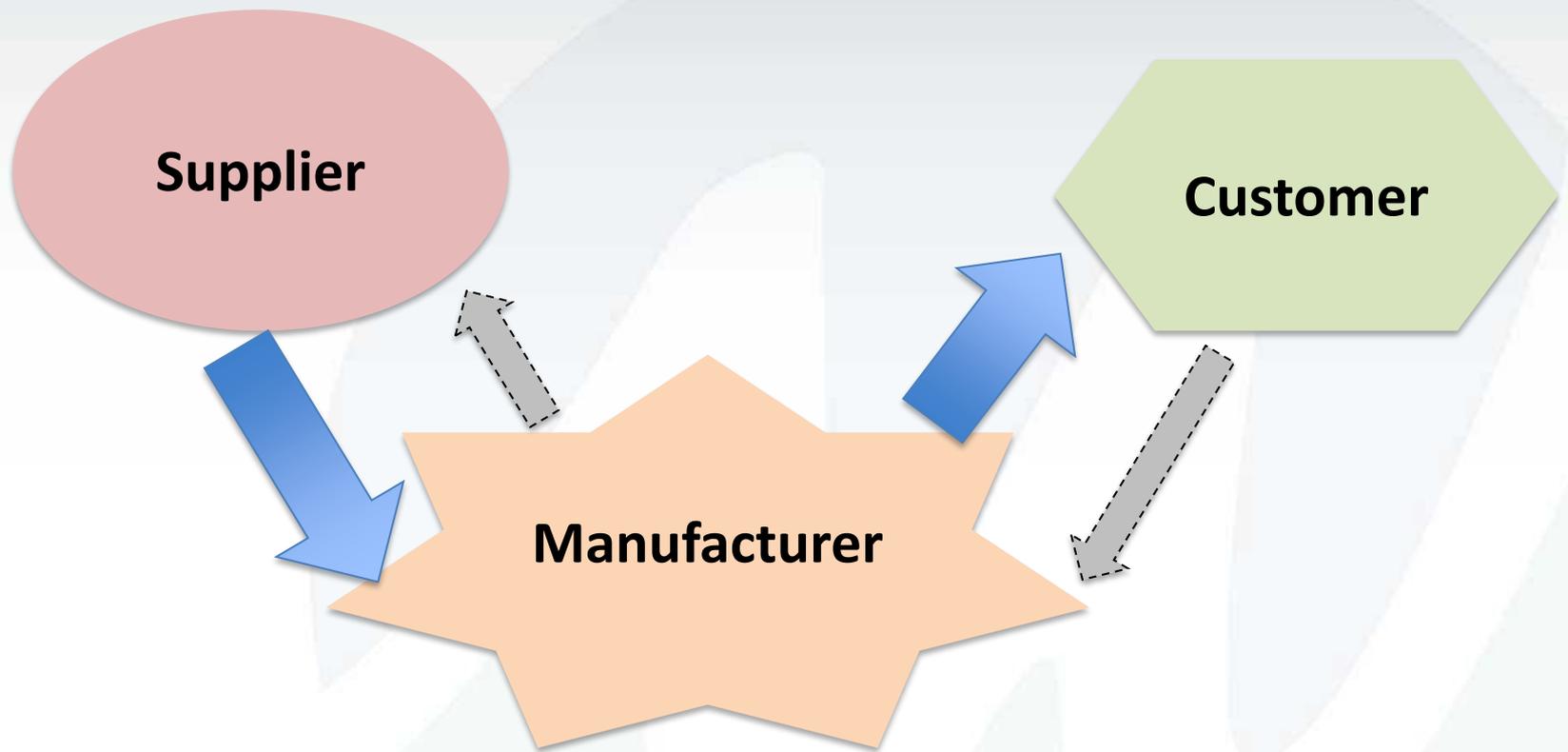
Customer vs. Supplier

- Who is the Customer?
 - User of the material, product, service
 - Internal – within the company / department
 - External – outside the company
- Who is the Supplier?
 - Provider of materials, products, services, etc.
 - Internal vs External

Customer vs. Supplier

- Who is the Customer? Who is the Supplier?
- Internal versus External

Example: restaurant, education

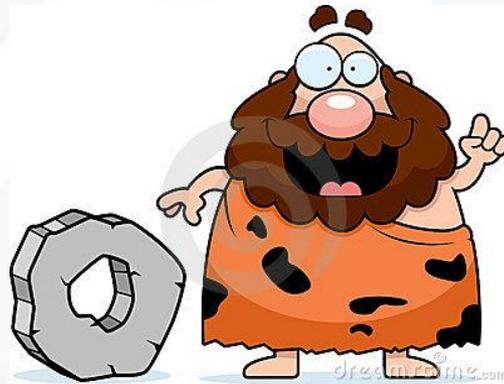


Supplier is who provides material/service
Customer is user of material/service

Roles are interchangeable to communicate expectations (requirements)

HISTORY OF QUALITY

- Quality has been around since beginning of time
 - Apprentice
 - Craftsman
 - Master Craftsman



History of Quality Improvement and SPC



Shewhart



Deming meets Shewhart

- Introduces SPC and control charts
- “Economic Control of Quality of Manufactured Product” (1931)

1924

1938

WWII

U.S. Army publishes SPC guide

U.S
Pre-1924



60



Ford and other U.S. mfgs. respond 1980s

1985-1988

- 1700-1900 Quality determined by individual craftspeople
- 1875 F.W. Taylor’s “Scientific Management”
- 1900 Henry Ford and the assembly line
- 1907 AT&T begins systematic inspection & testing

1940
Japan

1945
U.S. Allied Command Civil Communications Section introduces Quality Improvement and SPC to Japan

1950s
U.S. quality experts Deming, Juran, Feigenbaum lecture in Japan



Deming



Juran



Feigenbaum



1960-1970s
TOYOTA
Develops JIT production (Lean Mfg.)

1970s
Japan begins dominating many markets

2000

Taylor – Scientific Management

- Scientific management consisted of four principles:
 - Replace rule-of-thumb work methods with methods based on a scientific study of the tasks.
 - Scientifically select, train, and develop each employee rather than passively leaving them to train themselves.
 - Provide "Detailed instruction and supervision of each worker in the performance of that worker's discrete task".
 - Divide work nearly equally between managers and workers, so that the managers apply scientific management principles to planning the work and the workers actually perform the tasks.
- Management plans, workers perform tasks

Walter Deming

14 Quality Management Principles

1. Create constancy of purpose for improving products and services.
2. Adopt the new philosophy.
3. Cease dependence on inspection to achieve quality.
4. End the practice of awarding business on price alone; instead, minimize total cost by working with a single supplier.
5. Improve constantly and forever every process for planning, production and service.
6. Institute training on the job.
7. Adopt and institute leadership.

Walter Deming

14 Quality Management Principles

8. Drive out fear.
9. Break down barriers between staff areas.
10. Eliminate slogans, exhortations and targets for the workforce.
11. Eliminate numerical quotas for the workforce and numerical goals for management.
12. Remove barriers that rob people of pride of workmanship, and eliminate the annual rating or merit system.
13. Institute a vigorous program of education and self-improvement for everyone.
14. Put everybody in the company to work accomplishing the transformation.

Juran's Trilogy

- Juran first to write about the cost of poor quality
 - Without change there will be constant waste
 - During change there will be increased costs
 - After improvement margins higher and costs recouped
- Cross-functional management:
 - Quality Planning
 - Quality Control
 - Quality Improvement

TQM – Eight Principles

- Strategic and systemic approach
 - Quality integrated as component in overall strategic plan
- Continual improvement
 - Analytically and creatively find ways for competitiveness and efficiency
- Fact-based decision making
 - Collect and analyze data for decision making and predication based on history
- Communications
 - Effective communication maintains morale and motivation

TQM – Eight Principles

- Customer-focused
 - Customer ultimately determines level of quality
- Total employee involvement
 - All participate in working toward common goals
- Process-centered
 - Defined steps, monitor performance to detect variation
- Integrated system
 - Processes linked for defining and implementing business strategy

Homework Assignment

View video's on blackboard

Review slides on Frederick Taylor, Walter Deming, Joseph Juran and TQM

Complete worksheet –

- summarize the philosophies in your own words

- what's common

- do you see examples in current workplace



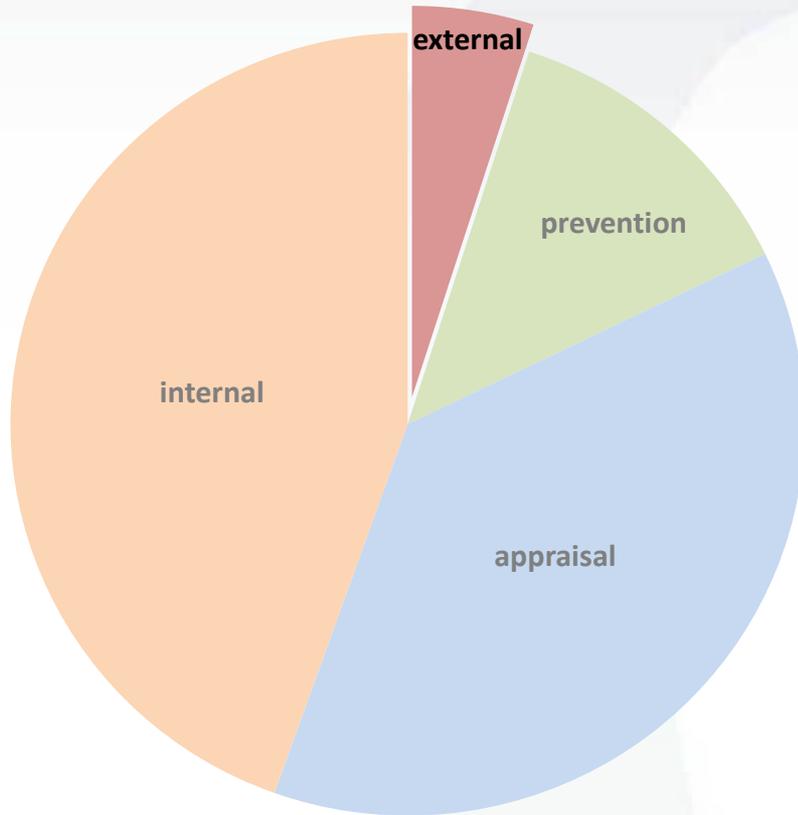
A large, light blue, stylized letter 'W' is centered in the background of the slide. The 'W' is composed of several rounded, overlapping shapes, giving it a modern, graphic appearance. It is semi-transparent, allowing the white background to show through.

QUALITY MANAGEMENT SYSTEMS

QUALITY IN MANUFACTURING

- *Quality is a product (or service) with the features and characteristics which determine desirability and can be controlled to meet certain basic requirements.*
 - Acceptable limits determined by customer requirements and company strategy
- **Variability in manufacturing processes affect product quality,**
 - Measure product quality using quantitative methods.
 - Statistical methods are used to characterize process variability and help to identify sources of variability (error).

COST OF QUALITY



- Internal
 - Scrap, Rework
- Appraisal
 - Material Receipt Measurement
 - In-process/Final Inspection
- Prevention
 - Improvement, Planning
- External
 - Returns, Warranty

QUALITY IN MANUFACTURING

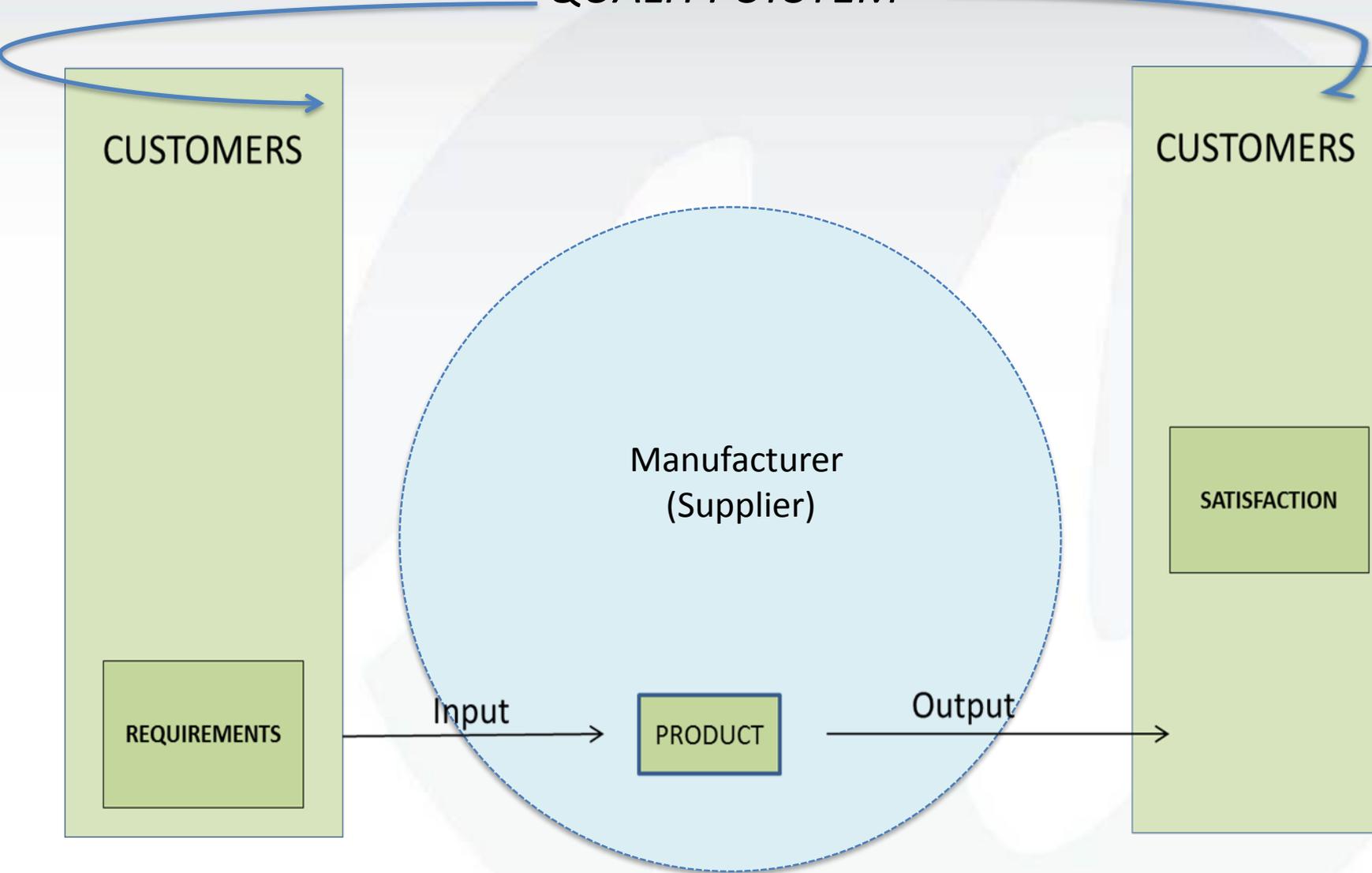
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 - Acceptable limits determined by customer requirements and company strategy
- Variability in manufacturing processes affect product quality,
 - Measure product quality using quantitative methods.
 - Statistical methods are used to characterize process variability and help to identify sources of variability (error).
- **Quality is an important component of cost of goods sold.**
 - Tracked through multiple measures
 - Lack of quality can lead to product and company failure

https://www.youtube.com/watch?v=jYj_R4oCTPI

QUALITY MANAGEMENT SYSTEM

- Method of doing business
 - Regulatory Requirements
 - US Food & Drug Administration
 - Europe, Japan, Canada, etc.
 - Customer Requirements
 - ISO (International Organization of Standards)
 - Specifications, etc.

QUALITY SYSTEM



QUALITY MANAGEMENT SYSTEM

- Method of doing business
 - Regulatory Requirements
 - Customer Requirements
- Basic Premise**
 - Say what you do
 - Do what you say
 - Record what you did
 - Check the results
 - Act on the difference

** Metrology Handbook, 2nd ed., Jay L Bucher, PhD

QUALITY MANAGEMENT SYSTEM

- Basic Premise
 - Say what you do (documents)
Standard operating procedures, measurement methods, assembly instructions, product requirements, etc.
 - Do what you say (training, day-to-day activities)
follow procedures, metrology, calibration, collect data
 - Record what you did (write it down)
good documentation practices, check sheets, automation
 - Check the results (analysis)
Graphical tools, uncertainty/variability
 - Act on the difference (improvement)
Root Cause Analysis, Validation, Lean Six Sigma

QUALITY SYSTEMS

- ISO 9001:2015 Quality Management Systems – Requirements
- ISO 13485:2016 Medical Devices – Quality Management Systems – Requirements for Regulatory Purposes
- ISO/IEC 17025:2005 General Requirements and Competencies of Testing and Calibration Laboratories
- AS9001C International Aerospace Quality System Standard
- ISO 22000:2005 Food Safety Management Systems – Requirements for any organization in the food chain
- ISO E14001:2004 Environmental Management Systems – Requirements with Guidance for Use

QUALITY SYSTEMS

- US Food & Drug Administration (FDA)
 - 21CFR (Code of Federal Regulations)
 - Part 210/211 Pharmaceuticals
 - Part 600/601/610 Biologics
 - Part 820 Medical Device
 - International Counterparts
 - Japan – Pharmaceutical & Medical Device Agency
 - Europe – European Directives
 - Canada –Health Canada

QUALITY SYSTEMS

- ISO
 - 9001:2015: General Quality Management Systems
 - 13485:2016 Medical Device Manufacture
- US FDA
 - 21CFR Part 210/211 Pharmaceutical
 - Part 820 Medical Device

ISO is voluntary

FDA is mandatory

QUALITY SYSTEMS

- Most common in this area (North Central Massachusetts)
 - ISO 9001:2015E
 - General manufacturing, including design
 - Also used by Service companies (i.e. healthcare, etc.)
 - ISO 13485:2016
 - International medical device
 - US FDA cGMP
 - 21CFR Part 820 (Medical Device)
 - 21CFR Part 210/211 (Pharmaceutical)
 - cGLP (Laboratory Practices) 21CFR Part 58
 - cGCP (Clinical Practices) 21 CFR Part 312
 - 21CFR Part 600/601/610 (Biologics)

ISO 9001:2015E

- Quality Management Systems Standard
 - “... designed to help organization ensure they meet the needs of customers and other stakeholders while meeting statutory and regulatory requirements related to a product...”*

GENERAL QUALITY PRINCIPLES

- Customer Focus
- Leadership
- Engagement of People
- Process Approach
- Improvement
- Evidence-based decision making
- Relationship management

REFERENCE: ISO 9001:2015

QMS – PRINCIPLES (ISO 9001:2015)

- **Customer Focus**

- understand current and future customer needs
- meet customer requirements
- strive to exceed customer expectations

Organizations depend on their customers.

- Leadership
- Engagement of People
- Process Approach
- Improvement
- Evidence-based decision making
- Relationship management

QMS – PRINCIPLES (ISO 9001:2015)

- Customer Focus
- **Leadership**

Leaders establish unity of purpose and direction of the organization. They should create and maintain the internal environment in which people can become fully involved in achieving the organization's objectives.
- Engagement of People
- Process Approach
- Improvement
- Evidence-based decision making
- Relationship management

QMS – PRINCIPLES (ISO 9001:2015)

- Customer Focus
- Leadership
- **Engagement of People**
 - People at all levels of an organization and their full involvement enables their abilities to be used for the organization's benefit
- Process Approach
- Improvement
- Evidence-based decision making
- Relationship management

QMS – PRINCIPLES (ISO 9001:2015)

- Customer Focus
- Leadership
- Engagement of People
- **Process Approach**
 - Desired result is achieved more efficiently when activities and related resources are managed as a process
- Improvement
- Evidence-based decision making
- Relationship management

QMS – PRINCIPLES (ISO 9001:2015)

- Customer Focus
- Leadership
- Engagement of People
- Process Approach
- **Improvement**
 - Continual improvement of the organizations overall performance should be a permanent objective of the organization
- Evidence-based decision making
- Relationship management

QMS – PRINCIPLES (ISO 9001:2015)

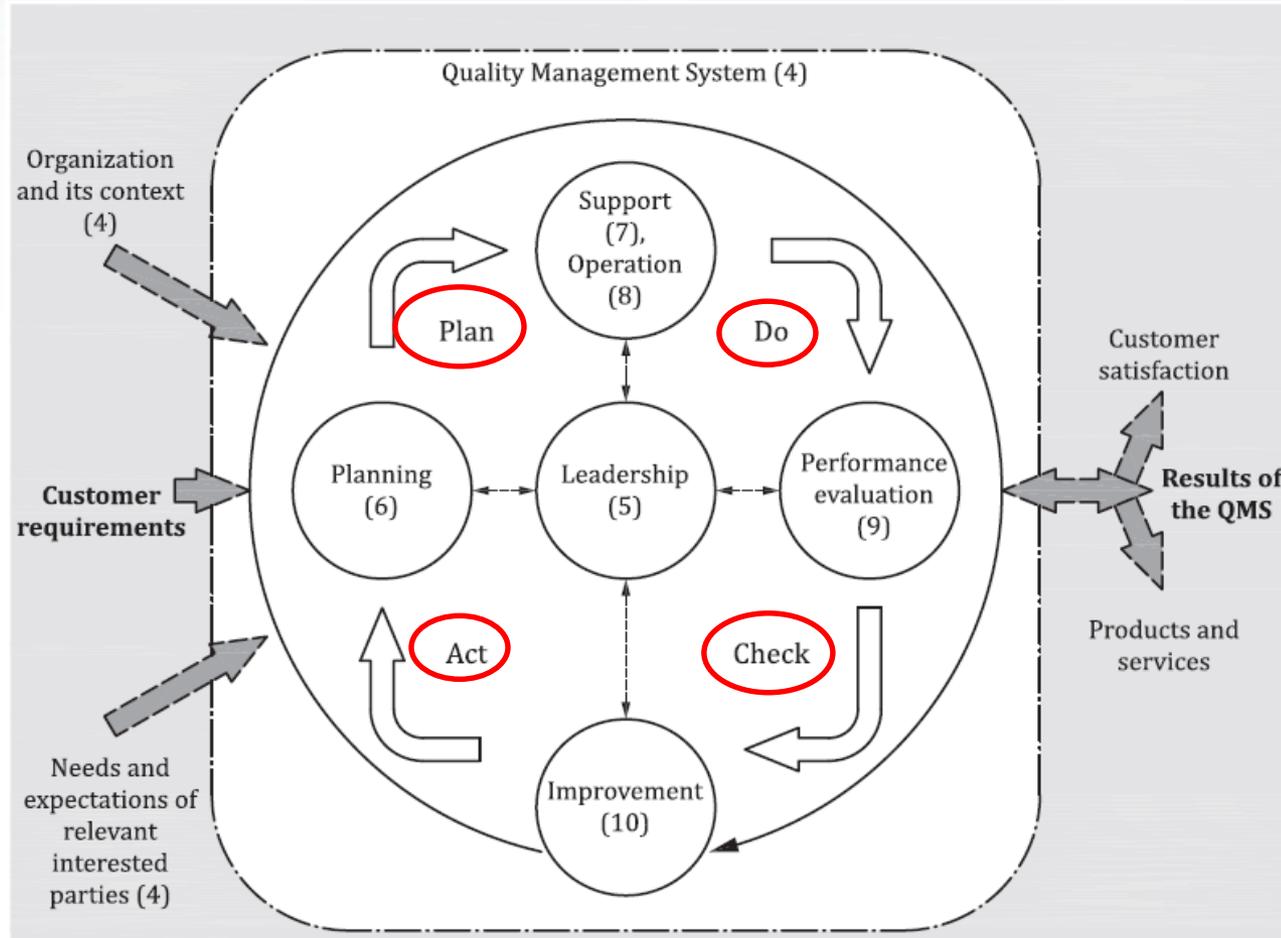
- Customer Focus
- Leadership
- Engagement of People
- Process Approach
- Improvement
- **Evidence-based decision making**
 - Effective decisions are based on the analysis of data and information
- Relationship management

QMS – PRINCIPLES (ISO 9001:2015)

- Customer Focus
- Leadership
- Engagement of People
- Process Approach
- Improvement
- Evidence-based decision making
- **Relationship Management**
An organization and its suppliers are interdependent and a mutually beneficial relationship enhances the ability of both to create value

Quality System Process Overview

ISO 9001:2015



Quality Management System Overview

ISO 9001:2015 --

- Section 4.0 Context of the organization
- Section 5.0 Leadership
- Section 6.0 Planning
- Section 7.0 Support
- Section 8.0 Operation
- Section 9.0 Performance evaluation
- Section 10.0 Improvement

ISO 9001:2015E

- 4.0 Context of the Organization
 - Determine internal/external issues that can impact or are relevant to strategic direction of the organization
 - Include interested parties (regulators, suppliers, subcontractors, etc.)
 - Overall QMS system scope, documents and records

* Reference ISO 9001:2015(E)

ISO 9001:2015E

- 5.0 Leadership
 - Management commitment, integration of the QMS into business processes
 - Customer Focus
 - Quality Policy
 - Organizational roles, responsibilities, authorities

* Reference ISO 9001:2015(E)

ISO 9001:2015E

- 6.0 Planning
 - Address business /product risks and opportunities
 - Quality (business) objectives
 - Changes
 - Controlled, address adverse consequences, resources, responsibilities & authorities

* Reference ISO 9001:2015(E)

ISO 9001:2015E

- 7.0 Support
 - Resources: personnel, infrastructure, environment, monitoring/measuring devices, intellectual property (organizational knowledge)
 - Training, Awareness, Communication, Documented Information

* Reference ISO 9001:2015(E)

ISO 9001:2015E

- 8.0 Operation
 - Contract review, purchasing, design control/validation, process control/product release, product traceability, handling & storage, change control, control of non-conforming

* Reference ISO 9001:2015(E)

ISO 9001:2015E

- 9.0 Performance Evaluation
 - Statistical methods, inspection/testing, audits, management review,
- 10.0 Improvement
 - Select opportunities and implement necessary actions to meet customer requirements and enhance customer satisfaction
 - Corrective Actions for non-conformity (root cause)
 - Continual improvement

* Reference ISO 9001:2015(E)

ISO 13485:2016

- Previously similar to ISO 9001:2008
 - General Requirements
 - Resource Management
 - Product Realization
 - Measurement, Analysis & Improvement
- Medical Device specific
 - Emphasis on regulatory requirements & efficacy
 - Risk Assessment and Management
 - Warranties (Adverse Events)
- Specific requirements in select areas
 - Handout for comparison to ISO 9001:2015 revision

FOOD & DRUG ADMINISTRATION (FDA)

- Federal agency; US Division of Health & Human Services
 - “... protect and promote public health through regulation and supervision of*
 - Food safety, tobacco products, dietary supplements*
 - Prescription, over-the-counter pharmaceuticals, vaccines, biopharmaceuticals, blood transfusions*
 - Medical devices, electromagnetic radiation emitting devices*
 - Animal foods & feed, veterinary products...”*

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 - *Medical devices, electromagnetic radiation emitting devices*
 - *Animal foods & feed, veterinary products...*”

Center for Biologics Evaluation & Research (CBER)

Center for Devices and Radiological Health (CDRH)

Center for Drug Evaluation and Research (CDER)

CODE OF FEDERAL REGULATIONS (CFR)

- CFR is the codification of the general and permanent rules and regulations (sometimes called administrative law)
- The titles are broken down into:
 Chapters, Parts , Sections , and Paragraphs

Example: 21 CFR 820.30(d) (1)

would read Title 21, Part 820, Section 30, Paragraph (d)(1)

CODE OF FEDERAL REGULATIONS (CFR)

Title 1	General Provisions	Title 18	Conservation of Power & Water Resources	Title 35	Reserved (Formerly Panama Canal)
Title 2	Grants and Agreements	Title 19	Customs Duties	Title 36	Parks, Forests, and Public Property
Title 3	The President	Title 20	Employee's Benefits	Title 37	Patents, Trademarks, and Copyrights
Title 4	Accounts	Title 21	Food and Drugs	Title 38	Pensions, Bonuses & Veterans Relief
Title 5	Administrative Personnel	Title 22	Foreign Relations	Title 39	Postal Service
Title 6	Domestic Security	Title 23	Highways	Title 40	Protection of Environment
Title 7	Agriculture	Title 24	Housing & Urban Development	Title 41	Public Contacts and Property Management
Title 8	Aliens and Nationality	Title 25	Indians	Title 42	Public Health
Title 9	Animals and Animal Products	Title 26	Internal Revenue (aka Treasury Regulations)	Title 43	Public Lands: Interior
Title 10	Energy	Title 27	Alcohol, Tobacco & Firearms	Title 44	Emergency Management & Assistance
Title 11	Federal Elections	Title 28	Judicial Administration	Title 45	Public Welfare
Title 12	Banks and Banking	Title 29	Labor	Title 46	Shipping
Title 13	Business Credit and Assistance	Title 30	Mineral Resources	Title 47	Telecommunication
Title 14	Aeronautics & Space (aka Federal Aviation Regulations)	Title 31	Money and Finance: Treasury	Title 48	Federal Acquisition Regulations Systems
Title 15	Commerce and Foreign Trade	Title 32	National Defense	Title 49	Transportation
Title 16	Commercial Practices	Title 33	Navigation & Navigable Waters	Title 50	Wildlife & Fisheries
Title 17	Commodity and Securities Exchanges	Title 34	Education		

cGXP

- cGXP -- Current Good [] Practices
 - Manufacturing (*GMP*)
 - Pharmaceutical
 - Medical Device
 - Laboratory (*GLP*)
 - Clinical (*GCP*)

cGMP – Current Good Manufacturing Practices

“... practices required in order to conform to guidelines recommended by agencies that control authorization and licensing for manufacture and sale of ... drug products, and active pharmaceutical products. These guidelines provide minimum requirements that a ... manufacturer must meet to assure that the products are of high quality and do not pose any risk to the consumer or public ...”
(wikipedia.com)

cGMP – Pharmaceutical 21CFR210/211

- Subpart A: General Provisions
- Subpart B: Organization & Personnel
- Subpart C: Buildings & Facilities
- Subpart D: Equipment
- Subpart E: Control of Components, Drug Product Containers & Closures
- Subpart F: Production & Process Controls
- Subpart G: Packaging & Labeling Controls
- Subpart H: Holding & Distribution
- Subpart I: Laboratory Controls
- Subpart J: Records & Reports
- Subpart K: Returned & Salvaged Goods

<https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRSearch.cfm?CFRPart=210>

<https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRSearch.cfm?CFRPart=211>

cGMP – Medical Device 21CFR820

- Subpart A: [General Provisions](#)
- Subpart B: [Quality System Requirements](#)
- Subpart C: [Design Controls](#)
- Subpart D: [Document Controls](#)
- Subpart E: [Purchasing Controls](#)
- Subpart F: [Identification & Traceability](#)
- Subpart G: [Production & Process Control](#)
- Subpart H: [Acceptance Activities](#)
- Subpart I: [Nonconforming Product](#)
- Subpart J: [Corrective & Preventive Action](#)
- Subpart K: [Labeling & Packaging Control](#)
- Subpart L: [Handling, Storage, Distribution & Installation](#)
- Subpart M: [Records](#)
- Subpart N: [Servicing](#)
- Subpart O: [Statistical Techniques](#)

<https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=820>

cGLP – Good Laboratory Practices for Non-Clinical Studies

*“Good Laboratory Practice (GLP) embodies a set of principles that provides a framework within which laboratory studies are planned, performed, monitored, recorded, reported and archived. These studies are undertaken to **generate data by which the hazards and risks to users, consumers and third parties, including the environment, can be assessed** ... GLP helps assure regulatory authorities that the data submitted are a true reflection of the results obtained during the study and can therefore be **relied upon when making risk/safety assessments.** “*

(wikipedia.com)

cGLP – 21CFR 58 Laboratory Practices

“... These studies are undertaken to generate data by which the hazards and risks to users, consumers and third parties, including the environment, can be assessed ... GLP helps assure regulatory authorities that the data submitted are a true reflection of the results obtained during the study and can therefore be relied upon when making risk/safety assessments.” (wikipedia.com)

- Subpart A: **General Provisions**
- Subpart B: **Organization & Personnel**
- Subpart C: **Facilities**
- Subpart D: **Equipment**
- Subpart E: **Testing Facilities Operation**
- Subpart F: **Test and Control Articles**
- Subpart G: **Protocol for & Conduct of a Nonclinical Laboratory Study**
- Subpart H: (reserved)
- Subpart I: (reserved)
- Subpart J: **Records & Reports**
- Subpart K: **Disqualification of Testing Facilities**

cGCP – Current Good Clinical Practices

*“... GCP enforces tight guidelines on **ethical aspects of a clinical study**. High standards are required in terms of comprehensive documentation for the clinical protocol, record keeping, training, and facilities, including computers and software... GCP guidelines include protection of human rights for the subjects and volunteers in a clinical trial. It also provides **assurance of the safety and efficacy of the newly developed compounds**...”*
(wikipedia.com)

cGCP – Current Good Clinical Practices

“... GCP guidelines include protection of human rights for the subjects and volunteers in a clinical trial. It also provides assurance of the safety and efficacy of the newly developed compounds...”
(wikipedia.com)

- ICH Guidance for Industry --
E6: Good Clinical Practice (Consolidated Guidance)
 - Glossary (Definitions)
 - Principles of ICH GCP
 - Institutional Review Board/
Independent Ethics Committee
 - Investigator
 - Sponsor
 - Clinical Trial Protocol & Protocol
 - Investigator’s Brochure
 - Essential Documents for Conduct
of a Clinical Trial

(ICH = International Conference on Harmonization of Technical Requirements; Europe, Japan & United States)

cGCP – Current Good Clinical Practices

“... GCP guidelines include protection of human rights for the subjects and volunteers in a clinical trial. It also provides assurance of the safety and efficacy of the newly developed compounds...”
(wikipedia.com)

- ICH Guidance for Industry --
E6: Good Clinical Practice (Consolidated Guidance)
- FDA adopted ICH E6, requirements are throughout 21CFR
 - Part 11 – Electronic Records & Signatures
 - Part 50 – Protection of Human Subjects
 - Part 54 – Financial Disclosure
 - Part 56 – Institutional Review Boards
 - Part 812 – Investigational Device Exemptions
 - Part 814 – Premarket Approval of Medical Devices

cGXP

- cGXP -- Current Good [] Practices
 - Manufacturing (*GMP*)
 - Pharmaceutical
 - Medical Device
 - Laboratory (*GLP*)
 - Clinical (*GCP*)

QUALITY MANAGEMENT SYSTEMS

- ISO 9001:2008: General Quality Management Systems
 - ISO 13485:2003 Medical Device Manufacture
 - ISO/TS 16949:2009 Automotive
 - SAE/AS9100C Aeronautics
- } voluntary
- 14CFR Aeronautics
 - 21CFR Foods, Pharmaceuticals, Medical Device, Cosmetics
 - 40CFR Pesticides (herbicides, sanitizers)
 - 49CFR Transportation
- } mandatory

– Basic Premise

- Say what you do (documents)
- Do what you say (training)
- Record what you did (write it down)
- Check the results (analysis)
- Act on the difference (improvement)

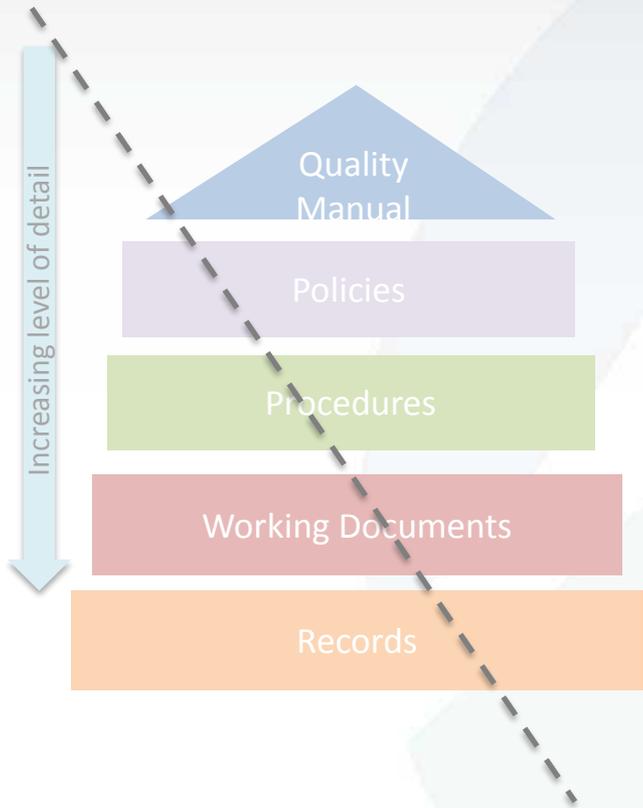


Say What you do - DOCUMENTATION

DOCUMENTATION



DOCUMENTATION



NOTE: ISO 9001:2015 revision no longer follows this model

Now refers to “Documented Information”

maintain documented information is equivalent to procedure

retain documented information is equivalent to records

Existing quality management systems built on original model – therefore, detail still provided

ISO 13485:2016 (medical devices) and 21CFR 210/211 (pharma) and 820 (medical devices) do specify where procedures are required

DOCUMENTATION



DOCUMENTATION



- **Quality Manual**
high level document providing overview of business operation and quality system

Note: No longer an explicit requirement for ISO 9001:2015

- **Policies**
provide general guidelines by which company conducts the various manufacturing (service) operations

DOCUMENTATION



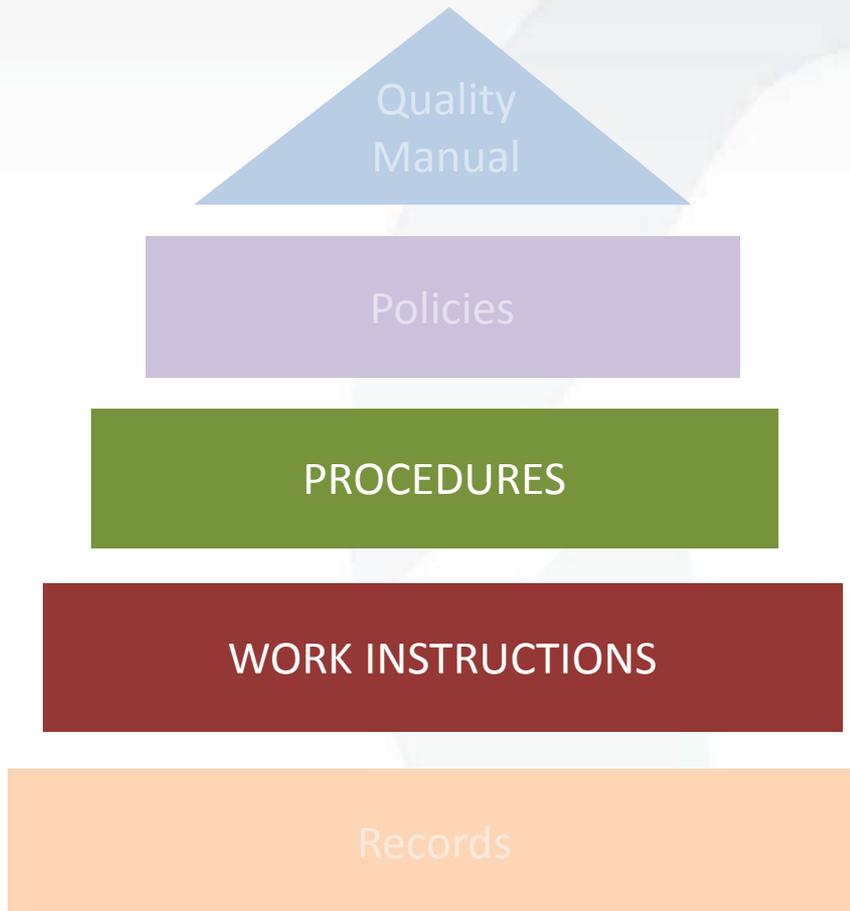
- Procedures – operational detail regarding how business has implemented policies and provide general information on day-to-day operations. (SOP)
- Working Documents
detailed steps to carry-out specific task(s)
 - Work instruction
 - Test Methods
 - Product / Process / Raw material Specifications
 - Protocols
 - Etc.
- Records
documented results completed tasks
 - Quality
 - Business

DOCUMENTATION

- Quality Manual – high level document providing overview of business operation and quality system
- Policies – provide general guidelines by which company conducts the various manufacturing (service) operations
- Procedures – operational detail regarding how business has implemented policies and provide general information on day-to-day operations. (SOP)



Say What You Do



- **Seven Quality Tools**
 1. Flow Chart / Run chart
 2. Check Sheet
 3. Control Charts
 4. Cause & Effect Diagram
 5. Histogram
 6. Pareto Chart
 7. Scatter Diagram

Documentation

- Standard Operating Procedures (SOP)
- Work Instructions (WI)

Either document type could include flow charts (process Maps) and/or written instructions

Check sheets (data collection forms) will be used to record what occurred during operation(s); However examples are typically included or referenced in the SOP / WI

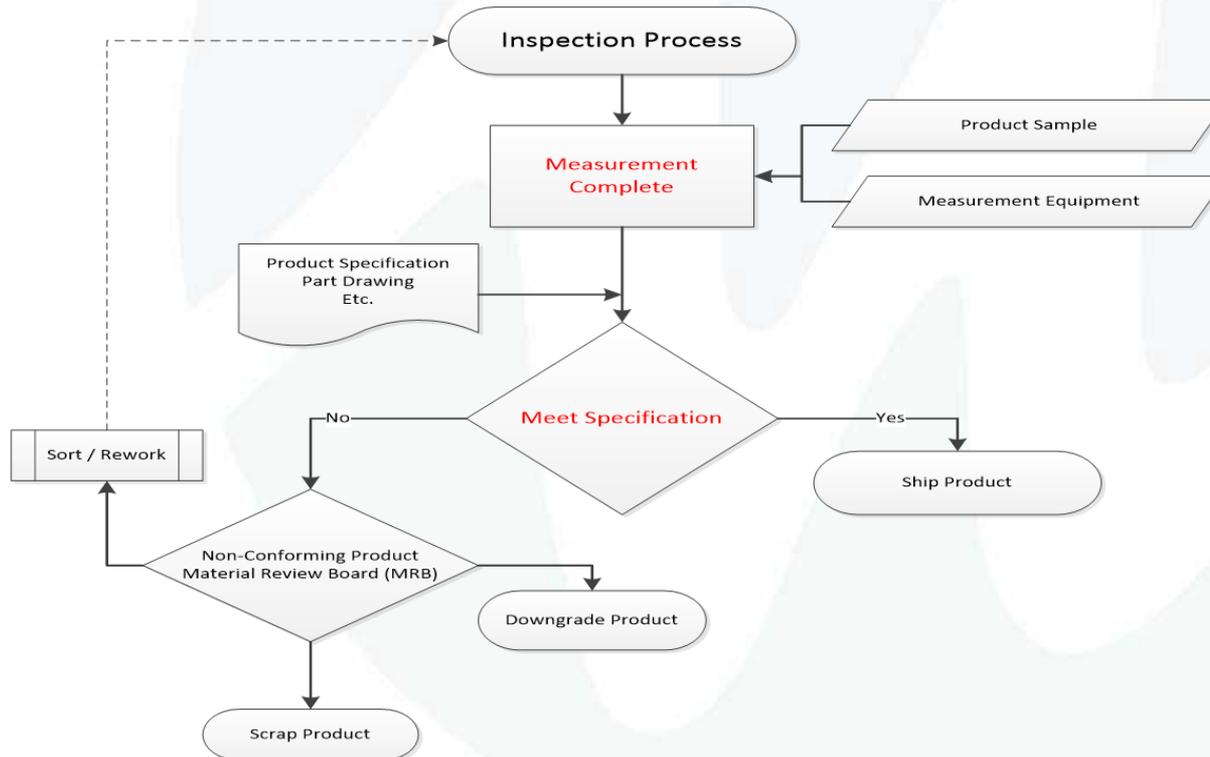
Seven Quality Tools

1. Flow Chart / Run Chart
2. Check Sheet
3. Histogram
4. Control Charts
5. Cause and Effect Diagram (a.k.a. Ishikawa or Fishbone)
6. Pareto Chart
7. Scatter Diagram

SEVEN QUALITY TOOLS

1. Flow Chart / Run Chart

- Documents process and associated steps
- Useful for delineating operational tasks



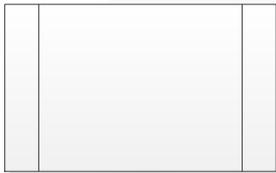
Flow Chart Symbol Key



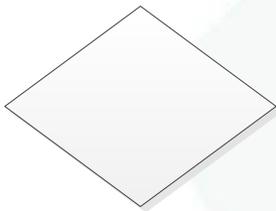
Start /End



Process



Subprocess



Decision



Document



Database

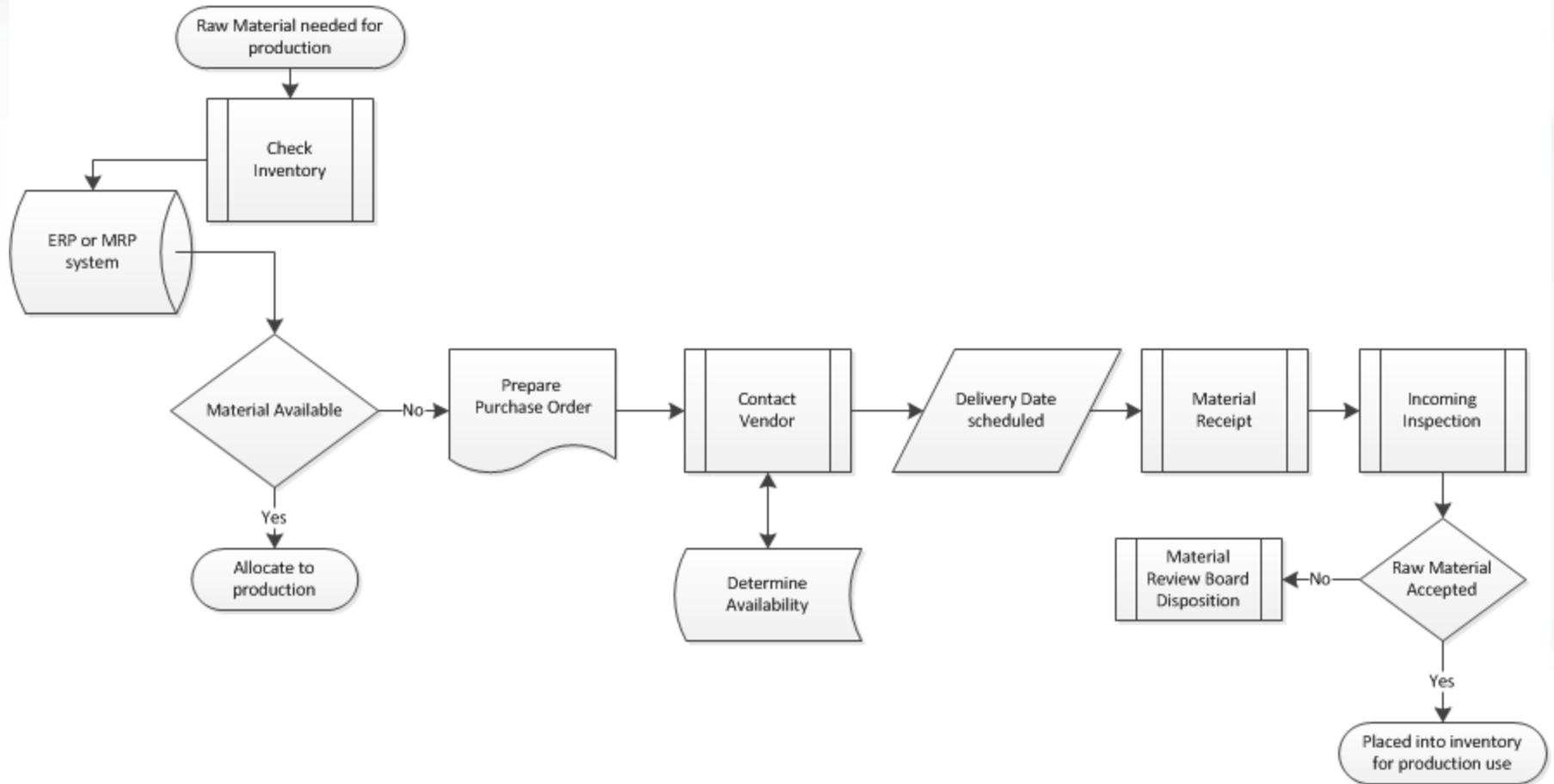


Data



External Data

Purchase Raw Materials



Process Map for Purchasing Raw Materials Standard Operating Procedure

Documentation

- Typical Policy or Procedure
 - Purpose
 - Scope
 - Responsibilities
 - Procedures
 - Quality Records
 - Revision History



Documentation

- Typical SOP

- Purpose
- Scope
- Responsibilities
- Process / Procedure
- Quality Records
- Revision History

- Typical Work Instruction

- Purpose
- Scope
- Materials
- Equipment
- Safety
- Responsibilities
- Tasks
- Quality Records
- Revision History



Documentation

- Example – verbal instructions
 - Full class
 - Pairs
- Homework – Laboratory Preparation

Do what you say - TRAINING



- Qualifications
 - Job Description
 - Resume
- Read and understand
- On-the-job Training (OJT)

Comprehension &
Effectiveness

Write it all down - RECORDS



QUALITY RECORDS



- Manual
 - Forms
 - Lab Notebooks
- Electronic
 - Automated systems
 - Validations (Reports)
 - Email

QUALITY RECORDS

- Relate to product
 - components used in manufacture
 - acceptance/rejection of finished product
 - storage, shipment, handling of finished product
- Relate to service provided

NOT Business records (i.e. financial records, personnel files, etc.)

QUALITY RECORDS

- Create permanent , official record of operation(s) conducted.
- Do not omit or falsify data
- Good Documentation Practices (GDP)
 - Terminology used in Pharmaceutical and Medical Device industries.
 - Standards by which documents are created and maintained.
 - Not codified by FDA, but are considered cGMP
 - ISO 9001:2008E also have requirements for legibility and document handling

GDP – Data Entry

- The **Do's** will be in **green**
- The **Don'ts** will be **red**

GDP – Recording Data

- Data recording shall be **timely** and **complete**
 - Recorded **at the time** the operation performed
 - Use the **forms provided**, **post-it[®] notes or scrap paper** are not allowed
 - do not **transcribe data**
 - **All data recorded**
 - do not use **ditto marks or continuation lines**
 - Do not **omit data**

GDP – Recording Data

- Make entries in permanent/indelible Ink (blue/black)
 - Pencil is not allowed
- Make entries Concise, Accurate and Legible
 - Enter data in English (unless otherwise directed)
 - Do not leave blank spaces; cross out and N/A
 - Entries should be on front page only (unless otherwise directed)
 - If using the back of the form is necessary, this MUST be clearly marked on the front page

GDP – Recording Data

- All data/records (pages) shall be included
 - Number the pages to be added
 - Example: page 2 of 4
 - Do not **destroy or remove pages**
 - Use diagonal single cross-out, initial and date
- Follow company's format for **Date and Time:**
 - Do not **back date**.
 - Formats shall not have different meanings
- For Critical Entries, have a **second authorized** person **independently verify** activity/entry

GDP – Recording Data

- Follow company's format for **Initials and Signatures**
 - Signatures and initials serve as an employee's confirmation that activity performed was per procedure
 - Signatures and initials have **company-specific, legal, and/or ethical ramifications**
 - Don't sign/initial for **another person**
 - Don't use **signature stamps**

GDP – Recording Data Summary

- Data recording shall be timely and complete
- Recorded in permanent/indelible ink (blue/black)
- Data shall be concise, accurate and legible
- All data/records (pages) shall be included
- Follow company's format for date and time
- For Critical Entries, have an independent verification
- Follow company's format for initials and signatures

GDP – Data Correction

- The **Do's** will be in **green**
- The **Don'ts** will be **red**

GDP – Data Correction

- For incorrect data entries
 - Use a **single line-out**, leave original data entry legible
 - Do not **scribble, overwrite or obscure** original data
 - Do not use **Wite-Out® or corrective tape**
 - **Sign or initial** (per Company procedure)
 - **Date** for when the correction made
 - **Concise reason/justification** for the correction

GDP – Data Correction

- Do not **transcribe data**
 - IF transcription necessary, **must be clearly marked and original maintained**
- When there is insufficient space for the correction rationale
 - Use a **reference symbol** at the point of the correction
 - **Pharmaceutical/Medical Device prefer numbers to asterisks (*)**
 - **Follow Company procedure**

GDP – Data Correction Summary

- For incorrect data entries
 - Use a single line-out, leaving original data entry legible
 - Sign and date, with rationale for change
 - Do not use correction tape or fluid
- Do not transcribe data, original data shall be maintained.
- When there is insufficient space for the correction rationale use a reference symbol at the point of the correction.

GDP – Electronic Records

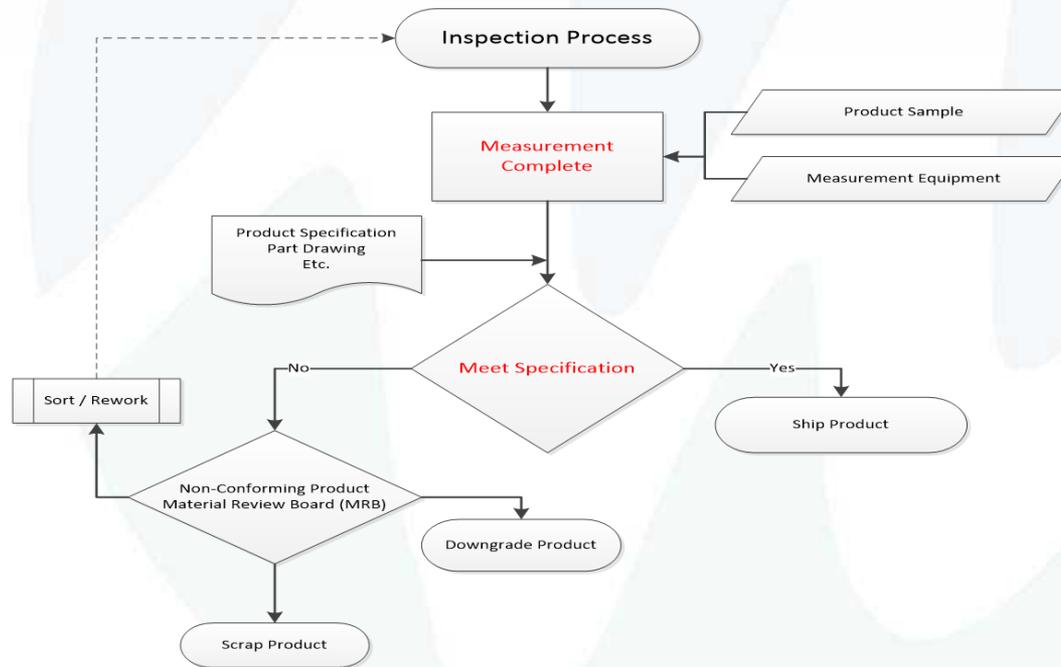
- 21CFR Part 11 for Pharmaceutical (Bio-Tech) and Medical Device
- Validated system and Electronic Signature
 - Replaces hand written signature
 - Unique login and password combination
 - Will change often

DO NOT SHARE

SEVEN QUALITY TOOLS

1. Flow Chart / Run Chart

- Documents process and associated steps
- Useful for delineating operational tasks

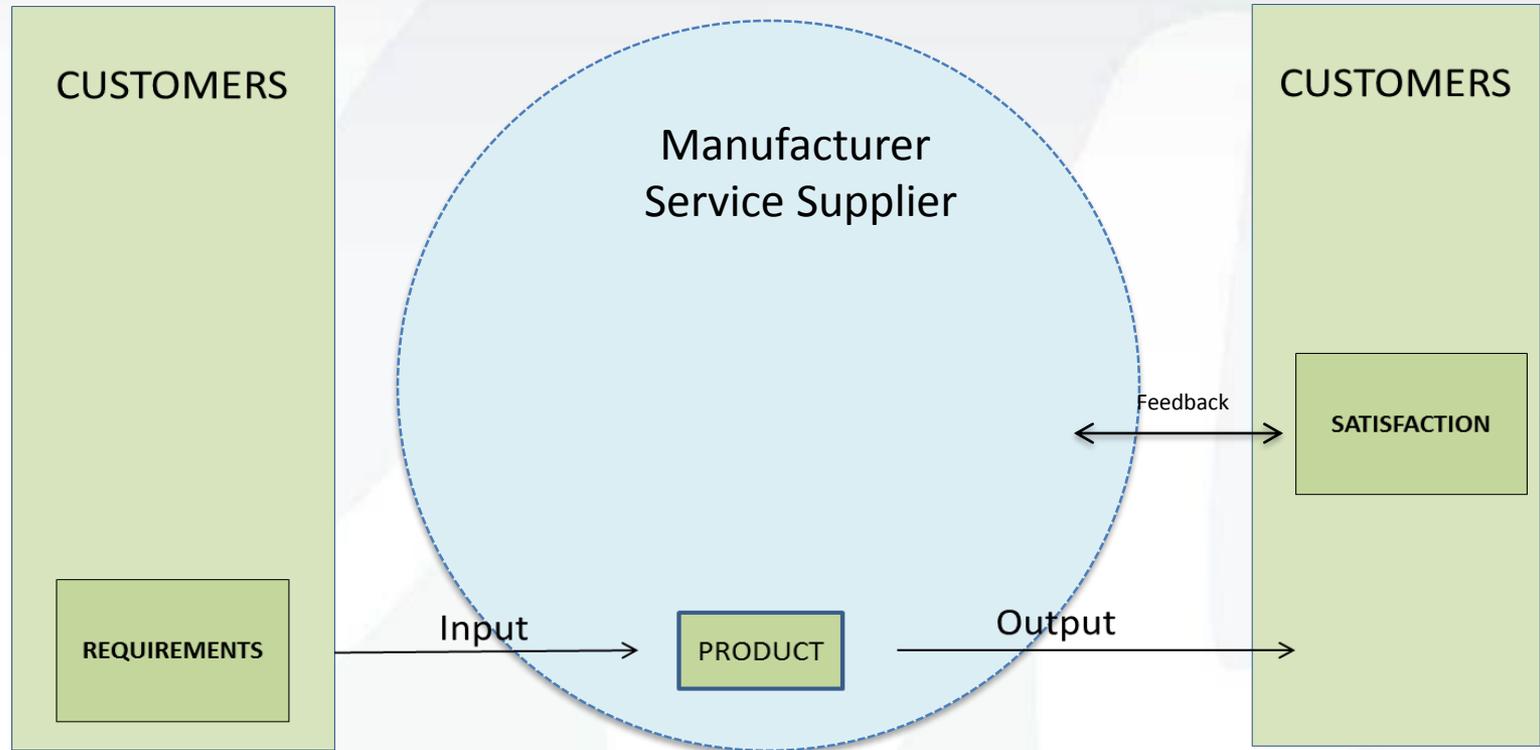




A large, light blue, stylized letter 'W' logo is centered in the background of the slide. The 'W' is composed of several rounded, overlapping shapes that create a sense of depth and movement.

QUALITY ASSURANCE QUALITY CONTROL

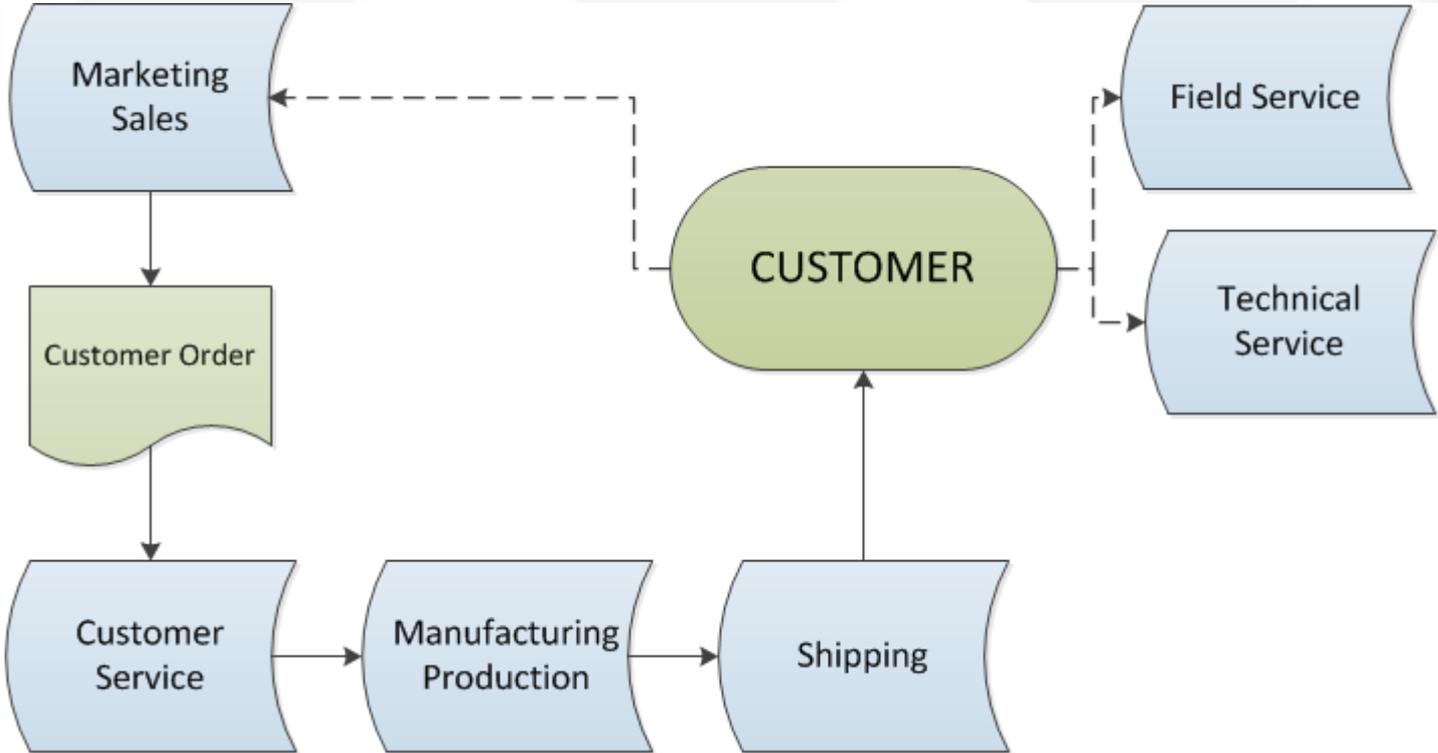
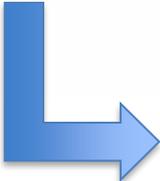
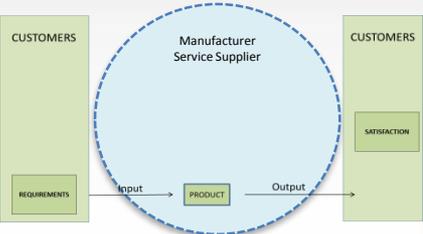
BUSINESS PROCESSES



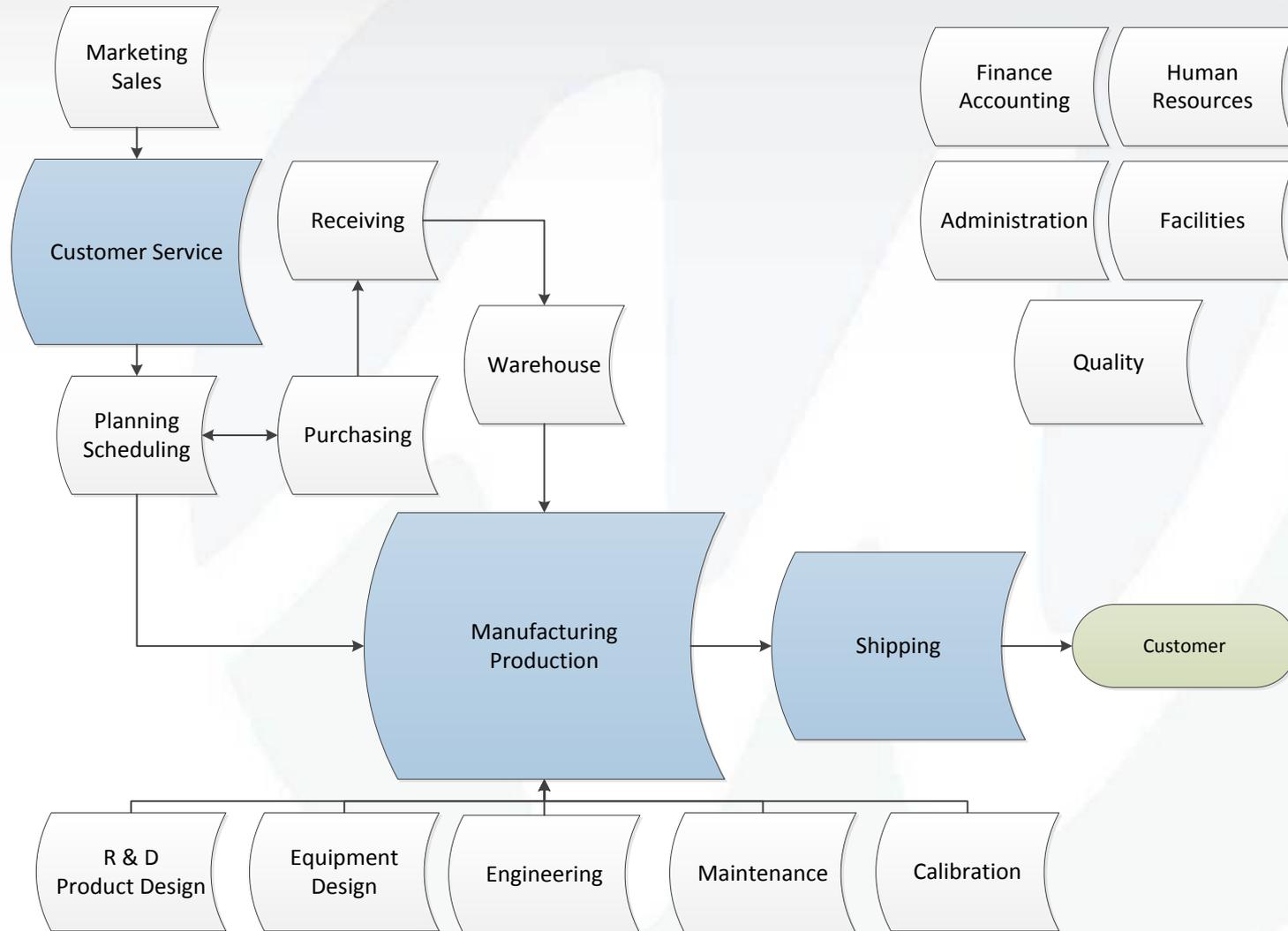
ISO9001:2008E Process Model

Quality is a product (or service) with the features and characteristics which determine desirability and can be controlled to meet certain basic requirements.

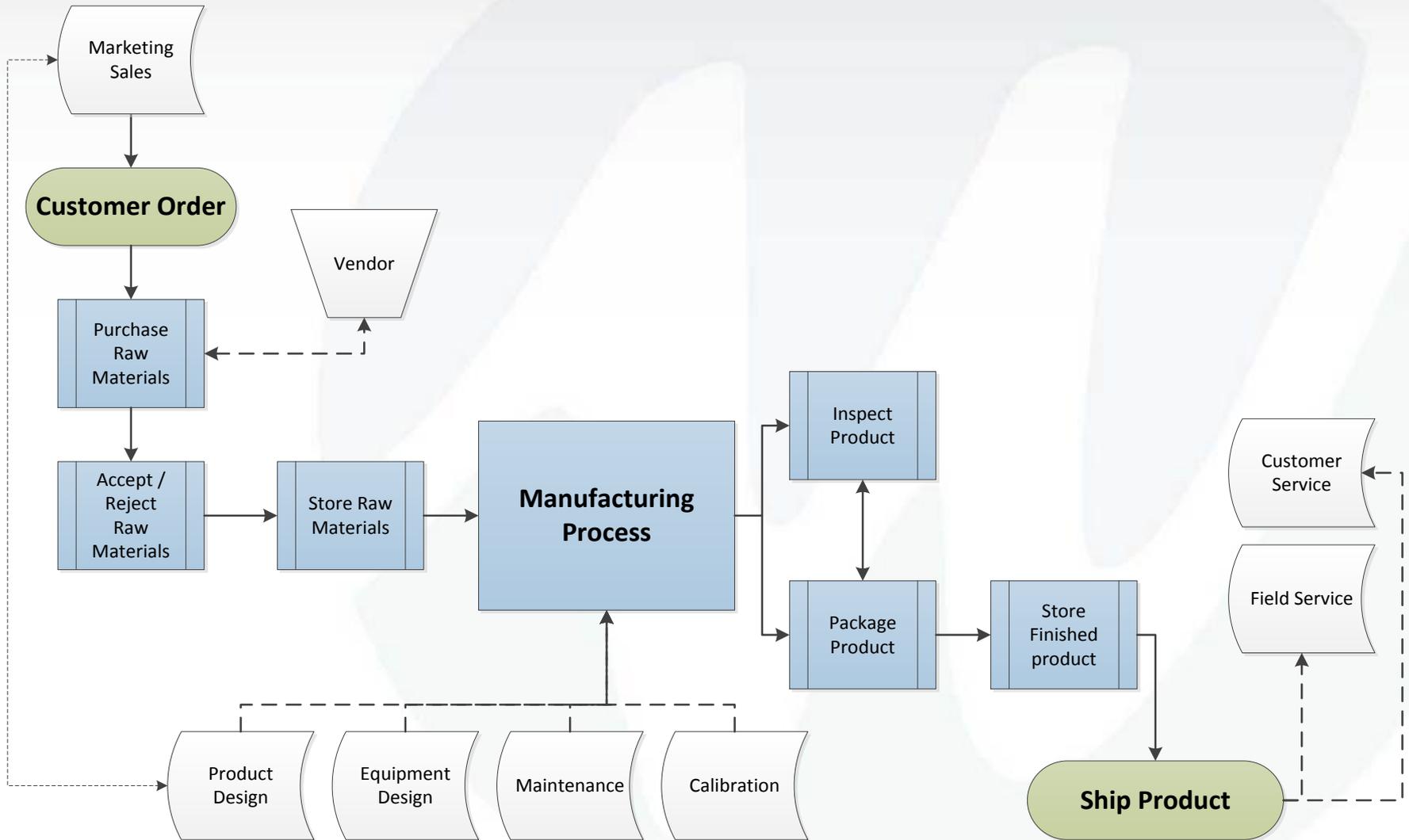
BUSINESS PROCESSES



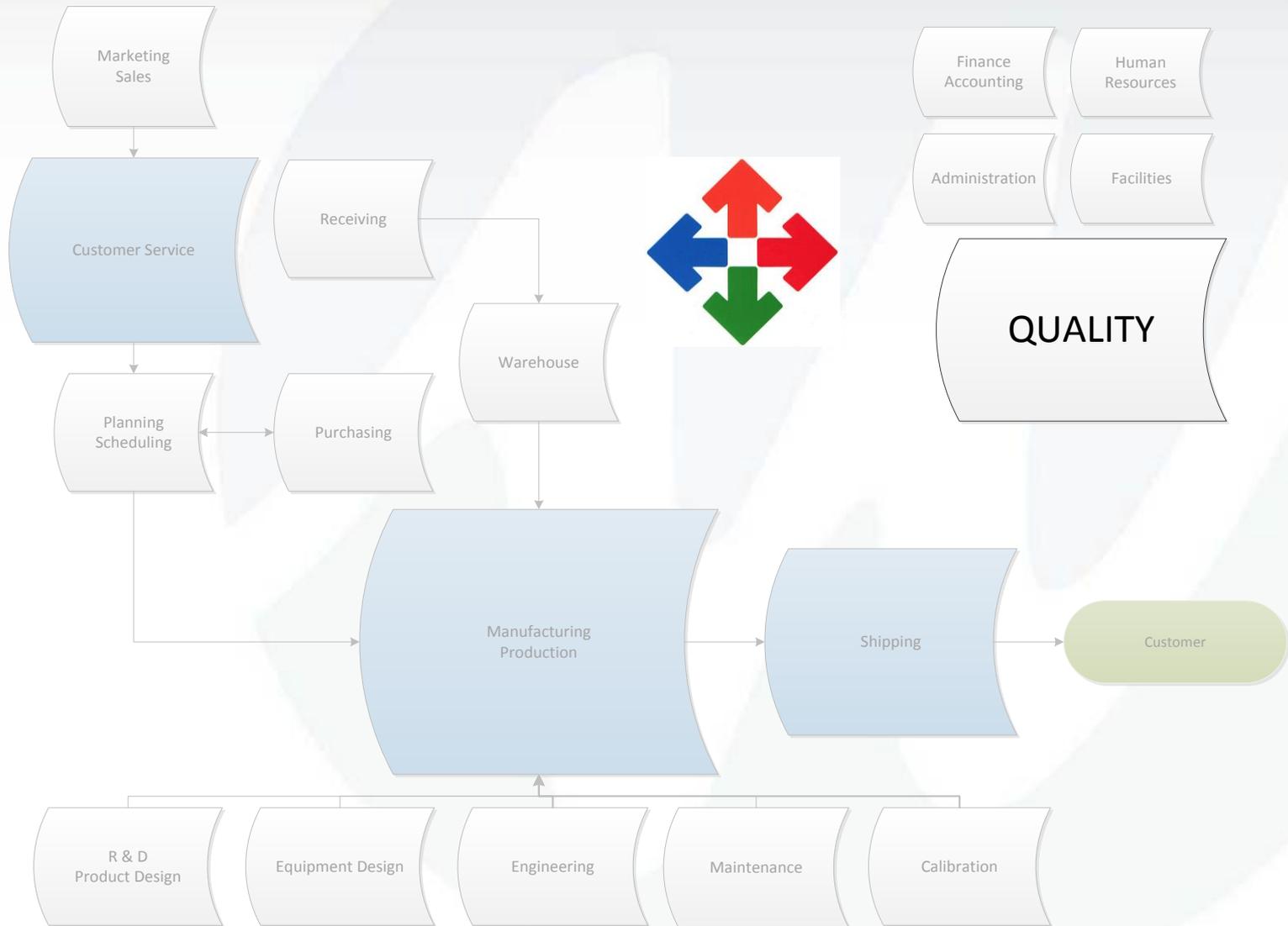
MANUFACTURING PLANT DEPARTMENTS



MANUFACTURING – MATERIAL FLOW



DEPARTMENT- QUALITY



QUALITY DEPARTMENT

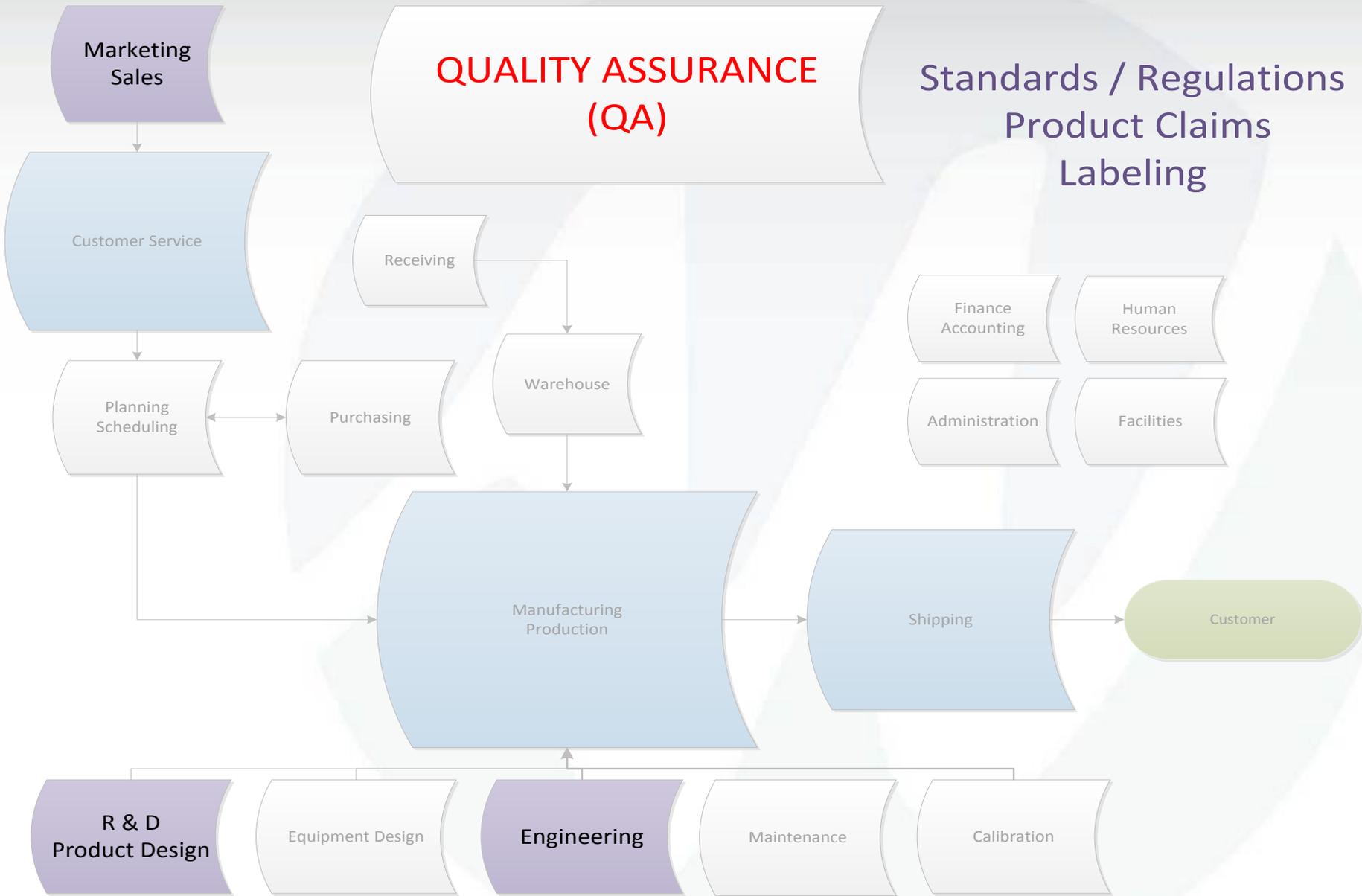
- Voice of the Customer
 - Quality is determined by the Customer (end-user) based on their expectation and needs
 - Internal and external
- Regulatory Review
 - Maintain industry relevant standards
 - Maintain awareness and communicate statutory requirements
 - File appropriate documents with government agencies
 - Domestic
 - International
- Support Function (manufacturing or service)
 - Quality Assurance
 - Quality Control

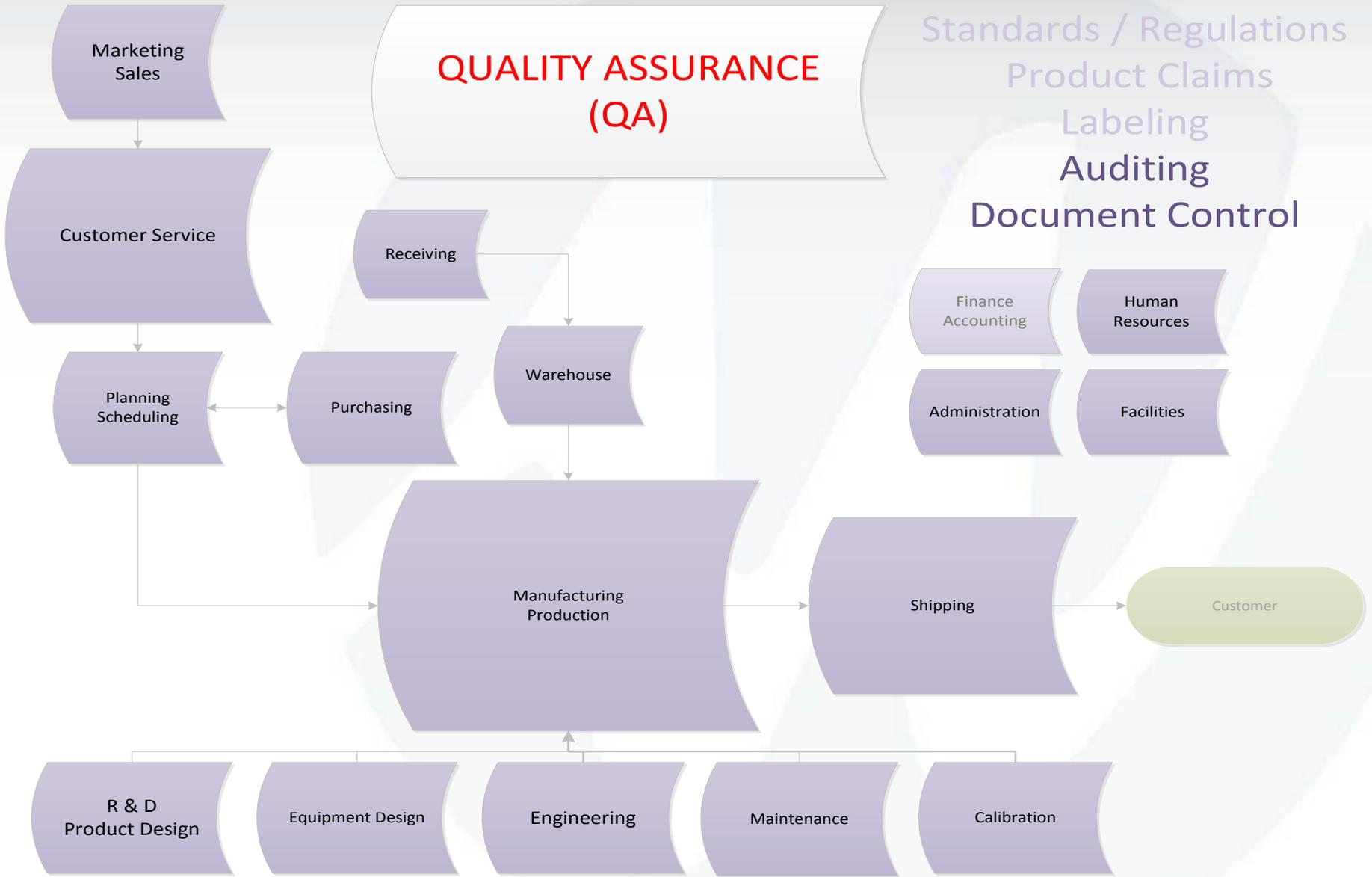
QUALITY ASSURANCE VS QUALITY CONTROL

- **Quality Assurance (QA)** plans, develops, documents processes that optimize objectives
 - Reviews and Evaluates
 - Systems based (oversight)

QUALITY ASSURANCE

- System Oversight
 - Standards Maintenance
 - Regulatory Review
- Document Control
 - Maintain records
 - Change Control
- Auditing
 - Internal Monitoring
 - Supplier Approval / Review
- Regulatory Department
 - Maintain Agency documents (filings)
 - Up-to-date on Regulations
 - Communicate changes



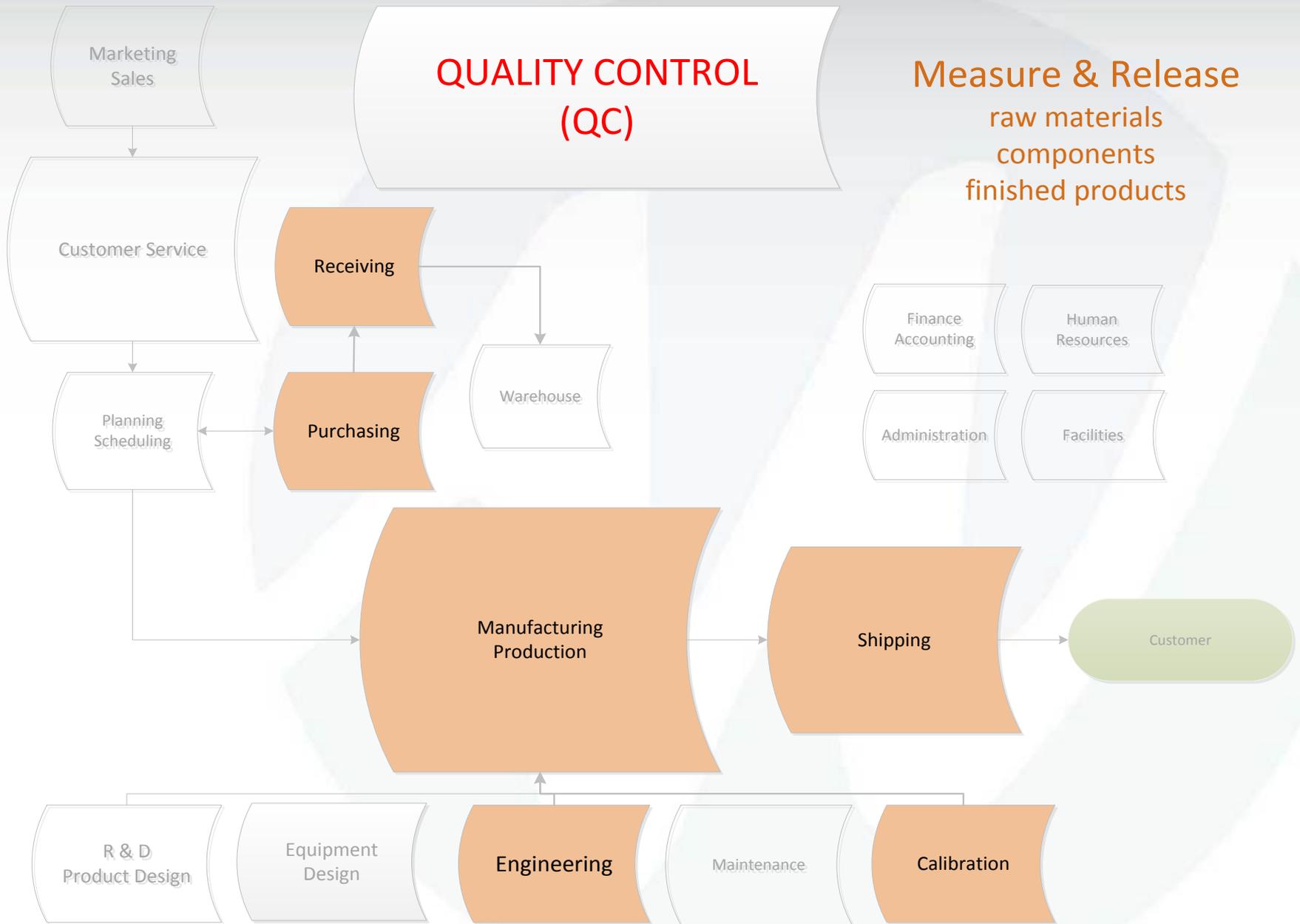


QUALITY ASSURANCE VS QUALITY CONTROL

- *Quality Assurance (QA)* plans, develops, documents processes that optimize objectives
 - Reviews and Evaluates
 - Systems based (oversight)
- ***Quality Control (QC)*** evaluates and respond to non-conformities
 - Measures & Releases
 - Manufacturing floor

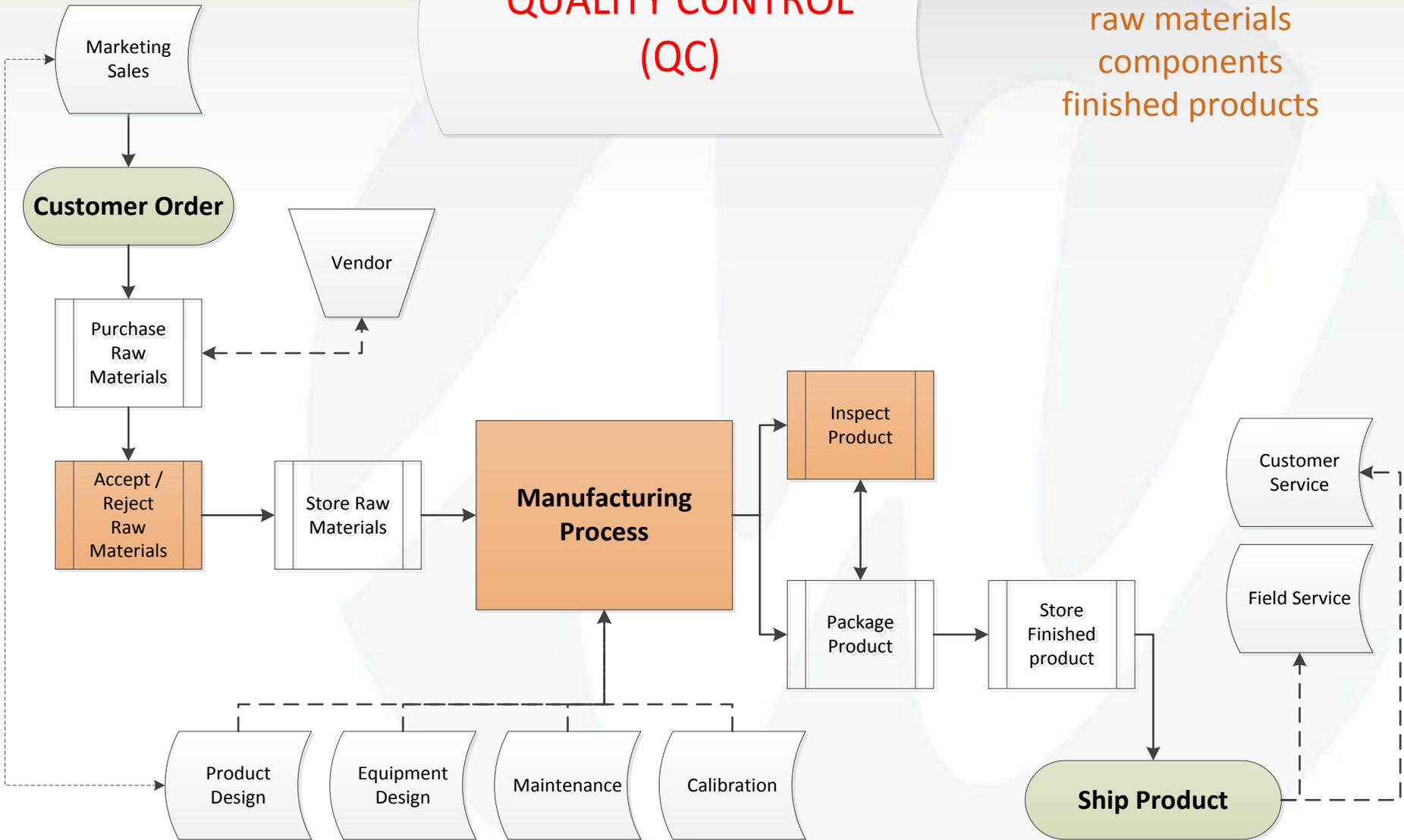
QUALITY CONTROL

- Incoming Quality
 - Material/Component Evaluation
 - Identity testing
 - Dimensional measurements
 - Physical testing
- Production Floor
 - Start-up of process(es)
 - In-process monitor
- Product Release
 - Final Inspection
 - Document (Batch/Lot Record) Review



QUALITY CONTROL (QC)

Measure & Release
raw materials
components
finished products



DEFINITION

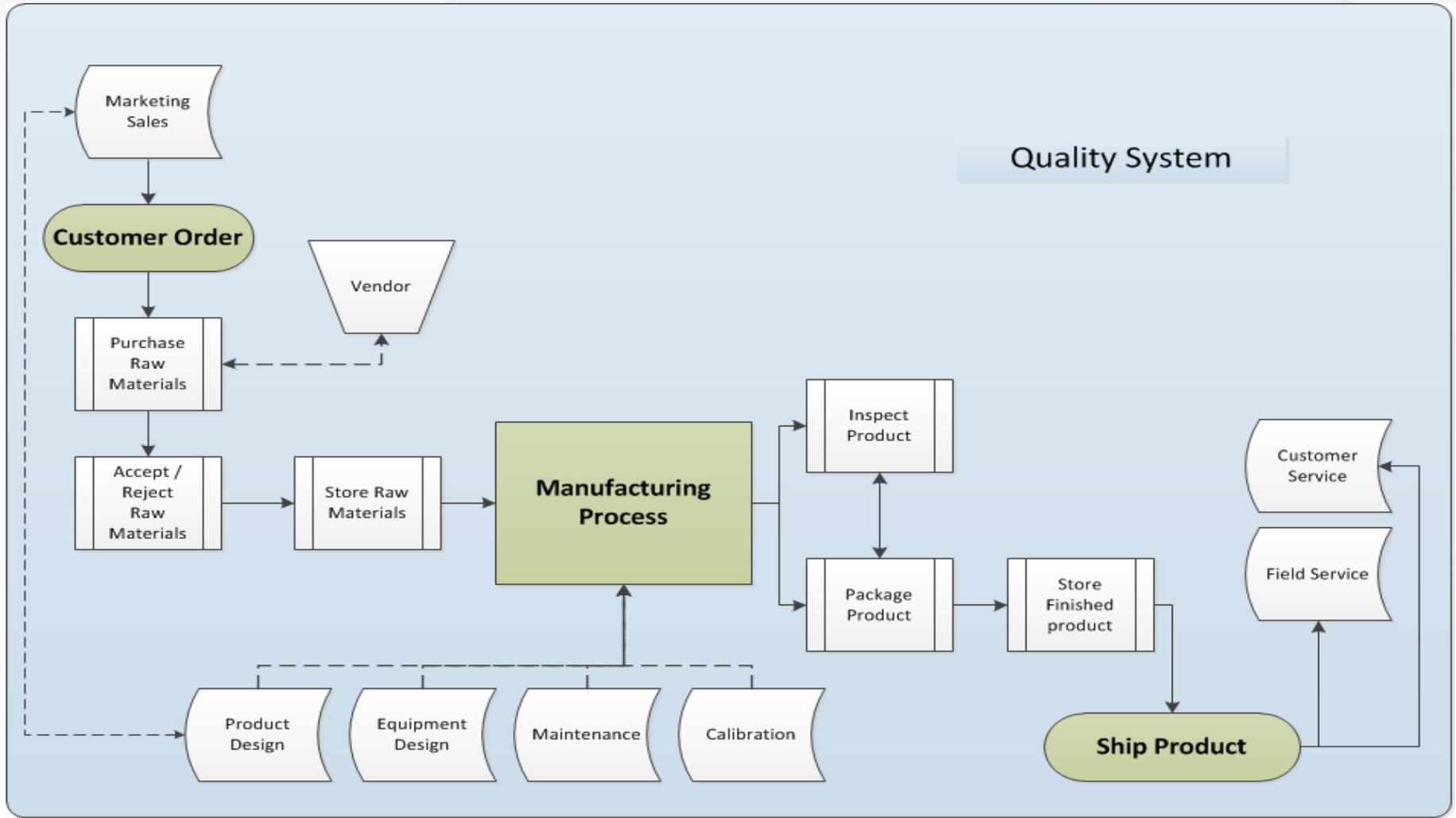
Quality is a product (or service) with the *features and characteristics* which determine *desirability* and can be *controlled to meet certain basic requirements*.

JURAN, DEMING, TQM:

Quality is a value that must be built into the product.
Quality cannot be inspected into the product

Quality is not just Quality's Responsibility

PROCESS FLOW - MANUFACTURING



Quality is not just Quality's Responsibility

- Marketing / Sales
 - Translate Customer requirements
 - Contract review
- Customer Service
 - Technical support
 - Complaints
- Engineering (design, process, manufacturing)
 - Quality is built into product, not inspected in
 - Process needs to be repeatable
 - Manufacturing maintains equipment, looks for improvements

Quality is not just Quality's Responsibility

- Manufacturing/Production
 - In-process testing
 - Timely data recording
 - Following procedures
- Maintenance
 - Equipment PM
 - Spare Parts
- Calibration
 - Measurement Equipment
 - Production/Assembly Gages, scales, etc.

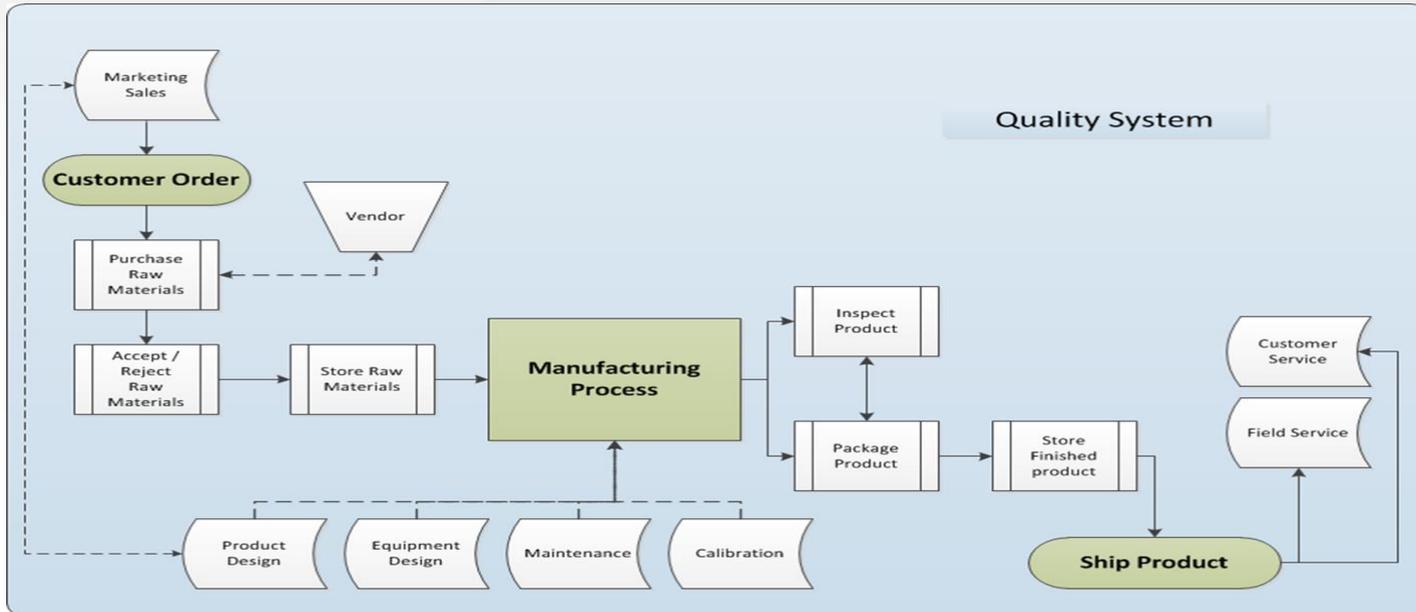
Quality is not just Quality's Responsibility

- Procurement / Purchasing
 - Supplier approval
 - Alternate Vendors
 - Raw Material Specification(s)
- Packaging / Shipping
 - Product protection
 - Stacking processes
- Storage / Warehouse
 - Environmental (i.e. cold storage, dry, etc)
 - Stacking
 - Delivery to production (material transfer)

Quality is not just Quality's Responsibility

- Facilities
 - Controlled Environments
 - Clean Rooms
 - HVAC
- Field Service
 - Customer Expectations
 - Customer Requirements
 - Technical Assistance

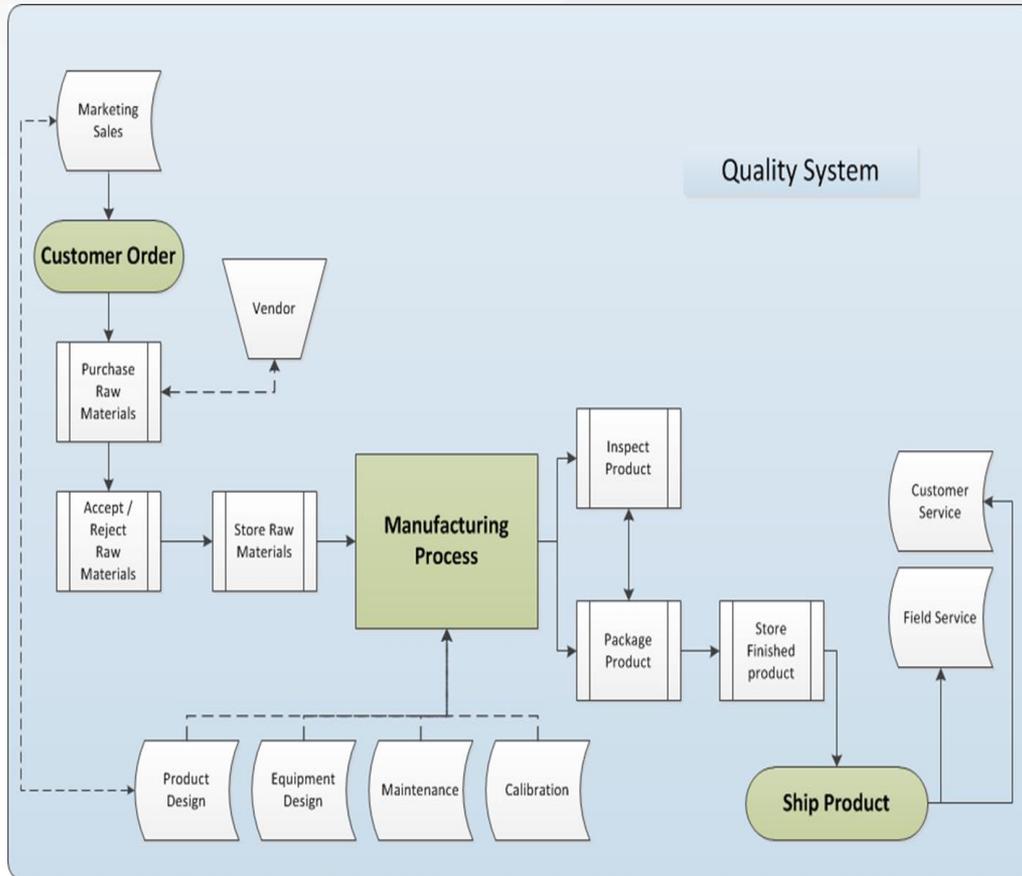
QUALITY IS EVERYONE'S RESPONSIBILITY



- Marketing / Sales
- Customer Service
- Manufacturing/Production
- Maintenance
- Calibration
- QA / QC
- Engineering
- Procurement / Purchasing
- Packaging / Shipping
- Storage / Warehouse
- Facilities
- Field Service

**Quality is determined by the
Customer (end-user)
based on their expectation and needs.**

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- Marketing / Sales
- Customer Service
- Manufacturing/Production
- Maintenance
- Calibration
- QA / QC
- Engineering
- Procurement / Purchasing
- Packaging / Shipping
- Storage / Warehouse
- Facilities
- Field Service

What are the Customer / Supplier relationships between departments?





QUALITY ASSURANCE
QUALITY CONTROL

PROFESSIONAL PRACTICES

PROFESSIONAL PRACTICES

- Company's Code of Ethics
 - Adopted by companies to enable employees to:
 - Understand difference between 'right' and 'wrong'
 - Apply understanding to their business decisions.
 - Implies documents at three (3) levels:
 - Codes of Business Ethics
How they choose to do business
 - Codes of Conduct for Employees
Show up on time, Dress code, Follow policies, etc.
 - Codes of Professional Practice

PROFESSIONAL PRACTICES

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CODES OF PROFESSIONAL PRACTICE

- Honesty
- Integrity
- Transparency
- Accountability
- Confidentiality
- Objectivity
- Respectfulness
- Obedience to the Law

INTEGRITY - ETHICS

- American Society for Quality Code of Ethics (ASQ.org)
 - **Fundamental Principles:** ASQ requires its members and certification holders to conduct themselves ethically by:
 - Being honest and impartial in serving the public, their employers, customers, and clients.
 - Striving to increase the competence and prestige of the quality profession, and
 - Using their knowledge and skill for the enhancement of human welfare.

American Society for Quality Code of Ethics (ASQ.org)

- Members and certification holders are required to observe the tenets set forth below:
 - **Relations With the Public**
 - Article 1 – Hold paramount the safety, health, and welfare of the public in the performance of their professional duties.
 - **Relations With Employers, Customers, and Clients**
 - Article 2 – Perform services only in their areas of competence.
 - Article 3 – Continue their professional development throughout their careers and provide opportunities for the professional and ethical development of others.
 - Article 4 – Act in a professional manner in dealings with ASQ staff and each employer, customer or client.
 - Article 5 – Act as faithful agents or trustees and avoid conflict of interest and the appearance of conflicts of interest.
 - **Relations With Peers**
 - Article 6 – Build their professional reputation on the merit of their services and not compete unfairly with others.
 - Article 7 – Assure that credit for the work of others is given to those to whom it is due.

INTEGRITY - ETHICS

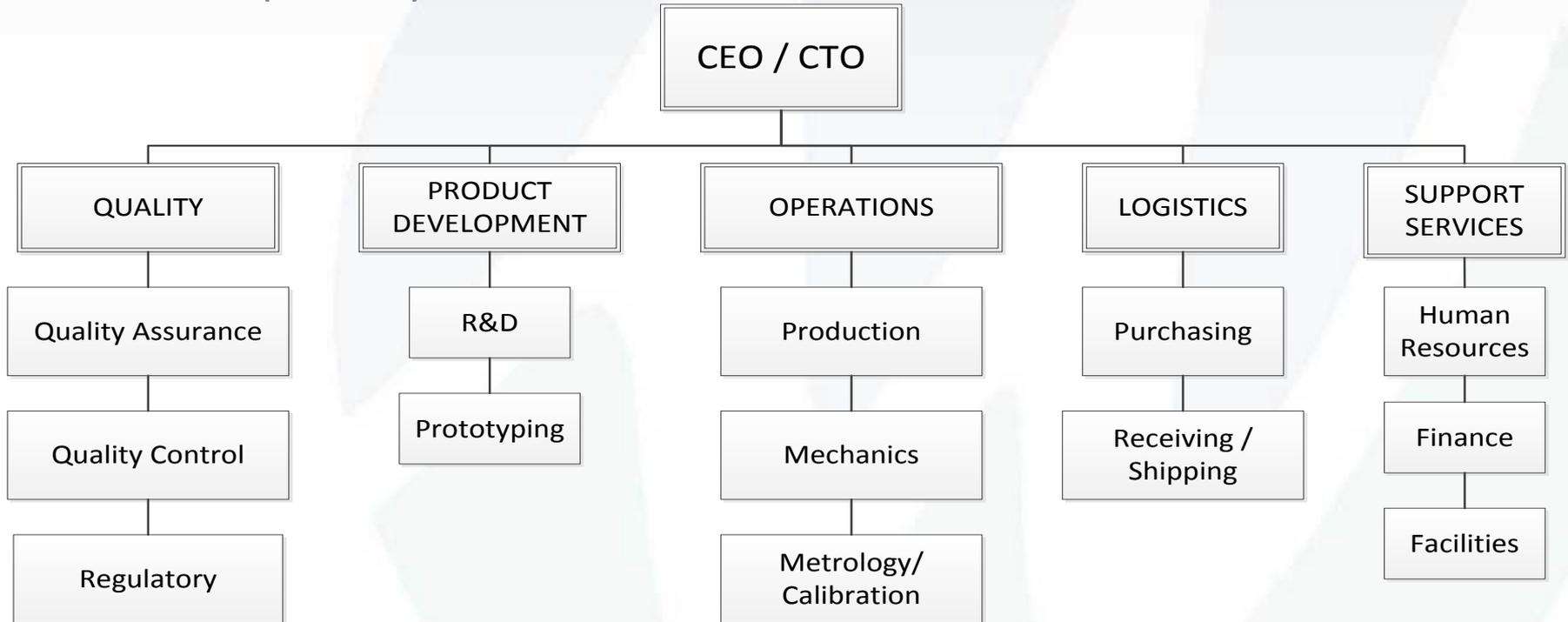
- Quality Assurance & Quality Control
 - Voice of the Customer
 - Is the product manufactured properly?
 - Does the product function as expected?
 - Was the product manufactured using the correct materials
 - Regulatory review
 - Does the product/service meet the Regulatory requirements (i.e. government, UL, etc.)
 - Does the product meet the Customer regulatory expectations?
 - Support function
 - Work with manufacturing, purchasing, etc. to meet Customer and Regulatory requirements

INTEGRITY - ETHICS

- Quality typically alternate reporting structure
 - Avoid conflict of interest
 - Required by FDA

INTEGRITY - ETHICS

- Quality typically alternate reporting structure
 - Avoid conflict of interest
 - Required by FDA



...”Being honest and impartial in serving the public...”

...”Using their knowledge and skill for the enhancement of human welfare...”

QUALITY ORGANIZATIONS

- **Regulatory:** Government organizations with legal oversight of industry
 - US FDA, European Union, etc.

QUALITY ORGANIZATIONS

- **Independent:** Organizations providing external review of industry processes
 - International Organization for Standardization (ISO)
International standard-setting body composed of representatives from various national standards organizations; various standards (documents) along with technical reports, specifications and guides.
 - American National Standards Institute (ANSI)
Oversees development of voluntary consensus standards for products, services, processes, systems and personnel in US; also coordinates US standards with international standards for worldwide American product use. (documents and physical standards)
 - US Pharmacopeia Convention (USP)
Establishes written (documentary) and physical standards (reference) for medicines, food ingredients and dietary supplements. Standards are used by regulatory agencies and manufacturers to help ensure products are of appropriate identity, as well as strength, quality, purity and consistency

QUALITY ORGANIZATIONS

- **Trade:** Organizations supported by industry representing common interests and processes
 - American Society for Quality (ASQ)
Advances the professional development, credentials, knowledge and information services, membership community, and advocacy on behalf of millions of individual and organizational members in 140 countries
 - ASTM International (American Society for Testing & Materials)
An international organization that develops and publishes voluntary consensus technical standards and test methods for a wide range of materials, products, systems, and services.

Quality Concepts - SUMMARY

- Quality is a product (or service) with the *features and characteristics* which determine *desirability* and can be *controlled to meet certain basic requirements*.
- Organizations
 - Regulatory: legal oversight of industry
 - Independent: provide external review of industry quality systems
 - Trade: provide support by representing common interests
- Manufacturing & Service Industries
- ISO Standards and FDA Regulations
- History of Quality (Taylor, Deming, Juran)

Quality Concepts - SUMMARY

- Quality System
 - Method of doing business
 - customer focused with everyone involved, process centered and continual improvement
 - Regulatory Requirements (FDA, EPA, FAA, etc.)
 - Basic Premise
 - Say what you do (documents)
 - Do what you say (training)
 - Record what you did (write it down)
 - Check the results (analysis)
 - Act on the difference (improvement)
- Codes of Professional Practice
 - Integrity (ethics)



MODULE 1

QUALITY CONCEPTS