cGMP Process Installation and Qualification Challenge

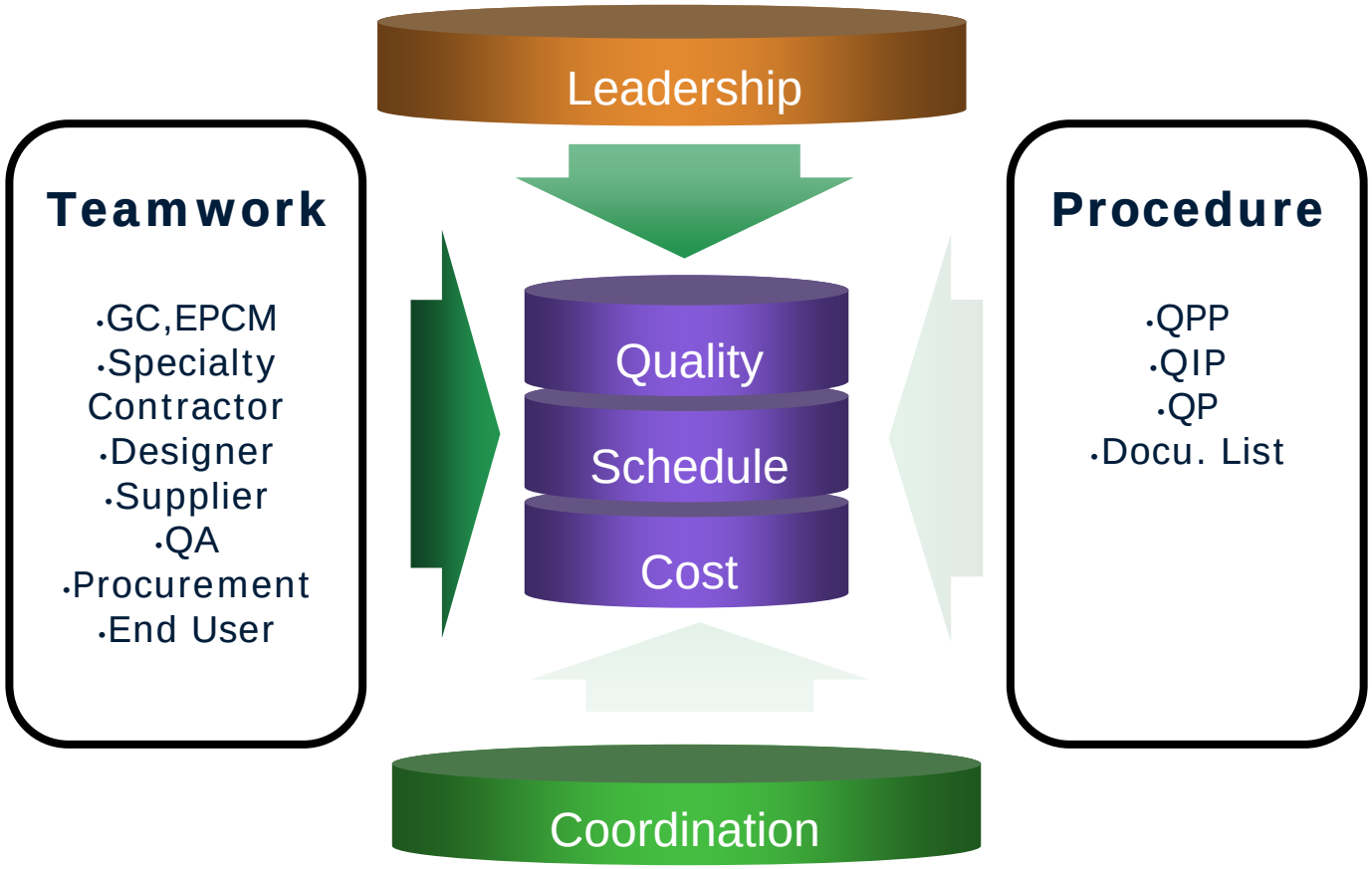
William Wang (Winatech Shanghai)

Contents

Section 1

cGMP Project Planning

Project General Plan Diagram



Quality Project Plan (QPP) -

- Details the Regulation and Requirement
- Details the Quality Procedures
- Details the Responsibility Matrix
- Details the Deliverables
- Including
  - Project Organization
  - Project Schedule

Quality Inspection Plan (QIP)

- Details the Quality Inspection Procedures
- Includes :
  - What to be inspected
  - How to inspect and the related procedures
  - Acceptance criteria
  - Who will witness
  - Report Form

Qualification Plan (QP)

- Details the Validation Procedures
- Includes :
  - DQ
  - IQ
  - OQ
  - PQ
  - SAT,FAT (For Packaged Equipment)

Other Important Documentation

- Safety Plan
- Change Control
- Deviation Control
- Schedule Report
- VO Report
- Space Management Plan
- Material Delivery Plan

Sample Procedure for Process Installation

Design Stage

- P&ID, Layout Preparation
- Equipment Specification
- FDS development
- Qualification Protocol
- Equipment List
- Material Takeoff List
- Equipment , Valve, Instrument data sheet
- Procurement Approval
- Project Schedule

Installation Stage

- Quality Plan
- Inspection and Testing Plan
- Material Acceptance Inspection
- Material Certification
- Welder Qualification
- Welding Procedure
- Welding Log and map
- Welding sample
- Boroescope Inspection
- Slope Inspection
- Deadleg Inspection
- Filter Integrity Testing

Installation Stage

- Pressure testing
- Flushing
- Degreasing
- Pickling and Passivation
- Mechanical Completion Verification
- Wiring test
- Instrument Calibration
- IQ report for approval
- Punch List

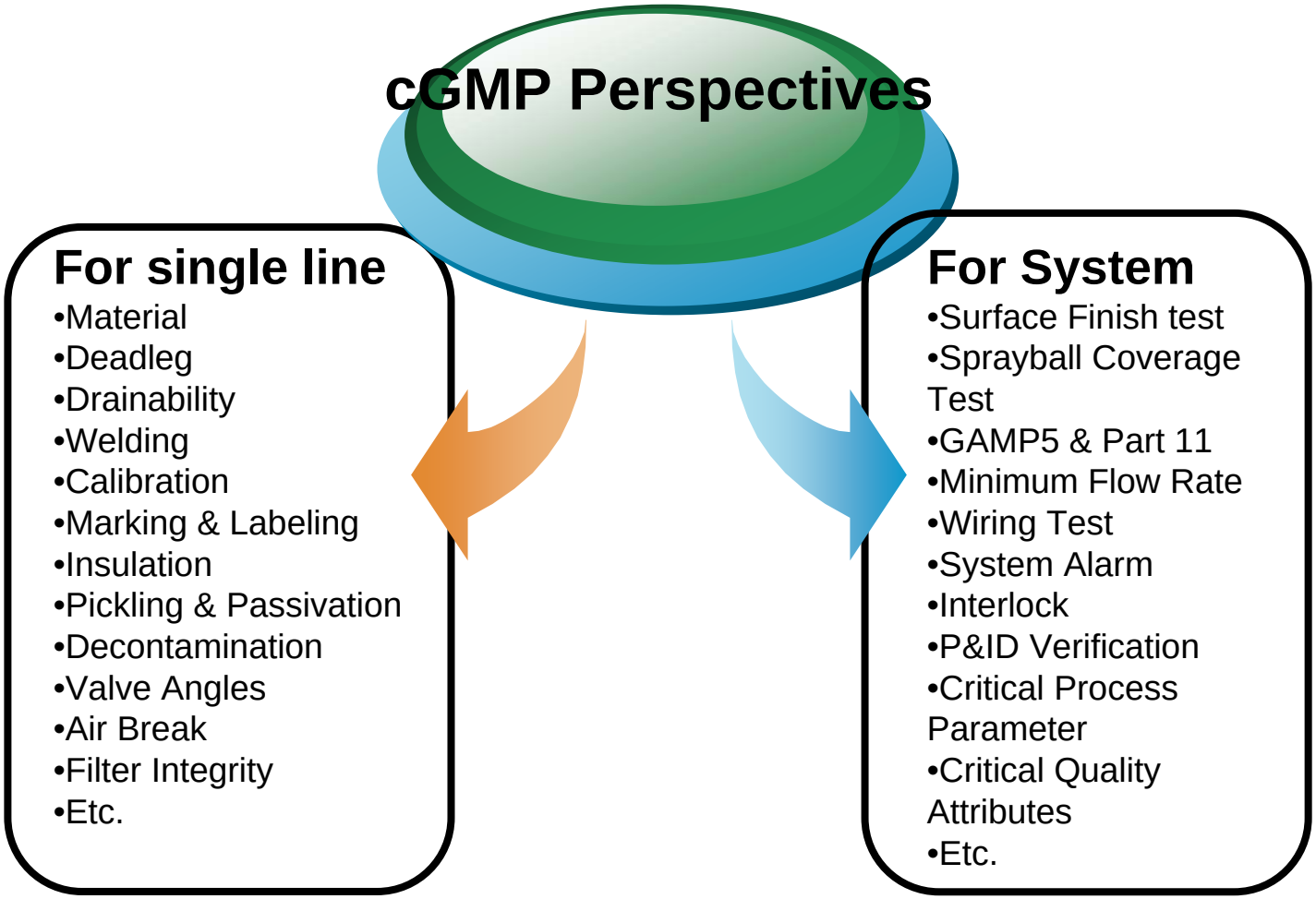
Commissioning and OQ

- Utilities Test
- Unit Test
- Dry and Wet Test
- Commissioning Report
- Performance test (such as flow, conductivity ,TOC etc.)
- Alarm test
- Cleaning & Sanitisation
- Training & report
- Deviation List and Analysis
- Spare Part List
- Operation and Maintenance Manual
- OQ report for approval
- Transfer for customer PQ

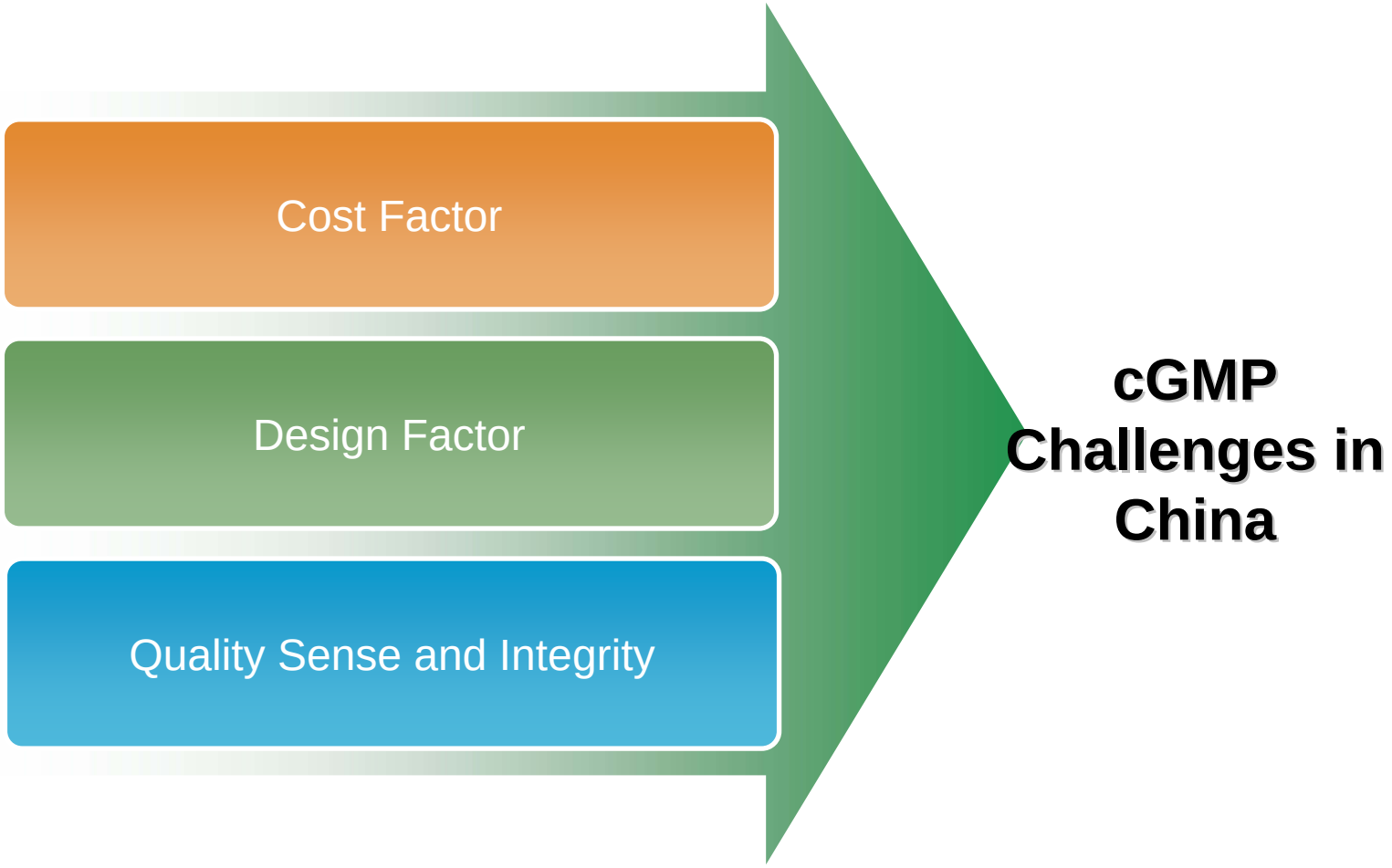
Section 2

cGMP Perspectives and Challenges

cGMP Perspectives



cGMP Challenges Root Cause



Zero Dead-Legs=Waste Money?

Old

Standard Zero Static
U-Bend Valve

New

Zero Static "T"
U-Bend Valve

Line Sizing Guidelines

- Maximum flow rate of 7-8 ft/sec
- Maximum pressure drop of 2 lb per 100 feet
  - Evaluate the “Equivalent Length”
- Minimum flow rate
  - 3 ft/sec
  - Turbulent flow (Reynolds Number > 3000 is turbulent. >10,000 – 15,000 is preferred)

User Information

AWFI System Use-Point Matrix					
Use Point	Room Name	Use-Pt. Temp.	Design Flow	Estimated Daily Volume	Estimated Peak Usage
A-1	Inactivation Wash Room CIP	25 Deg C	5 gpm	200 gals	5 gpm
A-2	Inactivation Wash Room	25 Deg C	4 gpm	100 gals	4 gpm
A-3	Inactivation Wash Sink	25 Deg C	2 gpm	50 gals	0 gpm
A-4	Fractionation Wash Room	25 Deg C	5 gpm	100 gals	5 gpm
A-5	Fractionation Wash Sink	25 Deg C	2 gpm	50 gals	0 gpm
A-6	Fractionation Buffer Prep	25 Deg C	2 gpm	100 gals	2 gpm
A-7	Purification Wash Room	25 Deg C	4 gpm	50 gals	0 gpm
A-8	Purification Wash Sink	25 Deg C	2 gpm	50 gals	0 gpm
A-9	Purification Buffer Prep	25 Deg C	4 gpm	200 gals	4 gpm
A-10	Q.C. Lab	25 Deg C	2 gpm	10 gals	0 gpm
A-11	CIP	25 Deg C	10 gpm	500 gals	10 gpm
A-12	Fractionation Diafiltration	25 Deg C	4 gpm	50 gals	4 gpm
A-13	Purification Diafiltration	25 Deg C	4 gpm	50 gals	0 gpm
C-2	Batching/Reactor Tanks	2 Deg C	7 gpm	1000 gals	7 gpm
C-1	Fractionization Freezers	2 Deg C	7 gpm	200 gals	7 gpm
		Maximum Possible Draw:	**64 gpm**	**2710 gals**	**48 gpm**

From	To	Distance
Tank	A-11	20 ft
A-11	A-4 / 5 / 6	40 ft
A-4 / 5 / 6	C-1	10 ft
C-1	A-1 / 2 / 3	90 ft
A-1 / 2 / 3	C-2	10 ft
C-2	A-7 / 8 / 13	60 ft
A-7 / 8 / 13	A-9	30 ft
A-9	A-6	20 ft
A-6	A-10	40 ft
A-10	Tank	60 ft
TOTAL		380 ft

Design Considerations

- Maximum Demand - 48 GPM
- Minimum Return Flow
- Future Expansion
- Storage Tank Sprayball flowrate
  - 2.5 - 3 GPM / ft of circumference
  - 1000 Gal Tk, 5.5 ft diameter -> 43 - 50 GPM
- Economics

Typical Quality Problem for some suppliers

- Tank
  - Wrong dimension twice (+/- 10cm)
  - QA Approval joke
  - CS/SS contamination
- Piping Material
  - Internal Surface Problem
  - EPOM gasket joke
  - Weldability and Tolerance
- Package Equipment Case
  - Full Documentation doubles the charge, does it mean double the quality?

Material Inspection

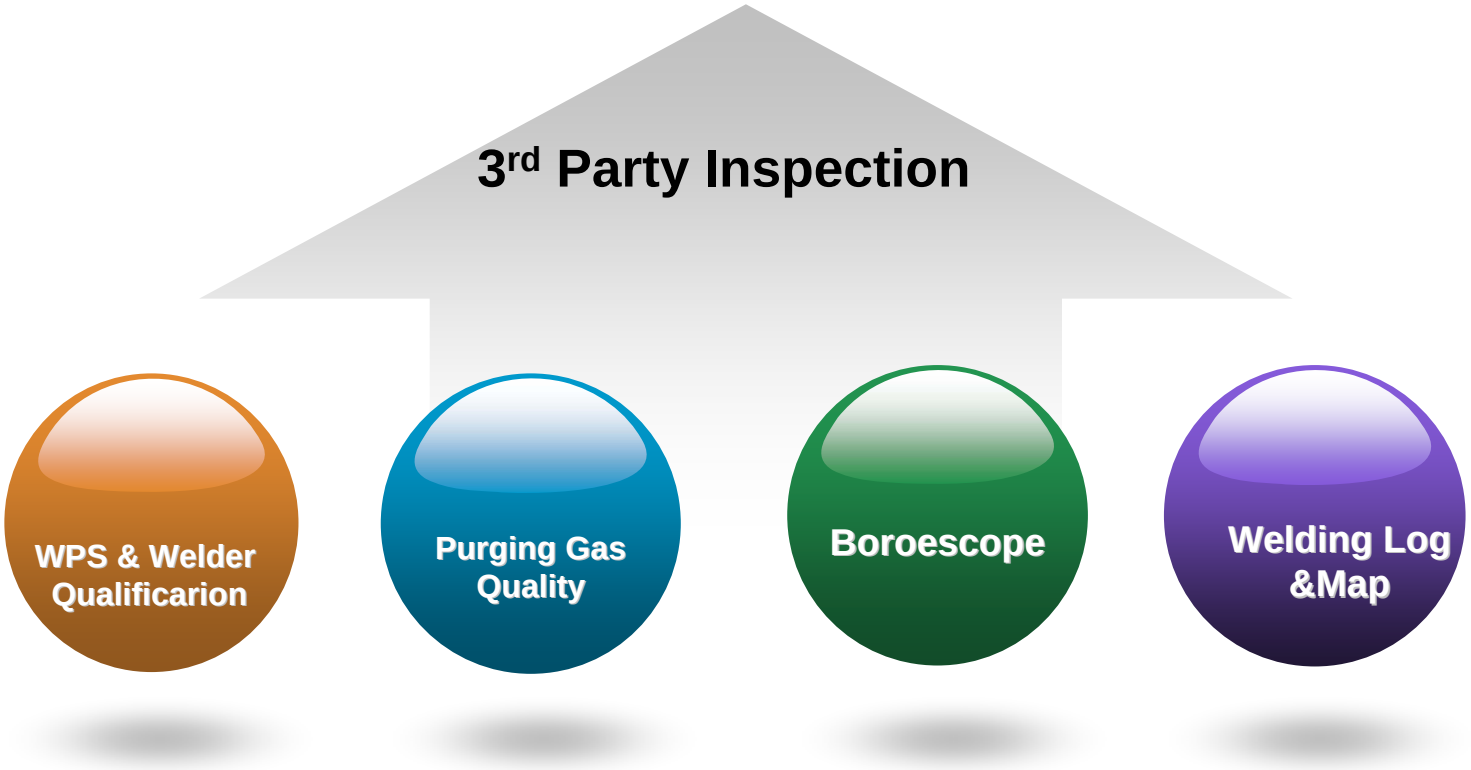
Qualified Materials

Sample Installation

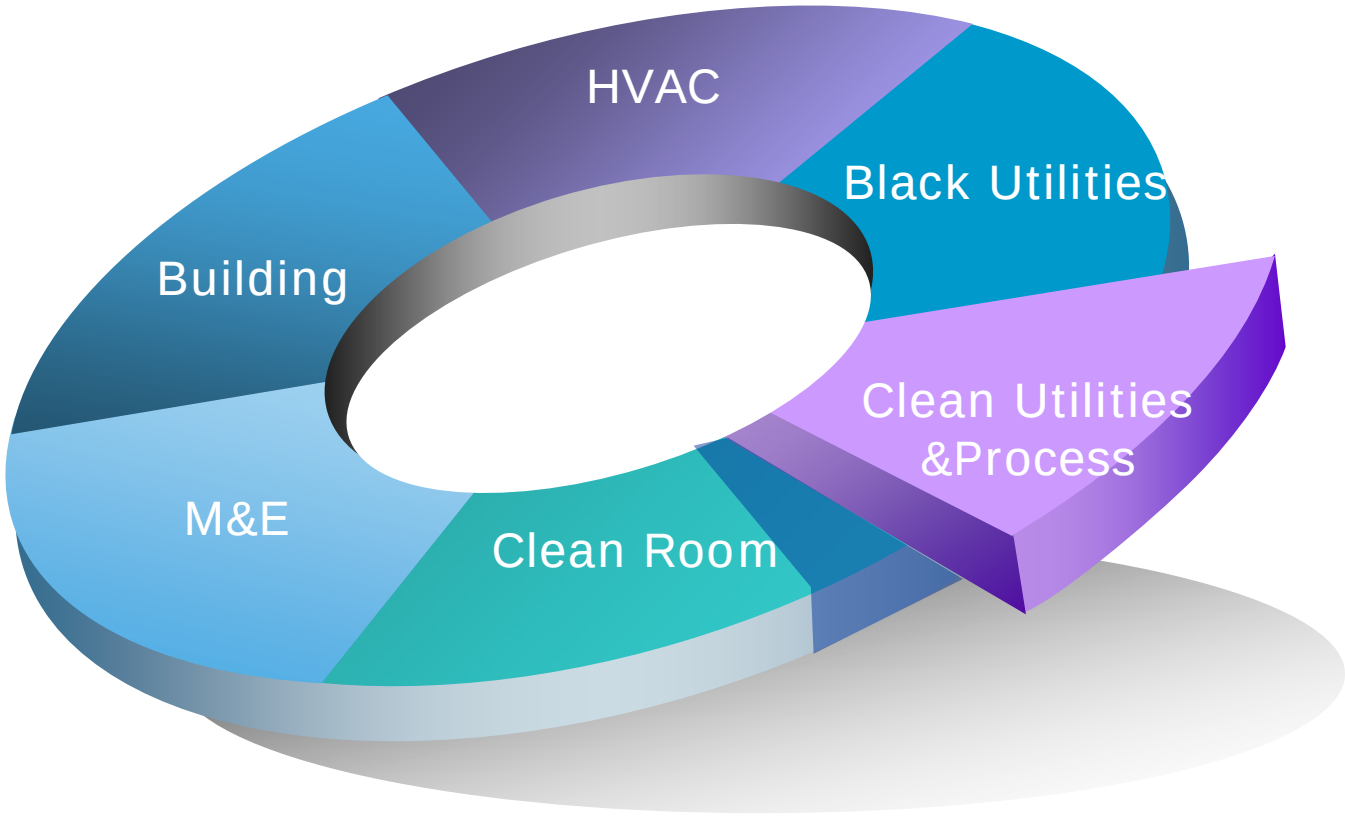
- Material Certificate
- Surface Finish Report
- Random Check
- 3rd Party Check

Welding Inspection

Qualified Welding



Site Coordination is a tough challenge



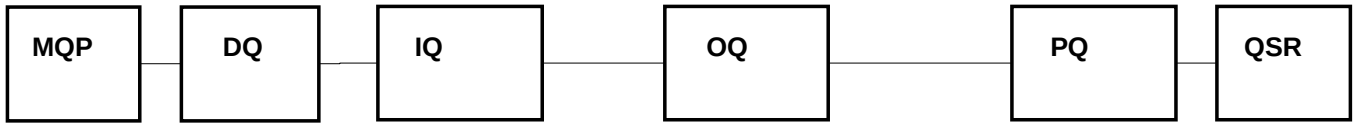
Real Lesson

- Leave the last for best sometimes means you need face the existing facts.
- Space management should start from the beginning
- Leave the hookup in the end
- Protect the finished work well.

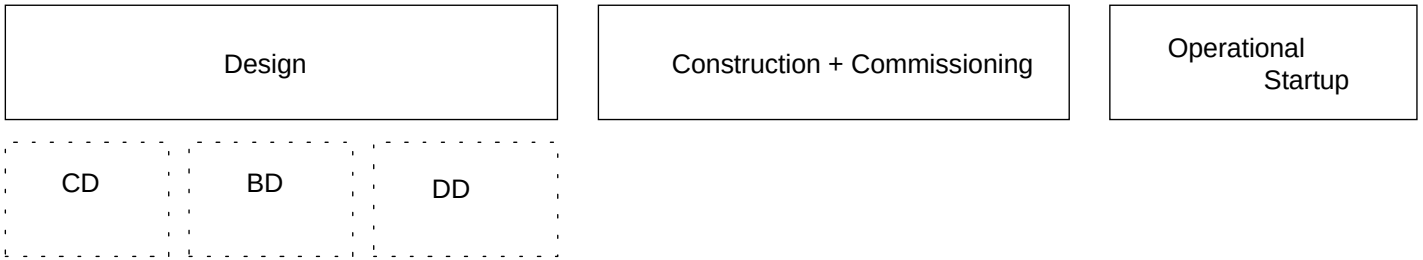
Section 3

cGMP Qualification

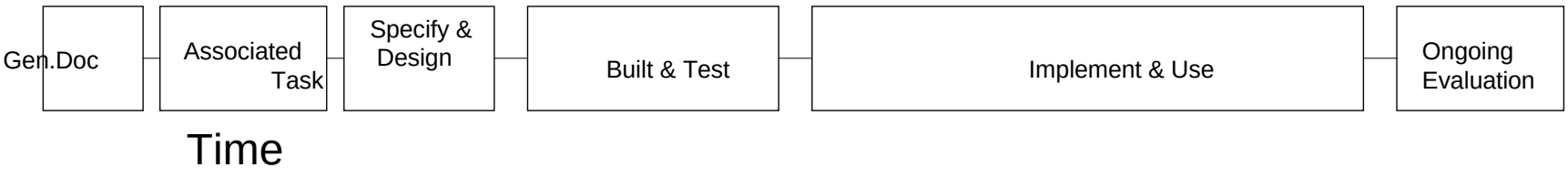
Qualification Program



Project Execution Sequence:

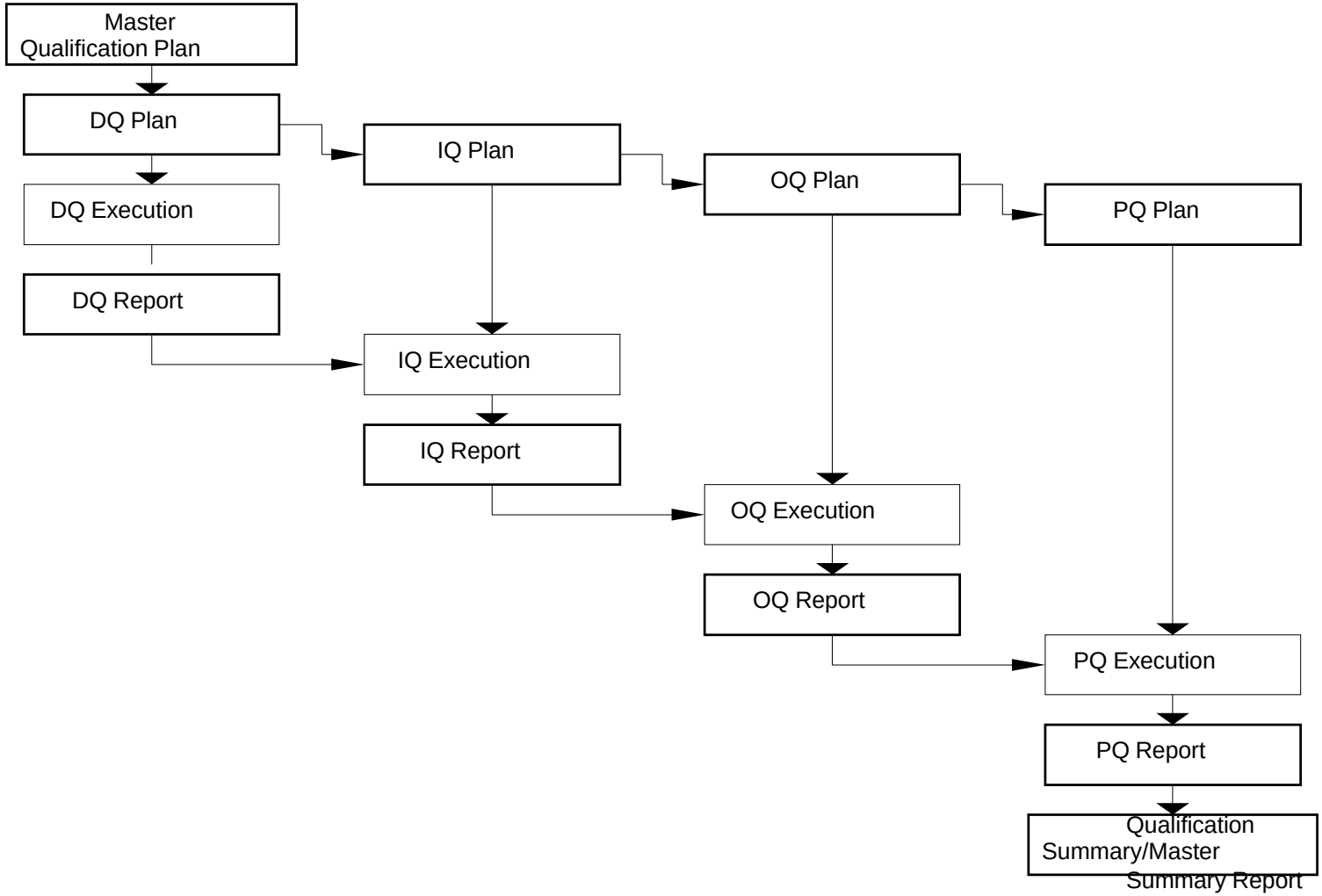


Other Activities, e.g. CSV:



Sequencing of qualification phases for new systems

Qualification Documentation



Sample Qualification of a PW/WFI System

DQ

- System Identification
- Reference Documentation
- Table of Critical Functions and Process Parameters (USP or Ph Eur)
- Checklist
  - General Rules (Change Control, Security, Training)
  - URS
  - Risk Assessment
  - P&ID
  - Layout
  - Technical Specification
  - Supplier Evaluation
  - Process Automation (ERES, FDS,HDS, SDS)
  - GMP Review(Appendix)GMP

IQ

- Objectives
- Responsibility
- System Identification
- Check List
  - Mechanical Completion Check
  - Material Inspection
  - Welding Qualification (WPS, PQR, Welder Qualification, Weld Map and Record)
  - Drawing Compliance Review (P&ID, Layout, Isometric)
  - Test Report (Pressure, Flushing, Degreasing, Pickling & Passivation)
  - Deadleg and Drainability Check
  - Labeling Check

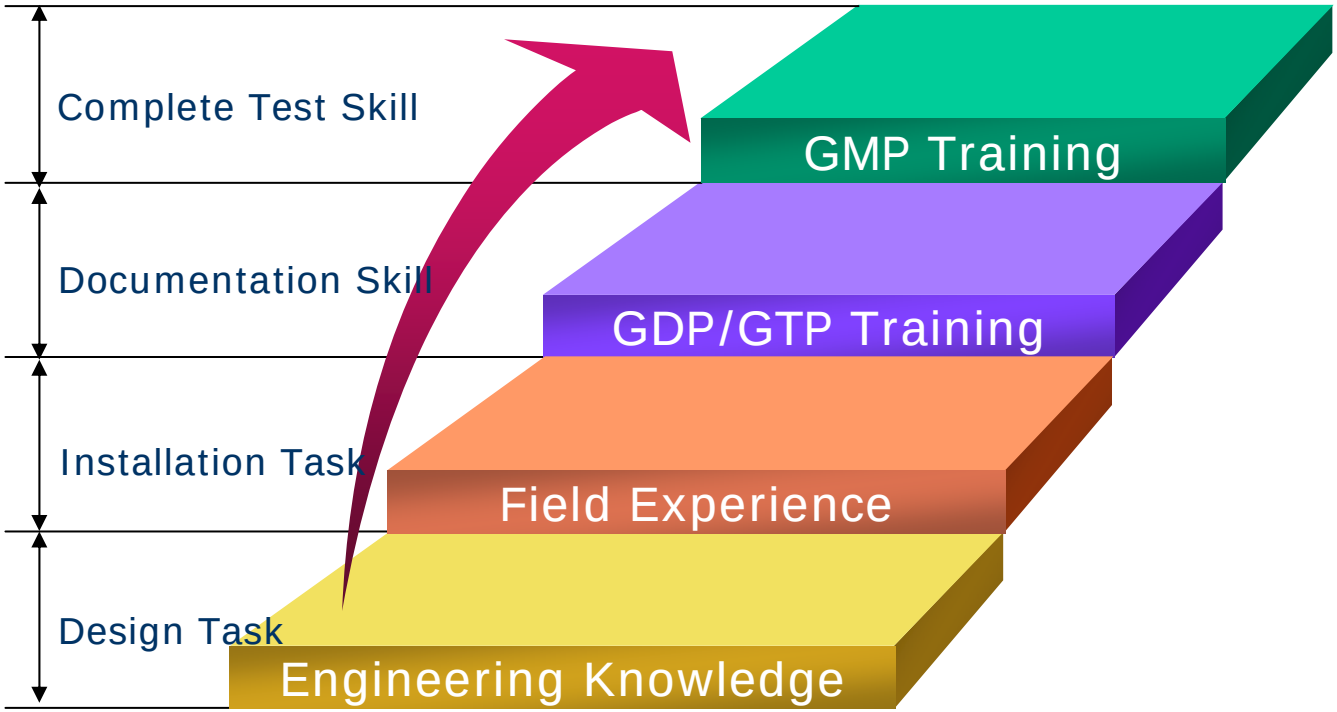
OQ

- Objectives
- Responsibility
- System Identification
- Check List
  - FAT and SAT for packaged equipment
  - Utilities Verification
  - Calibration Verification
  - Test (Operation Pressure, Flow, Temperature)
  - Process Automation (Software Backup, Hardware Connection, Network Connection, Code Review, I/O test, Alarm test, Parameter Test, Interlock Test)
  - Manuals (Startup ,Operation, Maintenance, Spare Part , Logbook)
  - SOP (Operation, Maintenance, Cleaning, Calibration, Training, Backup, Change Control)

PQ

- Objectives
- Responsibilities
- Sampling Planning (3 phases)
- Test Check list
  - Physical and Chemical Analysis(According to Ph Eur or USP) (such as condutivity, TOC, PH, Heavy Metal, Nitrate etc.)
  - Microbiological Analysis(According to Ph Eur or USP) (such as Bacteria, moulds and yeasts; Coliform bacteria; Pseudomonas aeruginosa ; Bacterial endotoxins)
  - Final Assessment

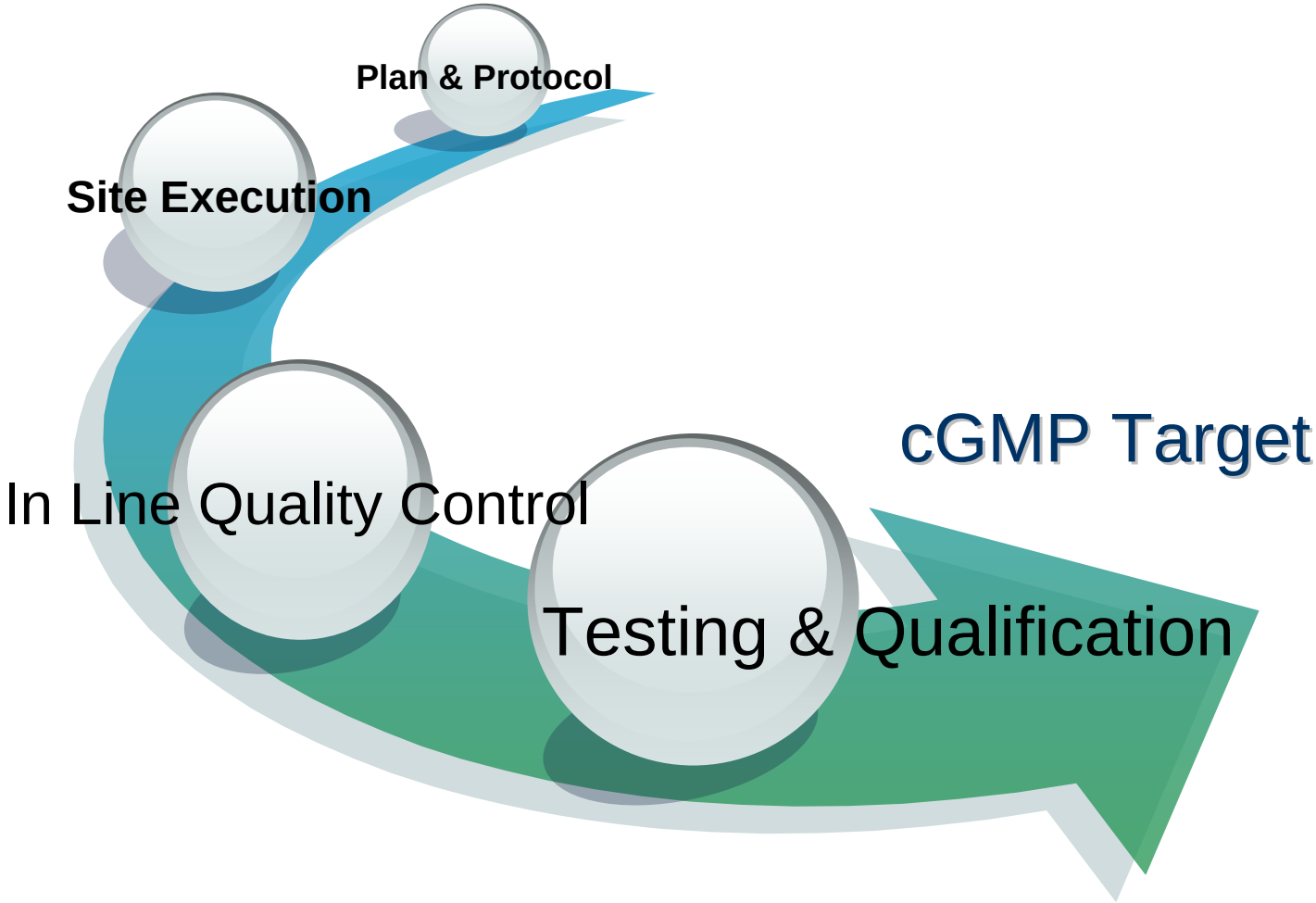
How to educate a qualification engineer



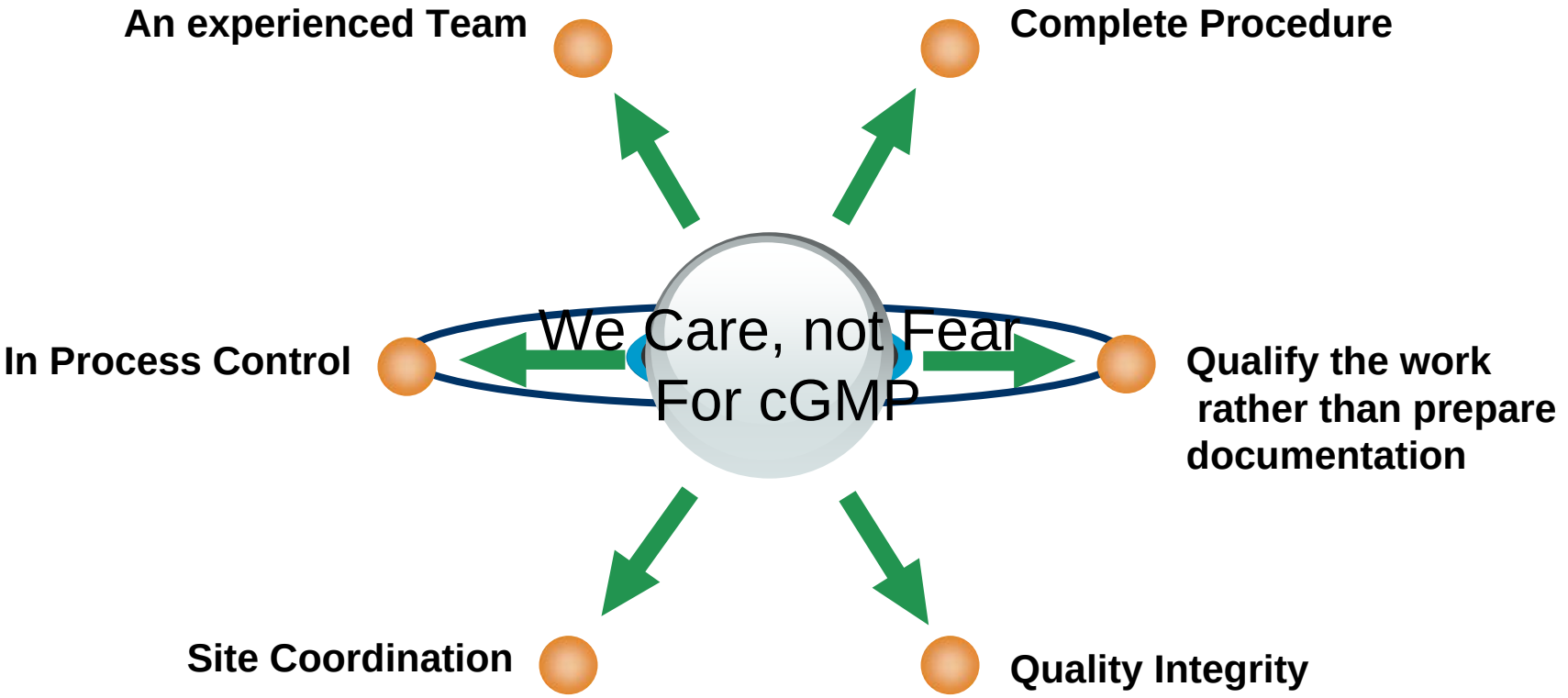
Section 4

Summary

cGMP Approach



Our understanding of cGMP



Acknowledge to our customers, they are our best teachers

Abbott Laboratories

Roche

MSD

NUTRICIA

Fresenius Kabi
Caring for Life

Baxter

nne pharmaplan®

AMO
ADVANCED MEDICAL OPTICS

NOVARTIS

gsk GlaxoSmithKline 葛兰素史克

发泰(天津)科技有限公司
PHARM-TECH(TIANJIN)CO., LTD.

Wyeth


Thank You !
More information please contact
williamw@winatech.com.cn