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#sharing challenges
and solutions in practice

Road from Design, Commissioning, Qualification to Process Validation for Fast Tracked Projects

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Introduction

Udara Yapa

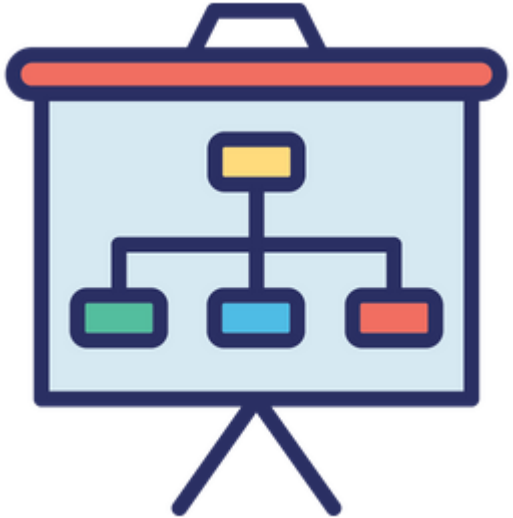
- Head of Validation at WuXi Biologics Global Solution Provider since April 2022.
- 10+ experience in GMP manufacturing/C&Q/R&D.
- Site expansion projects/Large facility modifications/ Green, Grey fields projects.
- C&Q Lead in CAPEX projects, Site Validation Lead.
- Several fast tracked concept to fill projects.

Presentation breakdown

- What is a Fast Tracked Project?
  9 months to 2 years from Basic design to Process Validation (PV).

- **Stages**

  - Purchasing and negotiation.
  - Quality Systems.
  - Design Qualification.
  - Commissioning and Qualification.
  - Handover to the user.
  - Time loss between end of OQ till start of PV.
  - Constraints during transition from PV to a routine manufacturing.



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Purchasing and negotiation

- **Referring to the stage:**
  - Purchasing order for complex equipment placed.

- **Pitfalls**
  - Procurement URS/GMP URS.
  - Agreeing to ‘‘cuts‘‘ during negotiation without consultation. (e.g. IOQ package for COTS/network connections/printing functions)
  - Techincal departments - Automation/Validation/Engineering/QA not involved in discussions.
  - Agreeing to design changes without understanding details.
  - Vendor not taking time to go through the requirements in detail.

Quality Systems

- **Referring to the stage:**
  - From Purchasing of equipment to start of Qualification.

- **Pitfalls**
  - No procedure to perform supplier assessments.
    - Could end up with systems that are not cGMP compliant.
    - Vendor software development (no change control/21 CFR part 11 non-compliant).
  - Deviation management not setup.
    - Difficult to evaluate criticality and to provide QA oversight.
    - Difficult to leverage tests into qualification.
  - QA under-resourced.
    - QA is a contractor - with limited access and oversight to global/site procedures.
  - Change control procedure not established.
  - Project change control + GMP change control.

"I see you getting into compliance verrry sooooooon. Okay, that will be 50 bucks."

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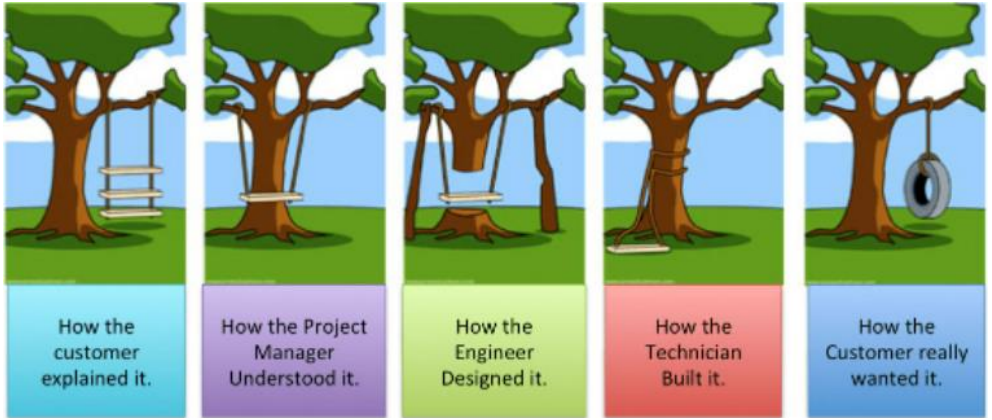
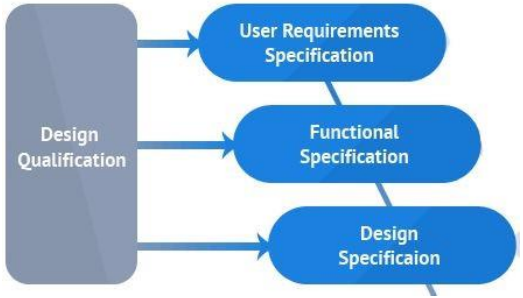
Design Qualification



https://nodeviation.com/what-is-design-qualification/

- **Referring to the stage:**
  - Vendor provides the detailed design and the qualification team review the design against customer requirements.

- **Pitfalls**
  - User/Automation/Engineering/QA/Process Engineer(s) not involved in design checks and non-compliances.
  - During the purchasing, costs for vendor DQ participation is not accounted for.
  - Vendor has not submitted the detailed drawings/specifications for DQ.
  - Vendor already building the installation prior to DQ approval.
  - HAZOPS (Hazard and Operability Study) ongoing as vendor is building the installation.
  - Interdepencies are not checked in detail.
    (e.g. Overlaps of piping connections from different vendors/ Compatibility of package units with cutomer network/DCS)



http://www.ysfc.co.kr/eng/companyIvalidation.php

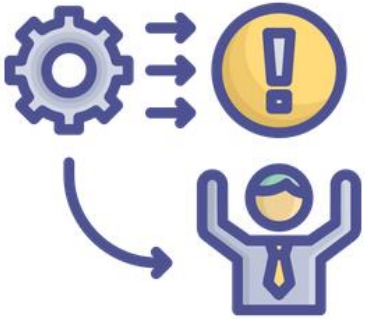
Commissioning and Qualification

- **Referring to the stage:**
  - Where installation performed and functionality checked and qualified.
- **Pitfalls**
  - Not appropriately resourced.
    - C&Q resources brought in too early when systems not fully mechnically/electrically complete or brought in too late.
    - Resources are not experienced enough. (e.g. C&Q suppliers bringing in graduates with limited GMP exposure).
    - Commissioning not witnessed.
    - User departments Production/Engineering not involved in C&Q works. (e.g. Parameter setups, rationale, fine tuning missed).
    - Vendor making changes to their commissioning teams.
  - Systems not construction complete.
    - Handover to C&Q acclerated due to timeline issues. (e.g. Large number of construction punches end up in qualification).
    - Non compliant in safety. (e.g. Documentation not complete for safety devices, Tie in`s are not properly LOTOed (Lock out Tag out), Electrical checks are not complete, Emergency procedures not tested, Interlocks not tested)

https://ahseeit.com/?qa=131022/when-you-apply-for-job-youre-not-qualified-for-but-anyway-meme

https://www.gettyimages.de/fotos/incomplete-bridge

Commissioning and Qualification



- **Pitfalls**
  - Communication
    - Speak out culture not established. Scare culture created by mangement who are not accepting/negotiating delays.
      (e.g. Vendors not communicating, team members not highlighting issues).
    - Yes culture, Schedule driven culture, forcing team members to make quick decision without detailed thinking.
    - Speaking culture in meetings.
      (e.g. Not being inclusive. Being harsh on vendors/employees. Egocentric behavious).

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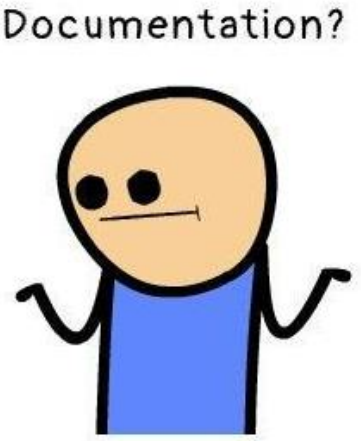
  - Not establishing a Change control procedure during C&Q
    - No clear stage gate for change controls to start.
      (e.g. Is it during commissioning or qualification or post qualification?)
    - Project change procedure exist to control costs but not quality.
      (e.g. QA left out of discussions/approval).
    - Changes control procedure has no verification/effectiveness check.

Commissioning and Qualification

- **Pitfalls**
  - Documentation
    - Customer does not specify documentation requirement at purchasing stage.
    - Vendor does not provide the documents in time or too many document errors leading to multiple review rounds.
    - Customer requests specific formats which vendor cannot provide. (e.g. Calibration Lists and Spare part lists).
    - Document handover not planned or responsibility not clear. (e.g. As built documents, Functional Specifications, Operating manuals).
    - Draft SOPs are acceptable at OQ stage but what is an acceptable draft?
  - Training
    - Vendor has no detailed training documents. Watch and learn is not enough!
    - Limited number of persons trained and training not cascaded to other team members. (e.g. Occasionally you find one team member trained and this person is on holiday or sick when you need him/her)
    - Trained persons leave the company or reallocated.



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Handover to User

- **Referring to the stage:**
  - Where OQ is completed and handed over to user + site.

- **Pitfalls**
  - PQ activities and pre-requisites not planned.
    - Autoclave load validation. Washing machine load validation.
      (e.g. Autoclave/Washing machine is ready for validation but load items not ordered, loading pattern, number of items not decided)
    - C&Q contractor leaves at this stage and site validation team not geared up to take the load validation.
    - Site team is so focused on CAPEX project completion and resource not allocated to SIP, Cleaning Validation or SOP finalisation.
    - System operability knowledge could also be lost with the leaving project team.

  - **Documentation**
    - No clear owner to receipt Qualification/Design drawings/Functional Specifications/Manuals etc.
    - Scanning not done.
    - Some documents are only interim approved with open non-critical deviations.

https://www.alamy.com/frustration-doubt-question-concept-young-businessman-office-worker-cartoon-character-standing-and-holding-big-sign-with-question-mark-in-hands-expr-image391403828.html

Time loss between end of OQ till start of PV

- **Referring to the stage:**
  - Where OQ is completed, till start of PV.

- **Pitfalls**
  - SOPs not issued
    - Scope for SOPs not established. Time lost for review and approval of the SOPs.
    - Gowning procedure, cleaning procedures, risk based clean room monitoring not established.
  - Receipes and Cycles
    - Production receipes not established.
    - Project has not allocated funds for vendor to support receipe development. (e.g. Time lost during cycle development for package units).
    - Operations/Engineering not involved in C&Q, leading to lack of knowledge on receipe development.
  - Loss of Staff
    - Due to high pressure, staff leaving for other jobs. Leading to loss of knowledge.

https://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.pinterest.com%2FMCMasterControl%2Fsop%2F&psig=AOvVaw13DrTlrir27OD5CMYCCYIQ&ust=1649930563910000&source=images&cd=vfe&ved=0CAgQjhxqFwoTCKCbyNjkkPcCFQAAAAAdAAAAABAJ

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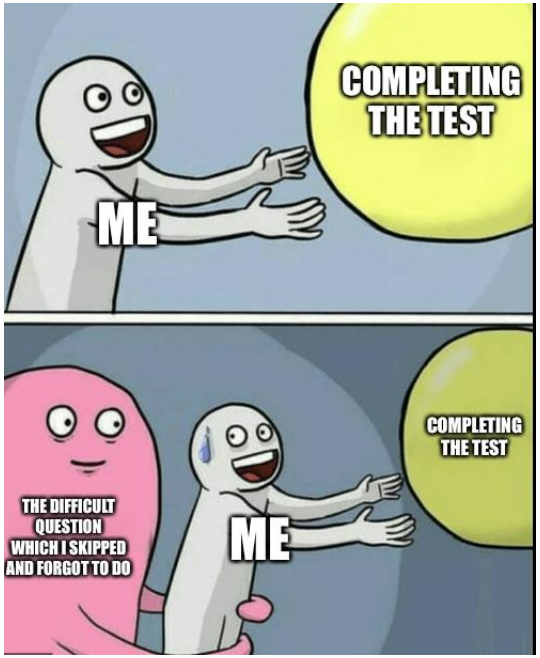
Time loss between end of OQ till start of PV

- **Referring to the stage:**
  - Where OQ is completed till start of PV.

- **Pitfalls**
  - Training
    - SOPs approved at rush and not enough time allocated for training.
    - As it is a new process, staff not confident on equipment, leading to errors.
  - Water runs
    - Due to schedule pressures, planned activities like water runs are scrapped.
      (e.g. Not able to see issues when all systems (utilities/process/waste facilities) are working together).
      (e.g. Not able to see and rectify utility supply/demand issues).
  - Media Simulations
    - Diving to media simulations without test runs.
    - Diving to media simulations without adequate training of staff.
    - Operator welding/sealing qualification not performed.



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Constraints during transition from PV to a routine manufacturing

- **Referring to the stage:**
  - Where PV has started and looking at routine manfuacturing.

- **Pitfalls**
  - CAPAs/Change Controls moved from Qualification - still open
    - Compliance gap – resources to complete the gap.
    - Effectiveness checks not completed.
  - Preventitative Maintainnance/Re-Calibration not planned
    - As Engineering is pulled into Qualification/Media simulations/SOP writing, no resource allocated to build up PM or plan recalibrations.
    - Causing deviations, equipment unavailability due to unplanned calibrations
    - HVAC re-qualification not planned.
      (e.g. Difficult to get a slot with HVAC testers, replacement of filters can result in production delays).

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Summary

- **Detailed planning**/proper scheduling is critical in a fast tracked project.
- **Realistic time** should be allocated for individual tasks.
- **Communication** up and down should be smooth and understanding.
- **Staff retention**, site staff is critical to be sucessful at PV and commercial manufacturing.
- Kicking the can down the road will only result in delays.
- Vendor/Third parties need to be fully aligned with the ambition.
- **Communicate** risks to sponsors upfront and **regularly** throughout the project.
- A good open work culture is esential for a fast tracked project to succeed. It is **people** who make **buisnesses work**!

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Thank you for your attention

QUESTIONS ?