Aligning Design Of Experiments with FDA Expectations

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Premise

- The focus by FDA on design and process validation underscores the need for well-planned experimentation.
- Such experiments can provide data that will enable device manufacturers to identify the causes of performance variations.
- They can then eliminate or reduce such variations by controlling key design and process parameters, thereby improving product quality.

MDDI Article: bit.ly/2A5VdEB

Validation Regulatory Expectations

- Validations are proof of performance.
- Characterization work done to ensure validations are smooth
- No surprises and/ or failures.
- Any validation failures should be
  - Easy to explain
  - A minor or no impact on the patient

Expectations for Design Control

- Design and Development Planning*
- Design Input*
- Design Output*
- Design Review**
- Design Verification
- Design Validation*
- Design Transfer**
- Design Changes**
- Design History File

* Direct benefit
** Indirect benefit

Design and Development Planning

- Planning is often limited to Validation planning, as other project plans are fluid and may contain proprietary information.
- However, having strong planning and evaluation of Development (Characterization) tests provides a strong submission and a strong audit, if that happens.
- We often hear about “Risk based sample size” but we also need “Risk based Characterization testing.”

Validation Planning

- An important part of a project schedule and an expectation from FDA is related to Validation planning.
- The validation plans should be tied to the development work, and thus referenced in the detailed validation plans.
- Test methods also need to be validated. They can also use DOE as support.

Design Input

- Requirements are real and known
- Clinical and/ or expert support
- Define early
- Some may need to float during development
- Design changes after freeze

Design Output

- DOE analysis provides a strong report for characterization work.
- Assumptions and interpretation are clear.
- Decision making, the ultimate output, has a clear basis.
- Validation reports are often provided to the FDA, thus important to have a strong basis from characterization work.
  - Tied to risk relationships.
  - Tied to design inputs

Design Review

- A well planned experiment will make reviews a quick and confident process.
- Planning should be done with multi-discipline input.
  - Marketing
  - Manufacturing
  - Design
  - Quality
  - Management

Design Verification

- This is testing to confirm conformance to requirements.
- This is the “exam.”
- Perform after development (characterization) tests to ensure we have the knowledge we think we have gained.

Design Validation

- This is confirming that customer needs are being met.
- Some confusion with this phrasing, as Process Validation is not directly meeting the customer needs.
- Validating a floating design is risky.

What about Development Tests?

- These are what I would call the “homework.”
- The focus is on learning and gaining understanding.
- Planning characterization work is also important, though not explicitly required by FDA. However, the benefit during an audit would be important.
- Risk driven – which is another FDA expectation.
- Understanding variation. A strength with DOE. A huge interest due to humans being involved, and being highly variable.

Design Transfer

- Creating a robust design through DOE makes transfer to manufacturing as smooth as reasonable.
  - Also makes thruput time as short as possible. Reduced checks and inspections, which are never 100% accurate anyway.
- Once, a new tool was being questioned during the transfer process. We reviewed our DOE testing and results with operations. This indicated our decision making process, and the tool was accepted quickly and performed well in manufacturing.

Design Changes

- Original design decisions are solid.
- Design changes during development are reduced and if needed, well justified.
- A huge ripple effect from changes, so potential for major delays and/ or mistakes when done late in the development process.

Design of Experiments

- An efficient and effective set of tools used mostly for development tests.
- Factorial or advanced designs can be selected to obtain the information required for the project.
- The set up strategy is as important as the statistics and math.
- Tools support obtaining a Robust Design.

DOE Process

- Define goal (User Needs, Risk Based)
- Define response(s) to measure progress to goal (Design Inputs)
- List all variables and down select to “key” variables using engineering judgment
- Select appropriate design matrix (Planning)
- Select safe/consistent test levels for variables
- Address tradeoffs between responses
- Perform test
- Analyze results (Design Output, Validation)
- Discuss next step (Support for Design Changes, Transfer and Reviews)

Smart Prototypes

- There is a push to reduce prototypes
- Prototypes are valuable but they consume considerable schedule
- Saving schedule by randomly “removing” prototypes is risky
- Need to build prototypes at the “lowest possible level” to reduce cost, and increase learning cycle. DOE helps with each portion of this.

Identify Problems Early

- Using a risk based approach, our testing should account for the key input variables and potential use environments.
- Design of Experiment application after preliminary testing of prototypes will provide comprehensive characterization testing (homework).
- DOE can be used to find solutions to the issues identified.
- Validations can be focused based on the learning from the characterization work.

Conclusion

- Early DOE work can provide the foundation for knowledge based decisions.
- If you want to see reference materials – visit our website.
  - www.PerrysSolutions.com
  - If interested, email us to be on our quarterly newsletter where we share recent trends and learning points
    - Newsletters are all archived on our publications page