| | |
|---|---|
| **Knowledge Area** | Regulatory Compliance |
| **Title:** | Design Space – What's the Link to the Project Process? |
| **Author:** | Dr Trish Melton, MIME Solutions Ltd |

**Introduction to the knowledge**

This paper looks at the impact of ICH Q8, and the definition of "Design Space", on the lifecycle of a typical pharmaceutical facility project and then highlights some further opportunities for the overall "Product Lifecycle".

Main areas covered are:

- The concept of "design space" and its integration into the project lifecycle – when & how the development should start
- The management of design space development – building in compliance using project management tools
- The management of design space implementation, managing compliance risk and the link to ICH Q9 – how the project team needs to work with the design space

**Main body of knowledge**

The project to design and build the facility which will manufacture a new drug is only a small part of the overall product lifecycle – however it is on the launch critical path. Therefore the engineering project team need to be efficient & effective in delivering a facility design & build which meets product and process needs:

- Compliance (cGMP, SHE, legal)
- Launch timetable
- Economic considerations – facility capital and lifecycle costs

The current "best practice" approach has been to make the technology transfer from the product development team a key part of the project process:

- In effect the project and development teams working together to transfer the process from clinical trial manufacture to full-scale production manufacture
- Integrating development team resources into the project team to support design and then eventual commissioning & start-up

Previous to ICH Q8, the project team communicated with the development team by discussing "equivalence" and by accepting empirically based process parameters and specifications. This lead to:

- Many parameters being denoted as "critical" when in fact they were either not critical at all or their criticality was linked to safety or yield, i.e. not quality critical
- Quality critical parameters with very narrow "control ranges"
- Unit operations expressed as equipment specifications
- A perception that the successful outcome of the three validation batches was not predictable
- Regulatory submissions which required post approval changes as manufacturing experience challenged the "control" limits

ICH Q8 and the concept of Design Space has given the Technology Transfer Team a more robust "envelope" from which the Project Team can "engineer" the process:

- A science based understanding of the chemical processes so that control ranges are based on quality by design, cause-effect thinking and a clearer appreciate of what "control" constitutes – thus supporting the development of a control hierarchy for quality critical parameters
- A science based understanding of the physical processes so that unit operations are specified NOT equipment

| | |
|---|---|
| **Knowledge Area** | Regulatory Compliance |
| **Title:** | Design Space – What's the Link to the Project Process? |
| **Author:** | Dr Trish Melton, MIME Solutions Ltd |

- Based on the above "equivalence" is built in rather than a challenge to be faced

Additionally, ICH Q9, Quality Risk Assessment, works with the design space concept to deliver an overall robust, science based understanding:

- It introduces a risk-based approach to control
- It allows engineers to focus on quality risk assessment as a tool to support "building in compliance"

However for the above to be delivered the development of the design space needs to be completed. This "project" is also on the launch critical path and requires a culture change to be successful:

- Integration of all required skills to support the scientific understanding of the chemical & physical processes, e.g. organic & physical chemists, chemical engineers and quality professionals, etc.
- Quality by Design – integrating new design methodologies to develop and measure process capability and to develop and ensure that the design space does minimise "risk to patient"

**Knowledge Summary and Conclusions**

The key messages can be summarised as:

- Design Space supports the effective technology transfer from pharmaceutical development to manufacturing via the traditional pharmaceutical facility project
- Design Space provides a project manager with the "answers" to the typical engineering and design team questions: it underlines the science based approach to "engineering" the manufacturing process
- Earlier involvement of engineers and project managers can deliver benefits in terms of:
  - Building a broader design space than can be "engineered"
  - Considering the product and regulatory lifecycle when developing the initial "project"
- "Best Practice" project management can support the effective management of the design space at all stages in its lifecycle:
  - Robust definition – to widen the design space through robust scientific understanding and consideration of how the production process is to be "engineered" to work within it
  - Risk Management – to ensure that appropriate risk assessment tools are used to assess and minimise "risk to patient"
  - Go/No Go Stage Gate Management – to provide the development team with clear goals as the design space is under development, e.g. linked to acceptable outcomes from chemical & physical process design work

**References**

ICH Q8 – Pharmaceutical Development

ICH Q9 – Quality Risk Management

ISPE Baseline Guides – Updated BPC; Technology Transfer

**Contact information**

Trish.Melton@mimesolutions.com