DOE Expectations for Tier I and II Medical Industry Suppliers

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Agenda

- **Recent history**
- **Current trends**
- **Approach to address**
- **Impact for your business**

Background

- **Five years ago, encouraged use of Design of Experiments in the product development process**
  - **Obtain a competitive edge with new products**
  - **Suppliers were insulated from FDA**
    - **Only need to "notify of changes"**
- **Today, movement toward application further up the supply chain**
  - **Application in R&D is recognized but still growing**
  - **Not just for companies dealing directly with FDA**

Expanding on Trend

- **Information transparency, clarity and speed is critical for data based decision making**
- **No longer a "big company" issue**
  - **All are expected to respond at a higher level with greater confidence**
- **Many suppliers are unclear what that may mean for them**
  - **Customer is too busy to provide direction**
  - **Supplier does not have internal experts**
  - **FDA does not give specific guidance of what to do**
- **While DOE is not directly required, there is no other tool that can answer the questions now being asked**
  - **Enough are using it, the expectation has been established**

Present Justification Needs

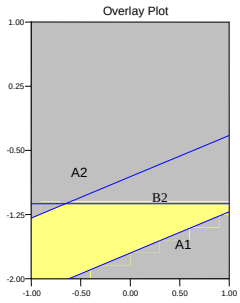
- **General Expectations**
  - **Key requirements/ processes**
  - **Testing and validation plans encompass many aspects of organization**
  - **Detailed processes and procedures**

Present Justification Approach

- **Comparative risk techniques**
  - **Failure Modes Effects Analysis (FMEA)**
  - **Fault Tree Analysis (FTA)**
- **Limited for developing the confidence expected for more mature products.**
  - **Ok to determine relative risk, but does not directly address the problems**

Present Customer Needs Approach

- **Understanding customer needs**
  - **Quality Function Deployment (QFD) analysis**
- **An area where finding the sweet spot is critical.**
  - **Balancing conflicting requirements**



Suggest Tool Blending

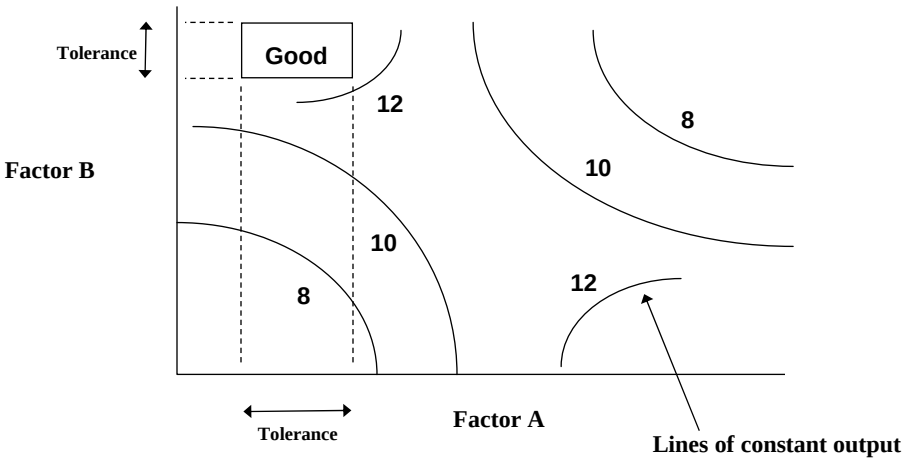
- **Knowledge from FMEA, FTA and QFD obtains relative and qualitative information.**
- **Desire to test for knowledge, establish essential steps for processes**
- **Complementing those results with strategic DOE usage can provide a more quantitative, confident message to the customer and ultimately for the FDA.**

$$Y = z + a[A] + b[B] + c[C] + d[AB] + e[AC] + f[BC] + g[ABC]$$

DOE Options - Design

- **In product development, use DOE to understand high product risk areas.**
  - **Design parameters**
  - **Tolerances**
  - **Robustness**

Tolerance Justification with DOE



DOE Options - MFG

- **In process development, use DOE to define key factors and their settings**
  - **Clear basis for initial conditions**
- **Also identify non-key factors that will not need prior approval if changed.**
  - **This knowledge can be used as a basis for future FDA submission needs; i.e. ability to simply provide an update in annual report**

MFG Implementation Example

- **Per our DOE testing, we found**
  - **Material A to be important**
  - **Variable M to be important**
    - **Nominal of x with a tolerance of +/- 2%**
- **We also found that**
  - **Material D could achieve performance with either vendor 1 or 2**
    - **We are choosing 1, but if volume grows and we need a second source – there is no need to obtain prior approval from FDA to make the change**
  - **Variable Q can be set with a lot of flexibility**
    - **We are choosing a level best for machine performance. Within the window tested, we could change for reasons other than product performance. If we do, this would be part of annual report**

DOE Options – On-going

- **If improvements are discovered down the road, a basis for change can be clearly supported.**
  - **Whether it is the refining of previous DOE work or generalized testing, propose new levels with a solid DOE basis**

Ongoing Implementation Example

- **Through our trend analysis (internal yields, field feedback, etc.), we found:**
  - **Variable E should be set in the range of y instead of z**
  - **Because this product is in high usage, we ensured the change by our vendor with a high confidence DOE**
  - **Our basis is solid thus we expect this to be covered with a 30 day change notification**

Impact

- **This proactive application**
  - **Improves time to market**
    - **Product development**
    - **Submission**
  - **Provides strong, positive company intent**
  - **Increases confidence**
  - **Speeds submissions**
  - **Increases reliability**
  - **Provides objective argument for new or changed designs**

Support to Customer

- **Knowing key factors, required setting levels helps initial submission**
- **Knowing if in-process changes impact submission, assists with updates**
- **Having criteria makes communication and decision making consistent**
- **Deeper understanding in important areas**

Summary

- **Trend is for more and deeper information available to FDA**
- **Higher confidence answers and timely approval will be key for competitive advantage**
- **Those who can provide this, likely via DOE, will be a viable business long term**