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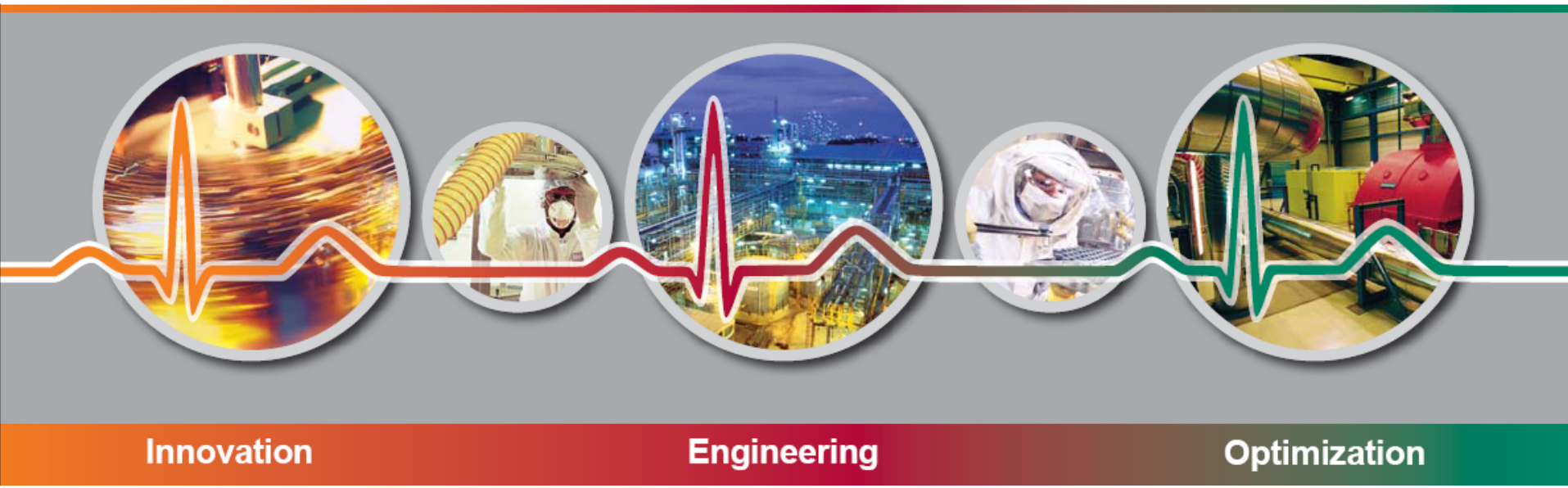

Design Qualification
设计验证

Speaker: Henry Tjong（张诚汝）

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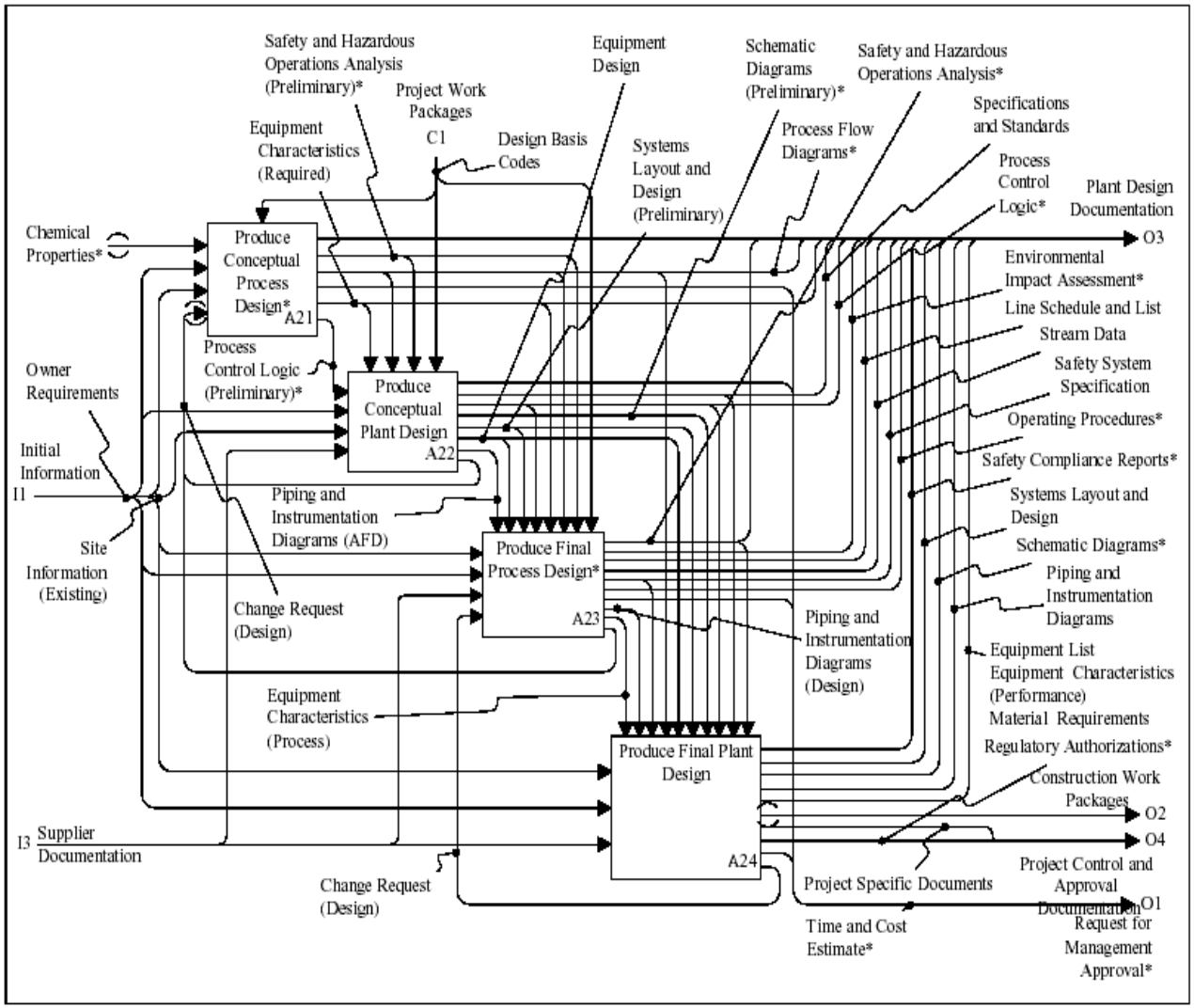
Bayer Technology Services

- Mr. Henry Tjong is a Senior GMP Consultant, works in the Healthcare Process Department, Bayer Technology and Engineering (Shanghai) Co. Ltd.
- 张诚汝先生任职于拜耳技术工程（上海）有限公司，他是医药保健工艺部门的高级GMP顾问。

- He is a dedicated and focused Professional Engineer with 26 years of progressive engineering/project/validation experience, including more than 20 years in the biotechnology and pharmaceutical fields.
- 一个在国际制药业具有丰富工程管理和验证经验的专家和项目经理，在制药行业从事工程管理和验证工作长达20年。

- In a pharmaceutical engineering project, design is complicated due to the complex nature of engineering project and in addition, to fulfill the GMP requirements. Design quality, will highly impact the quality, schedule and cost of a project, and ultimately the GMP compliance of the facility.
- 在制药工程项目中，设计是很复杂的，这是由于工程项目的内在复杂性及附加的GMP的要求。设计的质量直接影响着项目的质量，时间及费用，及最终设施的GMP符合性。

设计是复杂的



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- Systematic design review is a must to ensure design quality and a requirement of Good Engineering Practice. The importance of this activity is reflected in many regulations, for example, EMEA GMP, ICH, and PIC/S etc requires Design Qualification. In China, in the new GMP under discussion, DQ is required as the first step of the qualification practices.
- 系统的设计审核对于保证设计的质量是至关重要的，并且也是良好工程规范的要求。这一活动的重要性还进一步地体现在很多监管条例上，如欧盟的GMP，ICH， 及PIC/S中都要求设计确认。在中国，新版的GMP讨论稿中，也要求设计确认作为整个确认活动的起点。

- BTES as an International Engineering Company provides technology and engineering services to pharmaceutical industry worldwide. Through this presentation, we would like to share some of our knowledge and experiences; hopefully we would help the local pharmaceutical companies get ready for DQ implementations.
- 拜耳技术工程作为国际工程公司，为全球的制药工业提供技术和工程方面的服务。在这个讲座中，我们将分享我们的知识和经验，希望可以帮助中国本土的制药企业为设计确认的实施作好准备。

- **EMEA GMP**
- *The documented verification that the proposed design of the facilities, systems, and equipment is suitable for the intended purpose*
- *证实设施、系统和设备的拟用设计适合于既定目标所提供的文件证明。*
- ***EU GMP Annex15　欧盟GMP 附录15***
- *9. the first element for the new facility, system or equipment could be Design Qualification (DQ).*
- *9.新厂房设施、系统或设备的第一元素可为设计确认（DQ）。*
- *10. The compliance of the design with GMP should be demonstrated and documented.*
- *10. 为确保设计遵守GMP要求应证明和并记录成文。*

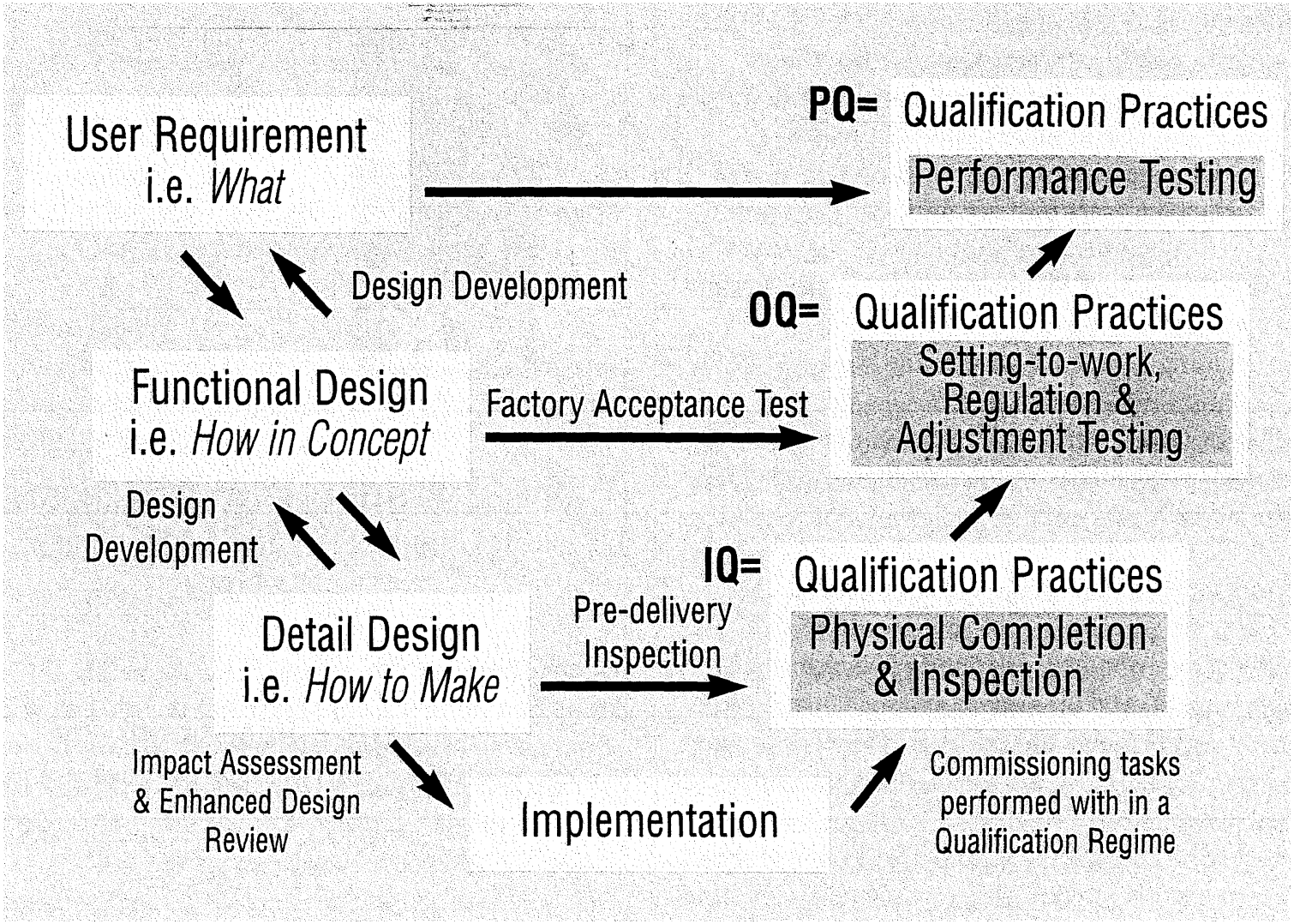
- **PIC/S**
- *1.8 The premises, the supporting utilities, the equipment and the processes have been designed in accordance with the requirements of the current GMP. This normally constitutes Design Qualification or DQ.*
- *1.8 建筑物、公用工程、设备和工艺的设计应符合现行GMP要求。 通常需进行设计确认或DQ。*
- **ICH Q7A**
- ***Design Qualification (DQ):** documented verification that the proposed design of the facilities, equipment or systems is suitable for the intended purpose.*
- ***设计确认（DQ）：**为证实厂房设施、系统和设备的拟用设计适合于既定目标所提供的文件证明。*

- **FDA**
- There is no DQ mentioned in the cGMP, however, design is well referenced in the cGMP.
- cGMP 未提及DQ 内容，然而cGMP适当的引入了设计。
- ***21 CFR Part 211 Subpart C— premises and facilities***
- ***CFR 21条, 211部分, C分部– 建筑物及厂房设施***
- ***21 CFR Part 211 Subpart D – Equipment***
- ***CFR 21条, 211部分, D分部– 设备***
- *211.63 Equipment design, size and location 设备设计、尺寸及安装位置*
- *211.65 Equipment construction 设备制造*
- *211.67 Equipment cleaning and maintenance 设备清洁及维护*
- *211.68 Automatic, mechanical, and electronic Equipment 自控，机械及电子设备*

- **SFDA**
- There is no DQ mentioned in the China GMP.
- 中国GMP没有提及设计确认。
- **China GMP 2009 中国GMP 2009**
- These are Validation requirements mentioned in New China GMP for Discussion 3rd Draft 新版GMP讨论稿第3稿中对验证的要求：
- Code 150: Documents and records of Qualification and validation should be constituted to verify that following predetermined objectives are achieved:
- 第一百五十条：应建立确认和验证的文件和记录，并能以文件和记录证明达到以下预定的目标:
- Design Qualification verify that premises, the supporting utilities, the equipment and the processes have been designed in accordance with GMP requirements. 设计确认(DQ)应证明厂房、辅助设施、设备和工艺的设计符合GMP要求.

- **DQ is an Authorities regulatory requirement!**
- **DQ 是监管机构要求!**

- The ISPE Baseline Volume 5, Commissioning and Qualification, First Edition/March 2001
- ISPE基准第五册，调试和确认，第一版，2001年3月
- *EDR（Enhanced Design Review） is defined as:*
- *“A documented review of the design, at an appropriate stage in the project, for conformance to operational and regulatory expectations”*
- *增强性设计审核（EDR）定义为：*
- *在项目的适当阶段进行设计文件审核以确认设计符合运行和规范的要求。*
- *The definition of EDR is the same as DQ’s.* ***Therefore EDR = DQ****.*
- *其对EDR的定义与DQ一致，即EDR=DQ。*


User Requirement
i.e. What
PQ= Qualification Practices
Performance Testing
Design Development
OQ= Qualification Practices
Functional Design
i.e. How in Concept
Factory Acceptance Test
Setting-to-work, Regulation & Adjustment Testing
Design Development
IQ= Qualification Practices
Pre-delivery Inspection
Detail Design
i.e. How to Make
Physical Completion & Inspection
Impact Assessment & Enhanced Design Review
Implementation
Commissioning tasks performed with in a Qualification Regime

1. DQ is an Authorities regulatory requirement.
2. DQ 是监管机构要求。
3. DQ would assure that the system (facility, utilities and equipment) owner would get what they want, as specified on the User Requirement Specifications (URS)
4. DQ将确保业主对系统（设施、公用工程和设备）的要求（在用户需求规范中详细说明）得以满足。
5. DQ would assure the regulatory authorities that the design process has been carried out in a control manner.
6. DQ将向监管机构证明设计过程是在控制下进行的。
7. DQ would provide an audit trail from conception of the project up to the completion of the detail design.
8. DQ将提供一个从项目立意直至详细设计完成的稽查追溯。
9. DQ would improve project delivery and streamline qualifications (IQ, OQ and PQ) efforts.
10. DQ将促进项目交付和确认流程（IQ、OP和PQ）的进行。

Owner Representatives 业主代表：

1. Project Manager 项目经理
2. Subject Matter Experts 各领域专家
3. QA 质量保证
4. Validation 验证人员
5. System Owners 系统业主
6. Engineering 工程师
7. Maintenance 维护人员

Design firm 设计公司:

1. Project Manager 项目经理
2. Subject Matter Experts (Discipline Engineers)
3. 各领域专家（各专业工程师）

Vendor / Contractor 供应商/ 承包商:

1. Project Manager 项目经理
2. Subject Matter Experts (Discipline Engineers)各领域专家（各专业工程师）
3. QA

- **This is the outmost important document该文件非常重要**
- Check if URS has to be written for each facility, utility system and equipment 核对URS是否包括所有设施、公用工程系统和设备
- All URS' should have been approved by QA (GMP Issue) and other Stake Holders (System owner, Engineering, Validation etc) 所有URS应经过QA（GMP相关问题）和其他参与方（系统业主、工程人员和验证人员等）审批

User Requirement Specifications (URS) (per GAMP 4) 用户需求规范（URS，GAMP 4）

- A User Requirements Specification defines, clearly and precisely, what the user wants the system to do.
- 用户需求规范正确、清晰的定义了用户对系统任务的要求。
- It defines the functions to be carried out, the data on which the system will operate, and the operating environment.
- 其定义了功能的执行，系统运行参数和环境。
- The URS defines also any non-functional requirements, constraints such as time and costs, and what deliverables are to be supplied.
- The emphasis should be on the required functions and not the method of implementing those functions.
- URS还定义了非功能性要求，以限制时间和成本和需提供的交付要求。强调了所需功能而非功能执行方法。

The following guidelines should be followed during the production of the specification:

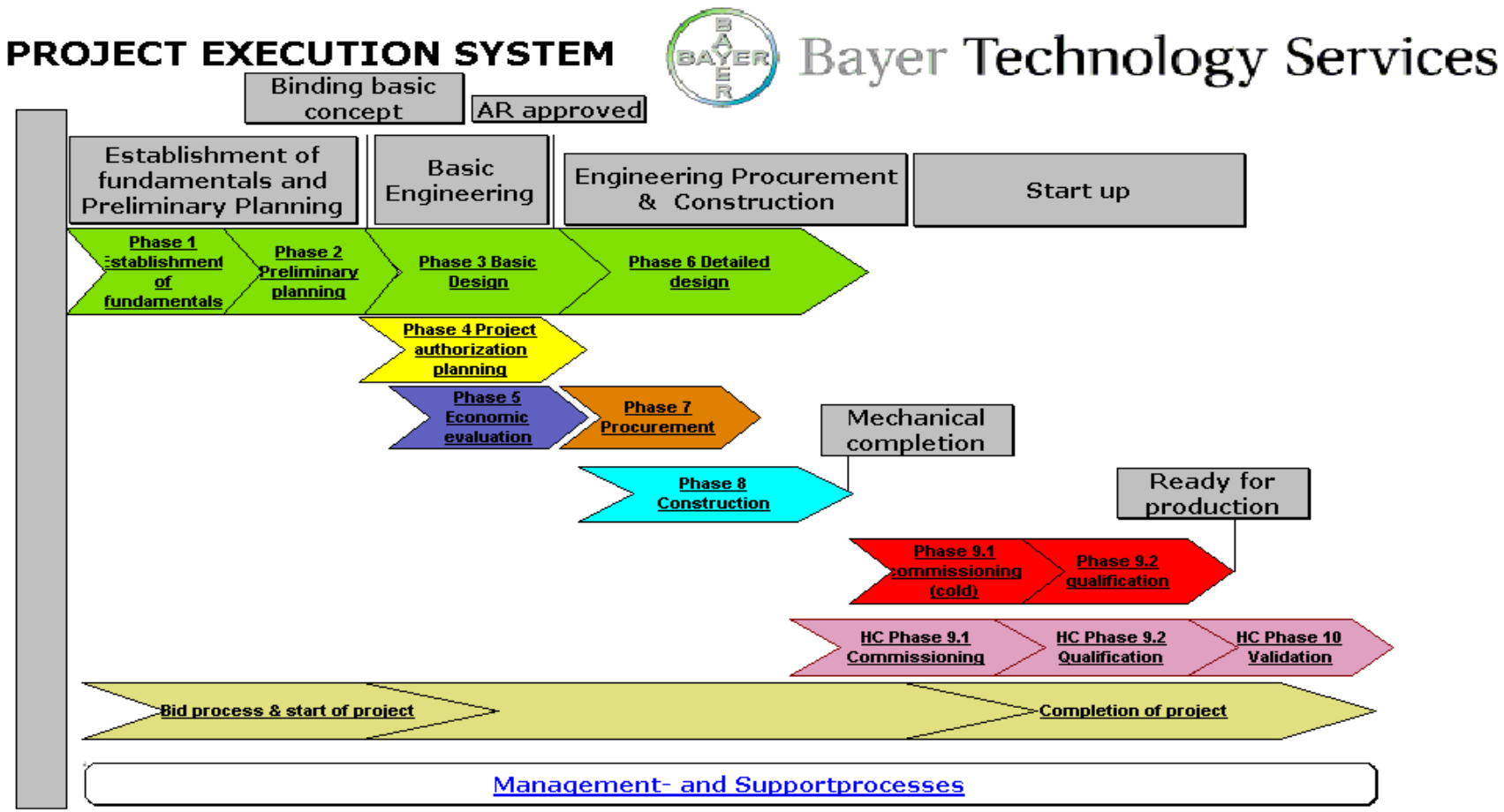
1. Each requirement statement to be uniquely referenced, and no longer than 250 words.
2. Requirement statements should not be duplicated nor contradicted.
3. **The URS should express requirements and not design solutions.**
4. **Each requirement should be testable**.
5. The URS must be understood by both user and supplier; ambiguity and jargon should be avoided.
6. Wherever possible, the URS should distinguish between mandatory/regulatory requirements and desirable features.
7. There may need to be a formal review of the URS between the user and supplier to check understanding and that requirements have been met (or not) in the Functional Specification.

The design reviews process shall follow the Bayer HealthCare Directive 24-09-01, “GMP Status Review for Facilities, Equipment and Utility System”.

- 设计审核应根据拜耳医药保健指南24-09-01“设施、设备和公共成系统GMP阶段审核”执行。

Procedures 程序：

- There will be 3 GMP reviews, namely Concept Review (B1), Planning Review (B2) and Detail Design Review (B3).
- GMP审核分3个阶段，分别为概念审核（B1）、计划审核（B2）和详设计（B3）。
- Write a DQ summary report based on the information above.
- 根据上述内容DQ 完成总结报告.



- Prerequisites先决条件
- System Level Product Impact Assessment. Only those systems have direct impact would go through DQ. Others will be managed by GEP.系统水平产品影响评估。定义为直接影响的系统进行DQ。其它系统将根据GEP要求管理。
- URS. DQ would not be able to perform without it.用户需求规范。DQ的执行必须以URS为基础。
- Do System Impact vs. System Complexity/Novelty assessment to determine the methods for DQ. The outcomes would be Structure Design Review only or Structured Design Review + FMEA.进行系统影响与系统复杂性/新颖性比较以确定DQ方案。评价结果为仅进行建筑设计审核或建筑设计审核结合失效模式与影响分析方法。

- Procedures程序
- After receiving the proposal from the vendor: the information provided by the vendor would be checked against the URS. Any discrepancies would be resolved prior to issue of PO.
- 供应商提供方案后，进行供应商提供资料与URS比较。所有偏差均应在发出采购订单前应将得以处理。
- After the Detail Design by the vendor is completed: check the information provided against the URS and any outstanding issues during tender analysis.供应商详细设计结束后，进行供应商设计方案与URS比较，并核对投标评估过程中出现的任何显要问题。
- Perform Components Criticality Assessment.
- 进行部件关键性评估。

- Perform FMEA (if required).
- 进行FMEA（如有要求）。
- Any deviations from the above 3 items would be resolved prior to release for fabrication/manufacturing.
- 上述3项提出的任何偏差需在制造/生产开始前得以处理。
- Structure design review consists of Verification Tables and Check List.
- 结构化设计审核包括确证表格和核对表。
- Write a DQ summary report based on the information above.
- 根据上述内容完成DQ总结报告。

- The DQ report is a document which will provide evidence that the system or equipment is designed for its intended use. Following is a proposed format DQ报告对设计指定用途的系统或设备提供证明。DQ提案格式如下：

The approval section 审批部分

- It contains the names, functions and signatures of the representatives for project team, usually Engineers, Operation (the system owner), Process, QA, and Validation。
- 包括姓名、职位和代表项目团队的签名，通常为工程师、运行人员（使用者）、工艺人员、质量保证人员和验证人员

The description section 描述部分

- A brief explanation of the equipment or system, it intended purpose, planned site location, phase in the production chain, process capacities, basic functional and automation capabilities, cleaning features, and peripheral items associated, where applicable.
- 设备或系统总体说明，内容包括目的、已规划厂区位置、生产线阶段、工艺产量、基本功能和自控性能、清洁特点和可利用的相关外围设施

The URS section URS部分

- This section contains the approved User Requirement Specifications, preferably the original set submitted to vendor for the initialization of procurement phase.
- 本部分内容包括审批的用户需求规范，最好将原件交付于买主以便开始采购阶段。

The attachment section 附录部分

- This section includes the list of all attached supporting document三, for example, engineering drawings, layouts, production process flowcharts, a summary of bid analysis, design review meeting minutes, and FAT reports.
- 本部分内容包括所有支持文件，如工程图纸、平面布置图、生产工艺流程图、投标分析总结、设计审核会议纪要和FAT报告。

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The project follows up section 项目贯彻部分

- This is a general synoptic table with major completion dates for the URS approval, PO placement, DDS approvals, FAT, and shipment.
- 本部分为URS审批、PO更换、DDS审批、FAT 和运输的主要完成日期一览表。

The qualification document section 确认文件部分

- This includes the Design Verification Tables, all the associated DQDRs, and summary reports. This makes the design phase follow-up completed traceable for the project – Refer to Appendix 6.It is actually the documented evidence that the design for the equipment or system was carried out to suit its intended use as defined at the URS.
- 内容包括设计验证表、所有相关DQDRs和总结报告。该内容使得设计阶段贯彻可追溯（参见**附录6**）。

The GMP assessment section GMP评估部分

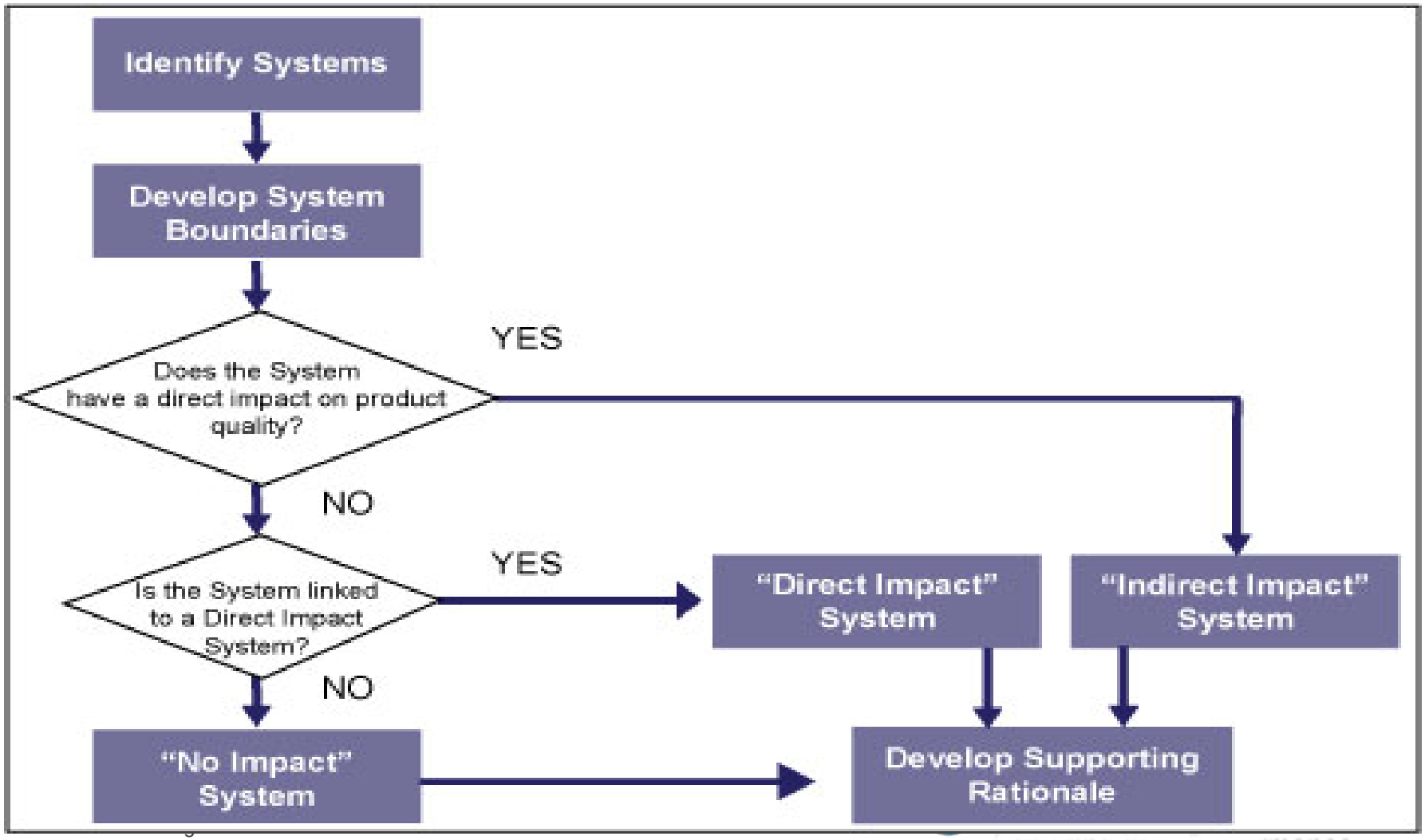
- This is a review section that includes a questionnaire considering items such as identifications of drawings and instrumentation, contact material suitability, calibrations, safety, and an adequacy concluding statement.
- 本部分为审核部分，包括问题表如图纸和仪表确认、接触材料适用性、校验、安全和充分的结论。

C&Q – Impact Assessment
影响评估

- Introduction 引言
  - Impact Assessment is the process by which the impact of a system on product quality is evaluated, and the critical components within those system are identified
  - 影响评估是对影响产品质量的系统进行评估的过程，和鉴别系统中的关键部件。

- Examples of Systems include:系统的例子包括：
  - Chilled Water 冷却水
  - Clean Steam洁净蒸汽
  - WFI注射用水
  - HVAC 空调系统

- System Impact Assessment Process Overview
- 系统影响评估过程概述



C&Q – Impact Assessment

- **System Impact Assessment Process系统影响评估过程**
  - Applicability of any of the following criteria will provide an indication that a system has a “Direct Impact”:下列情况都是系统的直接影响因素
    - The system has direct contact with the product (e.g., air quality)

      直接接触产品的系统（如：空气质量）
    - The system provide an excipient, or produces an ingredient or solvent (e.g., WFI)

      提供了一个辅料，一个生产组分或溶剂的系统（如WFI）
    - The system is used in cleaning or sterilizing (e.g., Clean Steam)

      用于清洁或消毒的系统（如灭菌蒸汽）
    - The system preserves product status (e.g., Nitrogen)

      保护产品性状的系统(如:氮气)
    - The system produces data which is used to accept or reject product (e.g., Electronic Batch Record System or critical process parameter chart recorder)

      产生用来接受或拒绝的产品数据的系统(例如，电子批记录系统或关键工艺参数图表记录器)
    - The system is a process control system (e.g., PLC, DCS) that may affect product quality and there is no system for independent verification of control performance in place.

      一种过程控制系统（如可编程控制器，集散控制系统），它可能影响产品质量，并且没有设置系统来单独确认控制影响。

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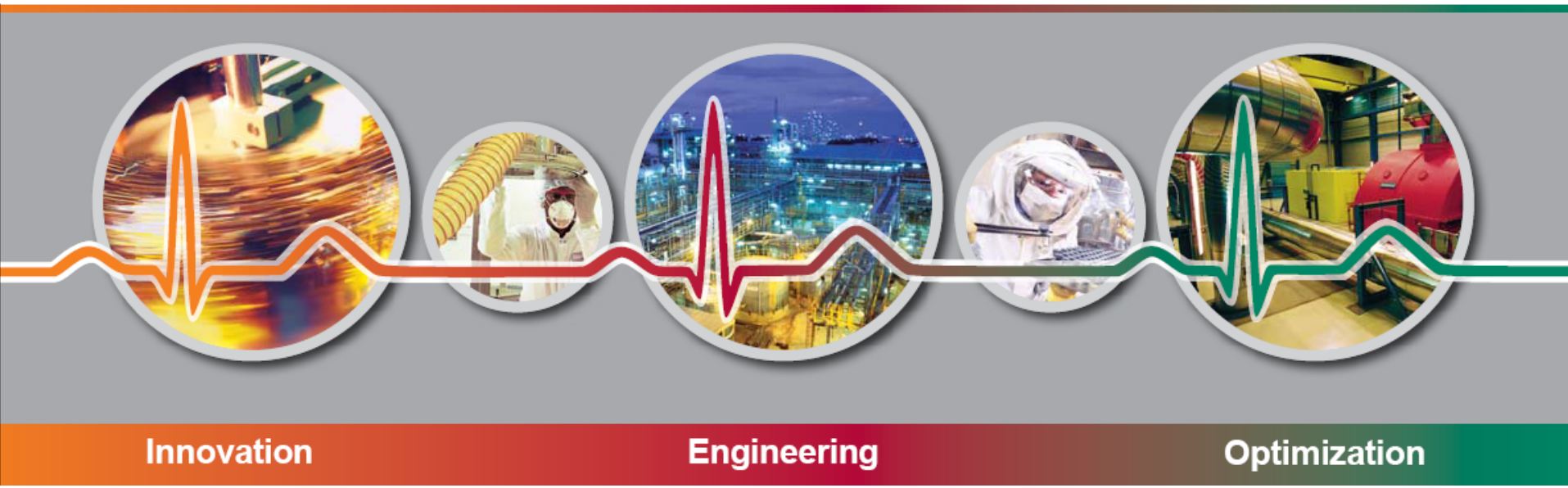

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