新版ISPE调试与确认变化解析

2nd ISPE C&Q Change Introduction

2020-9-28

变化综述

1. 系统分类：直接影响/非直接影响
2. 系统风险评估代替关键部件评估
3. 验证流程：流程图替代V模型
4. 对C&Q的测试理解提高
5. 基于风险和科学
6. 模板增加

7.问题和思考

8. C&Q 体系构建

1.系统分类

新

- 直接影响系统
- 非直接影响系统

旧

- 直接影响系统
- 间接影响系统
- 无影响系统

8个问题

- 8个问题中只要有1个问题回答为是，则为直接影响系统。8个都为“否”，则为 无影响系统。

问题序号	问题描述
Q1	系统是否包含CAs/ CDEs或执行满足包括CPPs在内的一个或多个工艺需求(CQAs)的功能?
Q2	系统是否与产品或工艺流有直接接触?这种接触是否有可能影响最终产品质量或对患者构成风险?
Q3	该系统是否提供辅料或生产一种成分或溶剂(如WFI)，该物质的质量(以及对其所需规格的遵守)是否会影响最终产品质量或对患者构成风险?
Q4	系统是否用于清洁、消毒或灭菌，系统故障是否会导致无法充分清洁、消毒或灭菌，从而给患者带来风险?
Q5	当该参数是产品CPP[illegible]是否为该过程建立适当的环境(例如氮气[illegible]气区空气质量、温度、湿度的[illegible]人构成风险?
Q6	系统是否使[illegible]拒绝产品、CPPs或电子记录的数据，[illegible]和欧盟GMP第4卷第11部[21]或本地同等标准?
Q7	该系统是否提供容器封口或产品保护，如果封口或产品保护失败，将对患者构成风险或产品质量下降?
Q8	系统是否提供产品识别信息(例如:、批号、有效期、防伪功能)无独立验证或系统是否用于验证该信息?

质量、CQA、CPP

直接影响系统案例

System Name	Typical CQAs	Typical CPPs
Autoclave System	• Sterile load (microbial levels reduced by ≥ log 6) (SAL ≥ 10^{-6}) • Load dryness Note: Steam quality is typically verified as part of the steam system	• Clean steam pressure and temperature (saturation) • Time • Vacuum level • Defined load pattern
Blending System	• Blend uniformity (potency)	• Number of revolutions • Rotational time
Buffer Hold System	• pH • Conductivity • Bioburden • Endotoxin	• Temperature (for buffer stability/ microbial control) • Weight/level (if not able to leverage unit operation readings)
Buffer Preparation System	• pH • Conductivity • Bioburden • Endotoxin	• Temperature (for proper dissolution) • Weight/level and/or flow (for proper batching quantities) • Most prep systems do not include, but if so: - *In situ* conductivity probe - *In situ* pH probe • Agitation rate, if critical for buffer preparation (not typical)
Capper RABS System	• Supply air quality	• Total particle count • Viable particle count • Air velocity
Capping System	• Container closure integrity	• Placing closure into container accurately • Maintaining closure pressure when capping

System Name	Typical CQAs	Typical CPPs
Chromatography Skid	• Product specific analytical data (can be measured using PAT or off-line) • Protein concentration • Bioburden • Endotoxin	• Flow rate of each channel • Total flow rate • Outlet UV wavelength • Temperature (if controlled)
CIP System	• Removal of material to a predefined level of detectability	• Flow rate or pressure • Temperature • Conductivity (% cleaning agent) • TOC (final rinse quality) of product residue indicating test
Clarification System	• Protein concentration and/or step yield	• Flow • Differential pressure across filters
Coating System	• Coating thickness • Coating uniformity • Moisture content	• Air supply temperature and humidity • Exhaust air temperature • Coater rotational speed • Spray rate • Airflow rate
Column Packing System	• HETP • Asymmetry	• Flow rate(s) • Feed pressure
Compressed Air System	• Moisture content (dew point) • Hydrocarbon content • Particle count (total and viable) • Capacity/Volume	• Pressure • Dew point
Controlled Temperature Unit (e.g., freezers, refrigerators, incubators)	• Stored material temperature	• Temperature uniformity (temperature range across all points in the storage area) • Chamber temperature • Airflow (if critical to achieve acceptable air temperature range) • Stored material layout
Debagger and Restricted Access Barrier System (RABS) System	• Sterility of the external surfaces of the tub	• Supply air quality • Supply air direction and velocity • RABS differential pressure
Decontamination/ Sterilization System	• Achieve SAL ≥ 10^{-6}	• Clean steam pressure and temperature • Time
Depyrogenation Oven System	• Removal of endotoxins	• Time at temperature • Temperature distribution
Dilution System	• Conductivity • pH	• Flow

直接影响系统案例

System Name	Typical CQAs	Typical CPPs
Fermentor/Bioreactor System	• Optical density (for fermentation) or viable cell density (for cell culture) • Contamination • Protein concentration (if production fermentor/bioreactor) • Mass yield (if production fermentor/bioreactor) Note: Organizations may consider yield a productivity issue. CPPs are product specific	• DO • pH • Temperature • Agitation speed • Feed flow rates (if controlled by fermentor/bioreactor) • Level/weight/volume (if used to partially transfer to seed the next fermentor/bioreactor in the train) • ATF permeate flow rate (for production fermentor/bioreactor, if present) • Airflow rate (for background air sparge and overlay)
Filler Isolator System	• Sterility	• Supply air quality • Supply air direction and velocity • RABS differential pressure
Filler System	• Liquid volume or tablet count	• (Tablet) quantity • Liquid volume (label claim)
Filter Press System	• Step yield	• Pressure
Filter/Filter Housing System	• Protein concentration and/or step yield • Bioburden and/or viral assay (based on purpose of the filter step)	• Differential pressure across filters
Filtration System	• Protein concentration and/or step yield	• Flow • Differential pressure across filters
Filtration System: Alternating Tangential Flow (ATF)	• Protein concentration in bioreactor • Viable cell density in bioreactor	• Permeate flow rate • Vacuum/pressure to ATF pump
Filtration System: Ultrafiltration/Diafiltration (UF/DF)	• Protein concentration • Yield • Bioburden • Endotoxin	• Flow • Vessel level/weight • Permeate P_{VV} • Transmembrane pressure
Formulation System	• Uniformity	• Time • Mixer speed
Harvest Collection System	• Bioburden (for cell culture processes)	• Temperature (pool stability/microbial control) • Agitation • Vessel pH (if used for control/titration)
Harvest Surge and Clarification System	• Protein concentration and/or step yield • Bioburden	• Differential pressure across filters • Agitation • Flow rate • Temperature

System Name	Typical CQAs	Typical CPPs
Homogenizer System	• Cell breakage efficiency (%) • Protein concentration and/or yield	• Breaking pressure • Flow rate (if controlled) • Cooler temperature
HVAC System (Classified Area)	• Room classification • May include specific ranges of temperature and relative humidity depending on product; all aseptic should include temperature and relative humidity due to impact on viable growth	• Room total particle count • Room viable count, if applicable • Temperature • Relative humidity • Room differential pressure or direction of airflow • Room recovery rate • Room airflow
Inoculum System	• Viable cell density (for cell culture) • Optical density (for fermentation)	• Incubator RPM • Incubator temperature • Water or heat bath temperature • Pressure for the hood • Weight (if not using pipette transfers)
Lyophilizer System	• Dryness	• Temperature • Cycle time • Vacuum level
Media Hold Tank System	• pH (media dependent) • Bioburden	• Temperature (media stability/microbial control) • pH (if control required) • Gas flow rates (media dependent) • Agitation rate (if agitation required)
Media Preparation Tank System	• pH • Osmolality (for cell culture) • Conductivity (for upstream solutions) • Bioburden	• Temperature (if controlled) • pH (if control required) • Weight/level and/or flow • Agitation rate
Microfiltration System	• Protein concentration • Yield • Bioburden	• Flow • Vessel level/weight • Transmembrane pressure
Milling System	• Solubility/dissolution • Particle size distribution	• Impeller speed and direction of rotation
Powder/Granule Drying System	• Granule size • Solubility/dissolution • Content uniformity	• Spray rate • Impeller speed • Granule moisture level
Roller Compaction (Dry Granulation)	• Ribbon density • Content uniformity	• Feed screw speed • Roller force • Roller speed • Roller gap
Sieving System	• No presence of lumps or particles above a predefined diameter	• Sieve size

直接影响系统案例

System Name	Typical CQAs	Typical CPPs
Single-Use Bioreactor System	• Viable cell density • Viability • Contamination • Protein concentration (if production bioreactor) • Mass yield (if production bioreactor)	• DO • pH • Temperature • Feed flow rates (if controlled by bioreactor) • Biomass (for production bioreactor only, if present and used for temperature shift) • Permeate flow rate (for production bioreactor only) • Agitation speed • Airflow rate (for background air sparge and overlay)
Single-Use Chromatography Skid System	• Product specific analytical data (can be measured using PAT or off-line) • Protein concentration • Bioburden • Endotoxin	• Flow rate of each channel • Total flow rate • Outlet UV • Temperature (if controlled) • Pressure • Break tank level (if break tank used)
Single-Use Vessel System	• Bioburden • Endotoxin • If used for reactions such as flocculation and viral inactivation: - Process specific analytical • pH	• Temperature • Agitation rate • pH (if controlled or monitored) • DO (if controlled or monitored) • Sparge gas flow (if utilized) • Weight/level/volume
SIP System	• Sterility	• Time • Temperature
Steam Sanitization	• Achieve SAL ≥ 10^{-3}	• Time • Temperature
Stopper Processing System	• Achieve SAL ≥ 10^{-6}	• Time • Temperature
Tablet Press System	• Tablet weight • Tablet hardness • Tablet thickness • Tablet friability/disintegration	• Material feed rate • Pre and main compression forces • Press rotational speed
Tank System (Fixed)	• Bioburden • pH (if pool titrated) • If used for reactions such as refold/ oxidization: - Process specific purity	• Temperature (pool stability/microbial control) • Agitation • Volume • Vessel pressure (if specified) • Vessel pH (if used for control/ titration) • If used for reactions such as refold/ oxidization: - DO

2.系统风险评估

新

系统风险评估

旧

关键部件

非关键部件

取消关键部件评估

降低工作量

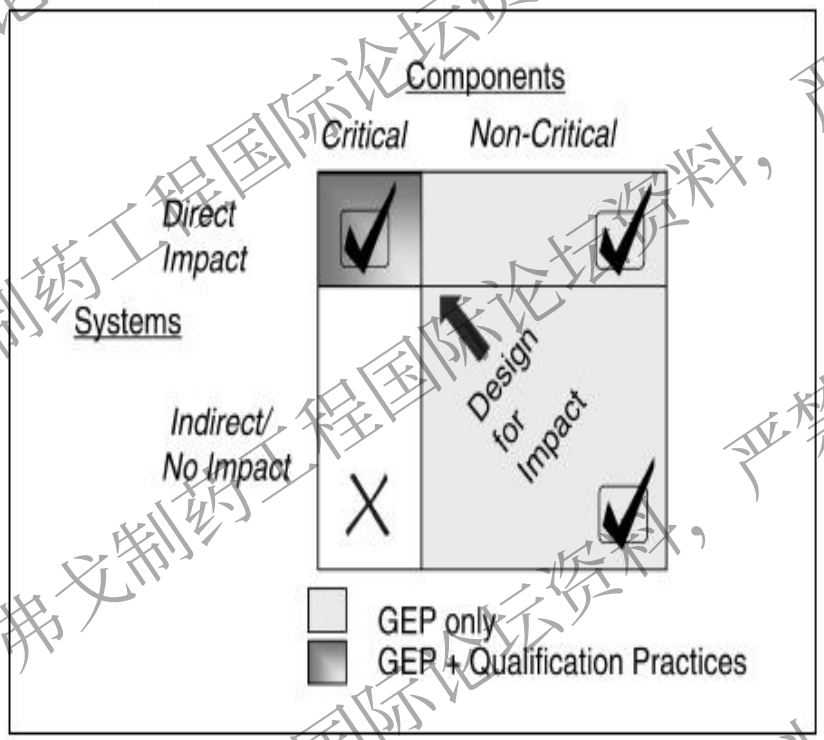


Figure 3-2 Relationship between Systems and Components

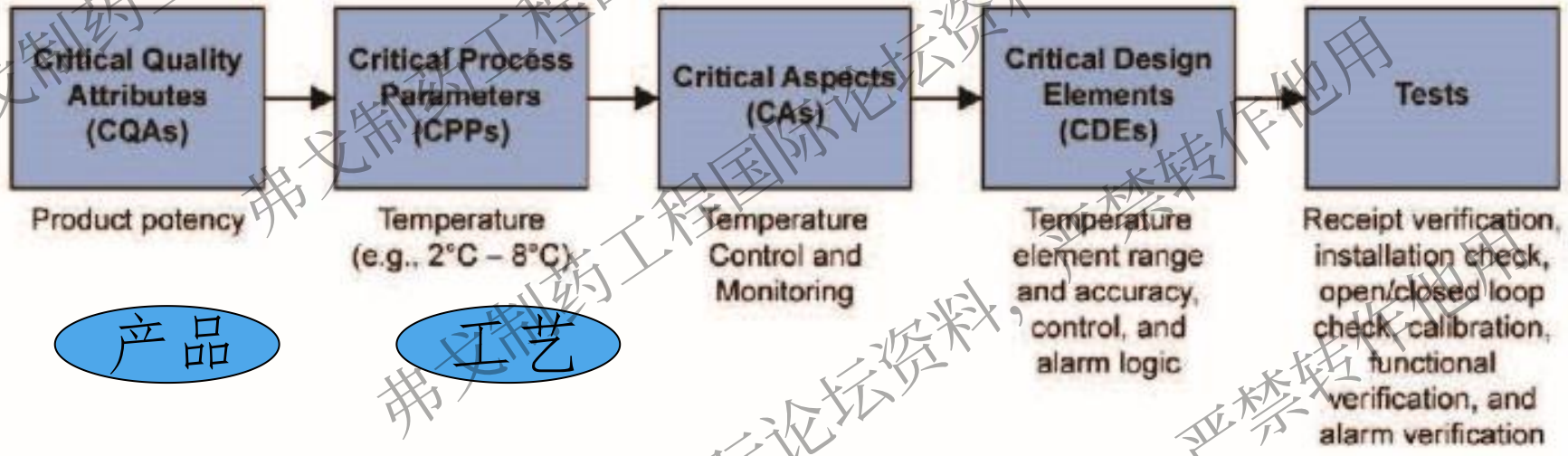
提升关注点和联系

系统风险评估

- 针对直接影响系统；
- 识别CAs/CDEs、程序控制；
- 系统评估完成后，检查URS是否包括CAs/CDEs，如果没有，则需更新URS并添加；
- SRA应在概念设计后，详细设计前。

CQA，CPP，CAs，CDEs之间的关系

Figure 1.2: Example of Automated Temperature Control and Monitoring of a Process Step



系统风险评估步骤

- 步骤一：分析直接影响系统的CQA和CPP

序号	操作顺序	工艺描述	CQA	CPP
1	压缩机	压缩空气(增加相对湿度、增加空气压缩程度)	压缩能力	体积/流速/压力
2	过滤器	允许冷凝水排出并去除粗颗粒	N/A	N/A
3	干燥机	干燥空气，防止水汽凝结并限制微生物污染	水分含量	干燥机设置（干燥机本身为调试系统，但输出需连续监测的CQA）

系统风险评估步骤

- 步骤二：详细系统风险评估

序号	操作/流程	操作描述	CQA	CPP	对CQA的影响	如何影响CQA	设计控制	控制参数	相关报警	程序控制	剩余风险等级
1	压缩机	压缩空气(增加相对湿度、增加空气压缩程度)	压缩能力	体积/流速/压力	直接影响	不符合下游设备的URS	低压力报警和行动限报警	特定压力操作范围	低压力	操作程序定义报警发生时所需操作	低
2	过滤器	允许冷凝水排出并去除粗颗粒	N/A	N/A	N/A	N/A	N/A	N/A	否	N/A	低
3	干燥机	干燥空气，防止水汽凝结并限制微生物污染	水分含量	干燥机设置（干燥机本身为调试系统，但输出需连续监测的CQA）	直接	水分含量高	报警控制	N/A	是	定义了报警发生时所需操作	低

风险等级

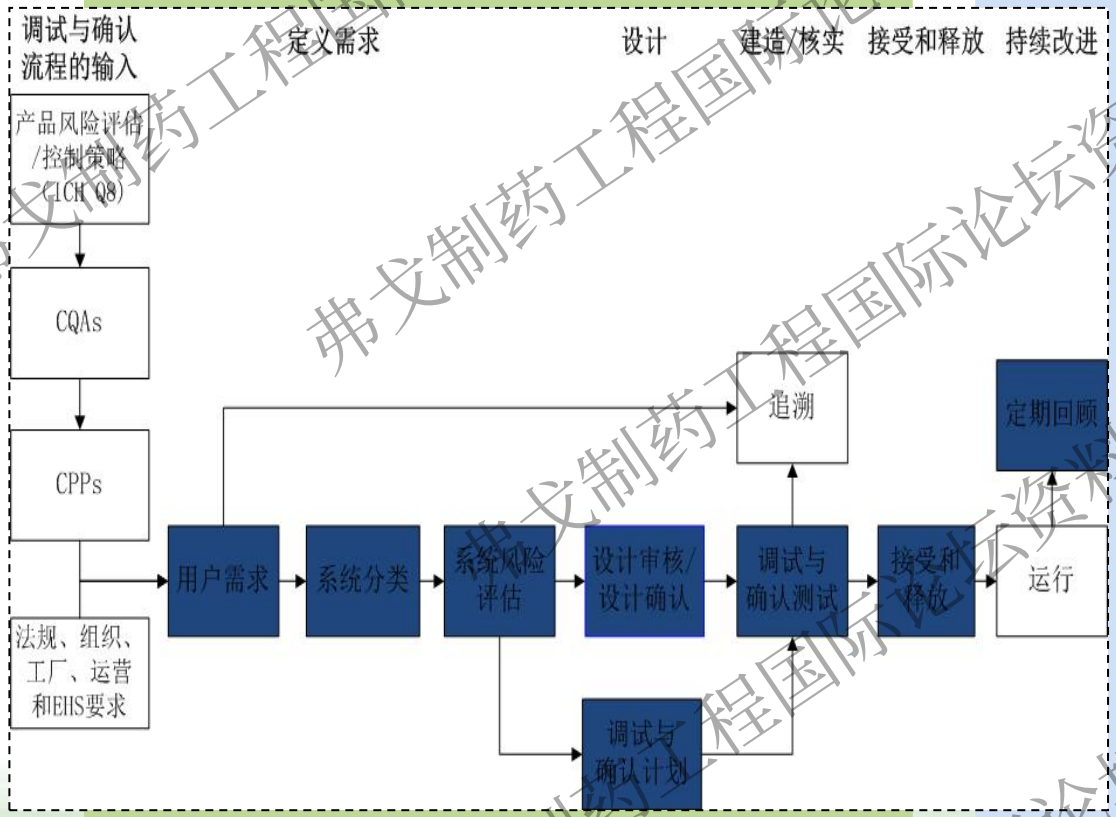
Table 4.1: Risk Level Definitions

Risk Level	Definition
Low	Considered acceptable with no actions needed. The likelihood of the risk occurring with the defined controls operating is considered low, and the detection is robust.
Medium	Normally considered unacceptable and requires mitigation through design (CAs/CDEs) and/or procedural controls. However, the SME reviewers may consider a medium risk as acceptable for the specific process/system and decide to accept the risk.
High	Considered unacceptable and requires mitigation through design and/or procedural controls. In certain situations, the SME reviewers may determine that these controls are not appropriate, e.g., implementation costs outweigh the incurred costs if the risk occurred, operational challenges, or other reasons. The SMEs may recommend acceptance of the system with the high risk; in this case, the assessment needs to be accepted by high-level management.

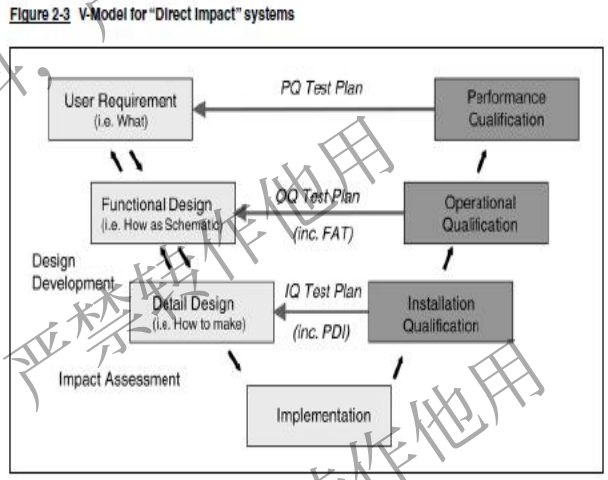
Note: The risk level is defined considering the overall process; thus, if the process is changed, the System Risk Assessments may need to be reviewed/updated. This aspect should be addressed through change management (see Chapter 12).

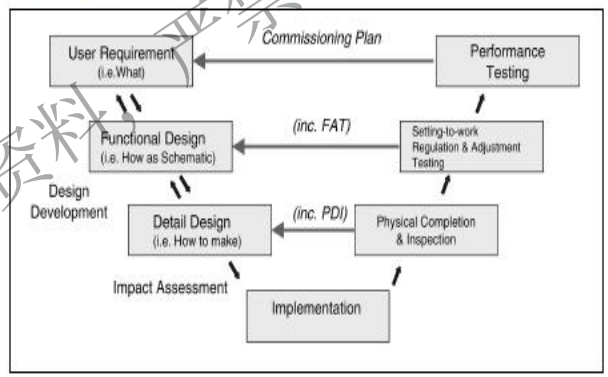
3. 验证流程

新

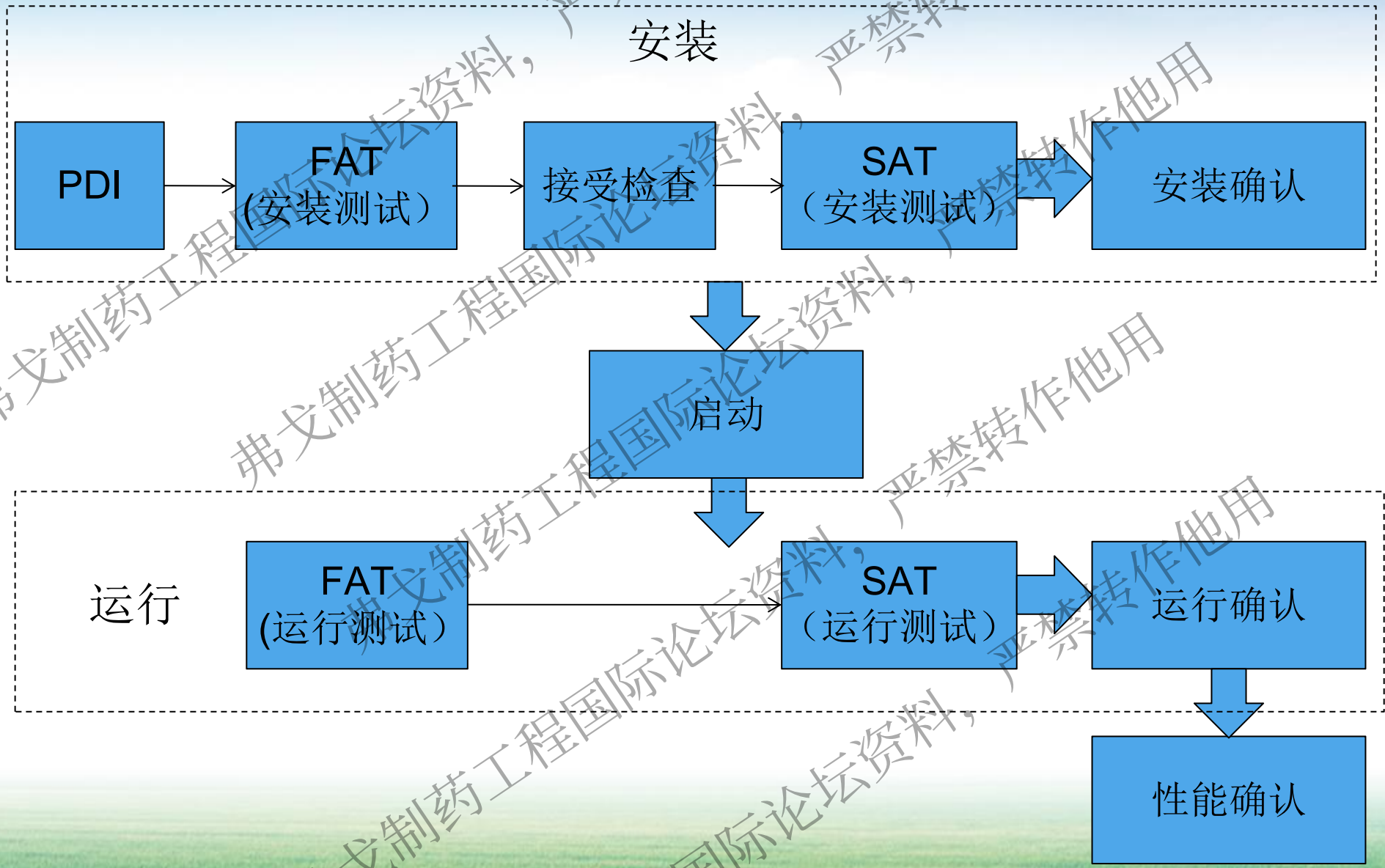


旧

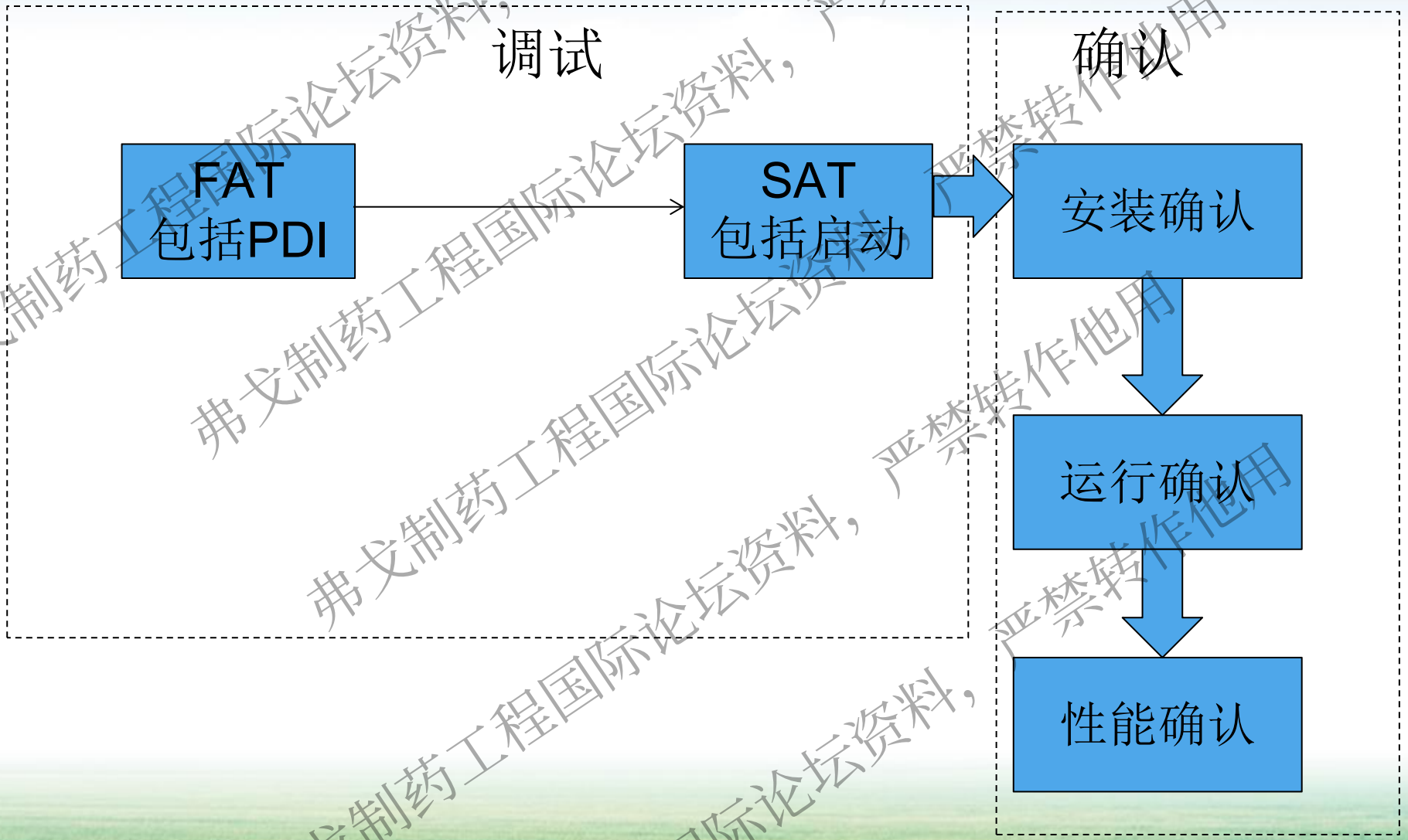




测试与确认测试流程



简化的调试与确认测试流程



4. 对C&Q的测试理解提高

新

一个章节介绍C&Q测试

12页

旧

5个章节，

独立章节介绍

C/Q/IQ/OQ/PQ测试

40页

附录1列举6个系统的实例介绍各测试的内容

新

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旧

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10.6 ORGANIZING AND WRITING THE PQ PROTOCOL
10.7 PQ PROTOCOL APPROVAL BEFORE EXECUTION
10.8 DOCUMENTS REQUIRED TO EXECUTE THE PQ PROTOCOL
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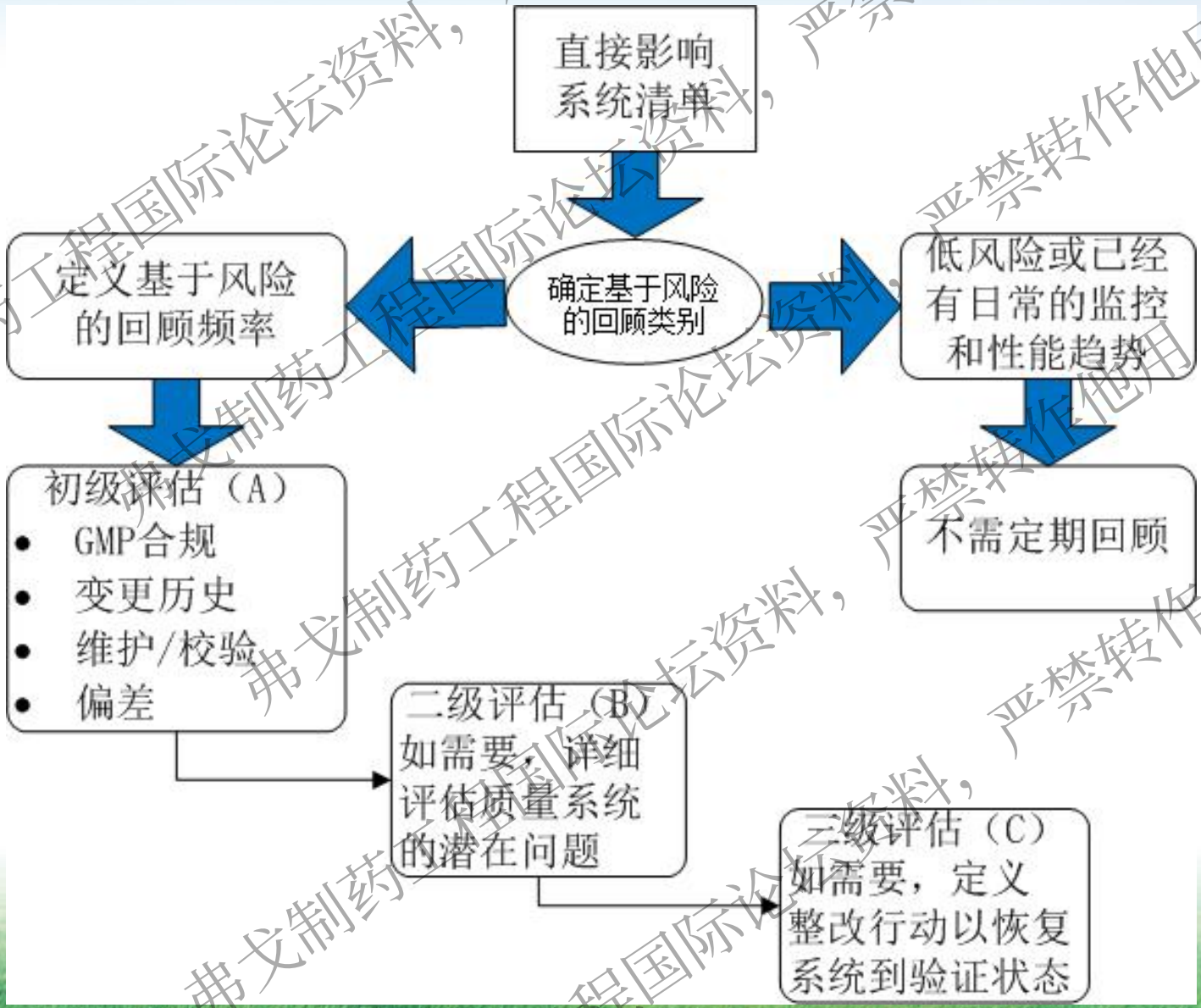
10.10 PQ PROTOCOL EXECUTION
10.11 PQ APPROVAL AFTER EXECUTION
10.12 PQ SUMMARY REPORT
10.13 PQ SCHEDULE
10.14 CHANGE CONTROL DURING PQ

5. 基于风险和科学

- 系统风险评估
- 定期回顾（新增）

定期回顾流程



定期回顾的频率类别 （基于风险）

Table 9.3: Example Periodic Review Schedule

Periodic Review Category	Periodic Review Schedule
0	This category relies on existing quality systems and performance monitoring programs; periodic review is not required, e.g., critical utility systems such as compressed air, purified water or WFI.
1	This category has established requirements from regulations specific to the system and is not subject to additional periodic assessment activities, e.g., autoclaves and depyrogenation tunnels.
2	Perform reviews at two-year intervals.
3	Perform reviews at three-year intervals.

各系统的频率分类案例

Table 9.2: Examples of Periodic Review Categories

Process	Periodic Review Category	System Types	Rationale
Sterilization	1	• Autoclave system • Decontamination/sterilization system (including equipment sterilization)	• Complex systems with a quality critical function subject to regulatory guidance or Standard Operating Procedures • Routine revalidation is already established
Sterile Filtration*	0	• Filter/filter housing • Filtration system	• Standard systems with pre- and post-use integrity tests used to monitor system performance

odic Review Categories (continued)

	odic Review Category	System Types	Rationale
Tablet Manufacturing (standard systems)	0	• Sieve • Granulator • Dryer • Mill • Blender	• Standard equipment with minimal configuration • System performance is generally monitored through in-process controls
Tablet Manufacturing (complex systems)	3	• Coater • Tablet press • Capsule filler	• Operationally and/or mechanically complex systems that process the final oral solid dose product
Fermentation	3	• Fermentation systems • Bioreactors	• Standard equipment with minimal configuration • System performance is generally monitored through in-process controls
Purification	2	• Chromatography skids • TFF systems	• Standard equipment with minimal configuration • System performance is generally monitored through in-process controls
Fill/Finish	2	• Buffer preparation/hold systems • Capper • Filler	• Systems are generally constructed from standard components • Quality of the output is routinely monitored
Utilities and HVAC	0	• Compressed air system • Argon gas system	• Systems are generally constructed from standard components

定期回顾内容

- 法规的变化
- 变更
- 维护、校验
- 偏差

定期回顾模板

Tier A
Validation Periodic Review Assessment Type and Instructions

1. GMP Compliance Assessment

Determine if there are any changes in the relevant regulations/regulatory guidance during the periodic review period that are applicable to the system undergoing periodic review.

GMP Compliance Assessment Results
- ☐ There were no applicable regulatory changes. Periodic Review is complete for this assessment type.
- ☐ There were regulatory changes. Refer to Tier B for further evaluation.

2. Change Control Assessment

Determine if there are medium/high risk changes with validation impact generated during the periodic review period that are applicable to the system undergoing periodic review.

Change Control Assessment Results
- ☐ There were no medium/high risk changes. Periodic Review is complete for this assessment type.
- ☐ There were medium/high risk changes. Refer to Tier B for further evaluation.

3. Maintenance/Calibration Assessment

Determine if there are repeated corrective maintenance records generated during the periodic review period that are applicable to the system undergoing periodic review.

Maintenance/Calibration Assessment Results
- ☐ There were no repeated corrective maintenance records. Periodic Review is complete for this assessment type.
- ☐ There were repeated corrective records observed. Refer to Tier B for further assessment.

4. Deviation Assessment

Determine if there were any deviations generated during the periodic review period that are applicable to the system undergoing periodic review, and have the potential to impact product quality.

Deviation Assessment Results
- ☐ There were no system related deviation records with the potential to impact product quality. Periodic Review is complete for this assessment type.
- ☐ There were system related deviation records with the potential to impact product quality. Refer to Tier B for further assessment.

Tier B
Validation Periodic Review Assessment Type and Instructions

1. GMP Compliance Assessment

GMP Compliance Assessment Results
- ☐ The system remains in a validated state. Periodic review is complete for this assessment type.
- ☐ The system requires further action to determine if it remains in a validated state. Refer to Tier C for further assessment.

2. Change Control Assessment

Change Control Assessment Results
- ☐ The system remains in a validated state. Periodic review is complete for this assessment type.
- ☐ The system requires further action to determine if it remains in a validated state. Refer to Tier C for further assessment.

3. Maintenance/Calibration Assessment

Maintenance/Calibration Assessment Results
- ☐ The system remains in a validated state. Periodic review is complete for this assessment type.
- ☐ The system requires further action to determine if it remains in a validated state. Refer to Tier C for further assessment.

4. Deviation Assessment

Deviation Assessment Results
- ☐ The system remains in a validated state. Periodic review is complete for this assessment type.
- ☐ The system requires further action to determine if it remains in a validated state. Refer to Tier C for further assessment.

Assessment Team:

Name: _____

Name: _____

Name: _____

Tier C **Validation Periodic Review Assessment Type and Instructions**		**N/A** ☐
Non-conformity record and CAPA tracking numbers		
Date system returned to a validated state		

6. 模板增加

新

URS
DR/DQ
启动
预功能测试
偏差表格
确认总结报告
定期回顾

旧

无

URS模板

6. Process Requirements-Capacity
7. Process Requirements-Product Physical Properties
8. Process Requirements-CQAs and CPPs
9. Automation and Records
10. Design and Considerations
11. Utilities Available
12. Operations and Maintenance
13. Miscellaneous

6. Process Requirements – Capacity

ID No.	Requirement	Type	Source
6.1	*This requirement is appropriate:* *<The system must process batches in the range of 50 to 83 containers per minute.>*	Business	Project Charter
6.2	*This requirement is appropriate:* *<The tank must have a working volume of 15,000 liters.>*	Business	Product and Process Requirements

7. Process Requirements – Product Physical Properties

ID No.	Requirement	Type	Source
7.1	*This requirement is appropriate:* *<The equipment will be capable of handling a range of clinical products with the following key physical properties.* *Density: 0.9 – 1.2 g/ml* *Viscosity: 1 - 20 cP* *Surface Tension 25 – 65 mN/m>*	Quality	Product and Process Requirements

8. Process Requirements – Critical Quality Attributes and Critical Process Parameters

ID No.	Requirement	Type	Source
8.1	*This requirement is appropriate:* *<The maximum shear rate is 122 000 s-1 based on water at 20 ± 2°C.>*	Quality	Product and Process Requirements
8.2	*This requirement is appropriate:*	Quality	Company

总结

新

- 流程图简单清晰
- 更具体的融入风险管理
- 更详细的阐述URS/PR

旧

- 侧重C&Q测试

7. 问题和思考

I. 风险评估的使用指导不明确，如SRA的风险定义，细化到什么程度（案例的压缩空气没有包括管路的材质）。

II. DQ模板：如何联系URS与设计没有体现。

III. 确认总结报告模板：对每个测试进行详细的描述，费时费力。

IV. 缺少设计说明（Design Specification）的阐述。

DQ模板

Concept GMP Design Review

A. General Project GMP Requirements
- Overall project scope and business case requirements
- Project type
- Regulatory design basis review

B. Facility Layout and Material Handling
- Overall facility layout
- Room classification/hygienic zoning schemes
- Product, people, material, and waste flow
- Transitions requirements
- Gowning levels
- Cold rooms, freezer rooms, and incubator rooms (locations and requirements)

C. Process and Operations
- Overall process summary
- Identification of sterile process steps
- Overall equipment cleaning philosophy
- Review of product quality risk assessment including risk of contamination from (1) particulates internal and external to the equipment, (2) microorganisms (for sterile products), and (3) other products or residues (i.e., cross-contamination)

D. HVAC
- Room pressurization
- Air handling unit zoning and segregation
- Temperature and relative humidity requirements
- Filtration

E. Support Functions
- Identification of approach for required support functions including Quality Operations labs, in-process test labs, warehouse space, sampling and dispensing areas, and offices impacting manufacturing areas

90% Detail Design GMP Design Review

The 90% detail design GMP design review is intended to be a detailed review of the GMP aspects of the design. The major topics to be covered in 90% detail design GMP design review meetings are listed below. Recommended items to cover under each topic are also listed. The items listed are not all inclusive. Items may be deleted or added depending on the type of project and GMP requirements specific to the project scope.

90% Detail Design GMP Review Meeting

A. General Project GMP Requirements
- Overall project scope and business case requirements
- Changes from BOD GMP Design Review
- Resolution of open items from BOD GMP Design Review
- Review of updated Regulatory Design Basis including:
  - Project type
  - Applicable Quality Guidelines and Standards and Engineering Design Standards, Equipment Standards and Standard Modules and anticipated variances to guidelines and standards
  - Project-specific GMP open issues and challenges including local regulatory requirements
  - Summary of risk assessment outcomes and identification of assessments to be done in next design phase
  - Product segregation and containment strategies in multiproduct facilities and antibiotic facilities
  - Licensing impacts, schedule, and documentation

UR Category 用户要求分类	UR # 用户要求文件的地址	User Requirement and Acceptance Criteria 用户要求和接受标准	Design Response 设计响应	Design Specification Location 设计规范文件中的位置
General 概要			Bisulfate dosing is designed instead of Carbon. 部分符合. 参考工艺有一些设计更改. 设计更改不影响系统性能. 紫外灯安装在预处理软化器之前. 碱加药口在 5u 过滤器之前安装. 设计用硫酸氢盐加药，而非活性碳.	
Process 流程	1A	The water supplying the Purified Water System must meet the specifications of GB 5749-2006 (please see note) to the entrance to the pre-treatment skid. • Coliform Count – Not detectable • Total Microbial Count – NMT 50,000 CFU/100ml • Hardness – NMT 2 ppm • Free Chlorine: 0.25-1.0 ppm Note: according to EG-210, city water will be sampled and tested by Suzhou disease control center (SDCC), the tests listed in the report from SDCC must meet the	Partially YES. The value of hardness – NMT 2ppm is not applicable. Our design is based on 550ppm hardness according to GB 5749-2006. 2. 3 部分符合. 硬度值– NMT 2ppm，不适用。设计根据 GB 5749-2006，基准为 550ppm.	PWTRG-DS-11002 DS 1.1

建议使用追溯矩阵

确认总结报告

2. Results

2.A Test 1

2.A.1 Test 1 Results

Summary of test conditions with justification and results compared against th
This may include tables, charts, etc.

2.A.2 Test 1 Discrepancies

None or summary of discrepancy.

2.A.3 Test 1 Data

Reference to where the execution and supporting data is stored.

2.B Test 2

2.B.1 Test 2 Results

Summary of test conditions with justification and results compared against the acceptance criteria.
This may include tables, charts, etc.

2.B.2 Test 2 Discrepancies

None or summary of discrepancy.

2.B.3 Test 2 Data

Reference to where the execution and supporting data is stored.

URS 号码	测试					结论（成功/失败）
	FAT	SAT	IQ	OQ	PQ	
1.1	x	x				成功
1.2			x			失败
1.3				x		成功

建议使用追溯矩阵

8. C&Q体系构建

- 验证总计划
- 文件架构
- 团队
- 职责

GMP要求

第一百四十五条　企业应当制定验证总计划，以文件形式说明确认与验证工作的关键信息。

第一百四十六条　验证总计划或其他相关文件中应当作出规定，确保厂房、设施、设备、检验仪器、生产工艺、操作规程和检验方法等能够保持持续稳定。

验证总计划

工厂验证总计划(VMP)）提供了工厂的验证状态和验证策略的概要。

验证通则考虑到了**所有产品、工艺、设备、方法、清洁和计算机相关的系统的确认、再确认和验证状态，以及计划的验证、再验证活动和遗留计划。**

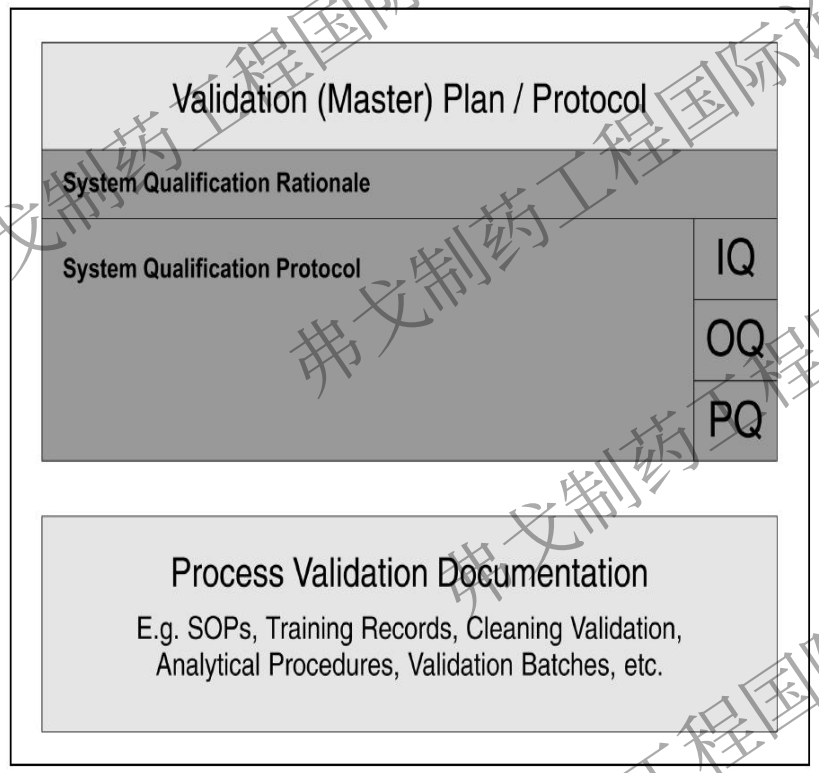
VMP 一般包括以下信息：

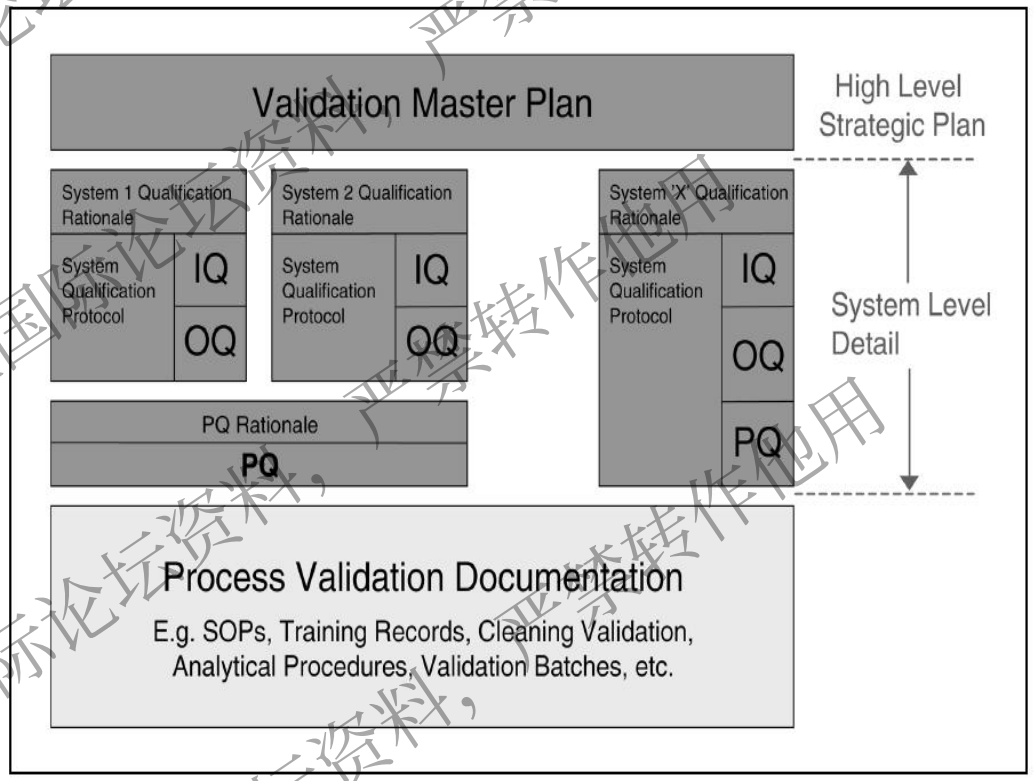
- 目的
- 范围
- 组织和职责
- 现行设施、设备、公用设施和工艺的描述
- 验证文件格式和流程
- 验证方法，包括一般准则和具体验证方法
- 验证系统维护
- VMP 管理
- 每年验证计划管理
- 参考文件和附件

项目VMP

小、单一系统的项目
Small Single System Project

多系统，复杂项目 Complex Project with Many Systems



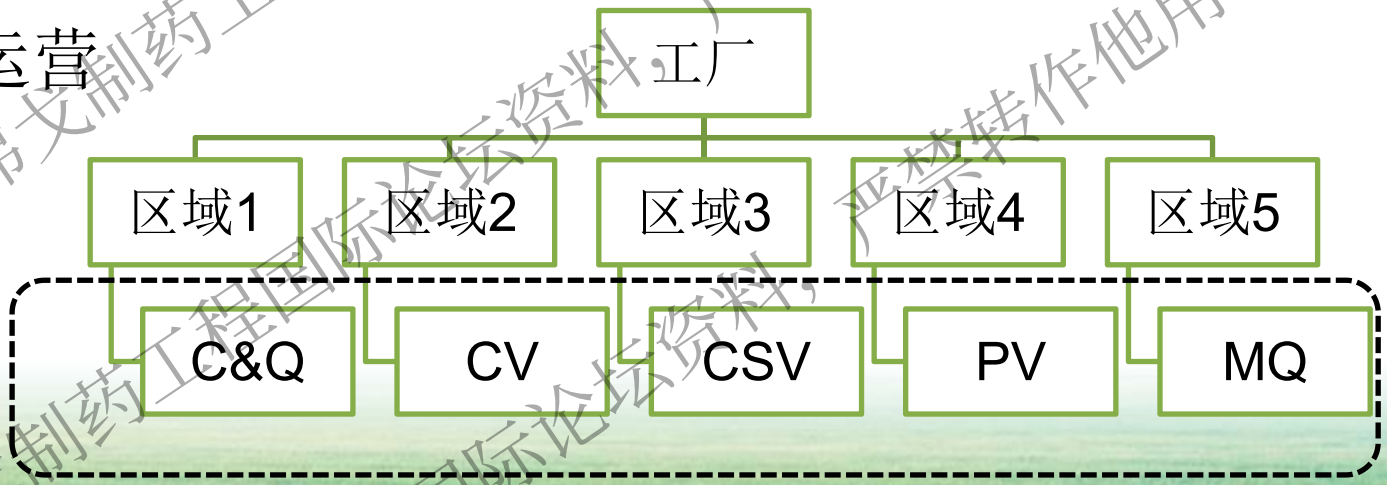


文件架构

团队

- 独立的C&Q团队
  - 大的项目

- 交叉区域的团队
  - 日常的运营



职责

- 四类职责
  - W: 写
  - R: 审核
  - A: 批准
  - E: 执行

活动	工程	质量	技术服务	生产
调试	W, R, A, E	NA	NA	E
确认	W, E	A	R (如需)	E
验证	NA	A	W, R	E

职责- 质量人员的参与

- 调试文件不需质量人员的参与
- 对直接影响系统，如果有些调试的测试结果、数据用于替代确认测试，质量人员需参与相应测试的监管。

Q&A?