

Day 2-Drug Product Breakouts

- ◆ Identify critical aspects of the drug product that support the product being characterized as low “Risk” and the boundaries on those characteristics
 - Gain feedback from breakouts on conceptual aspects of the objective
 - Get specific comments from participants on areas of most value

- ◆ Breakouts will cover:
 - Broad Concepts
 - Drug Product Attributes

Day 2-Drug Product Breakouts

•**Broad Concepts**

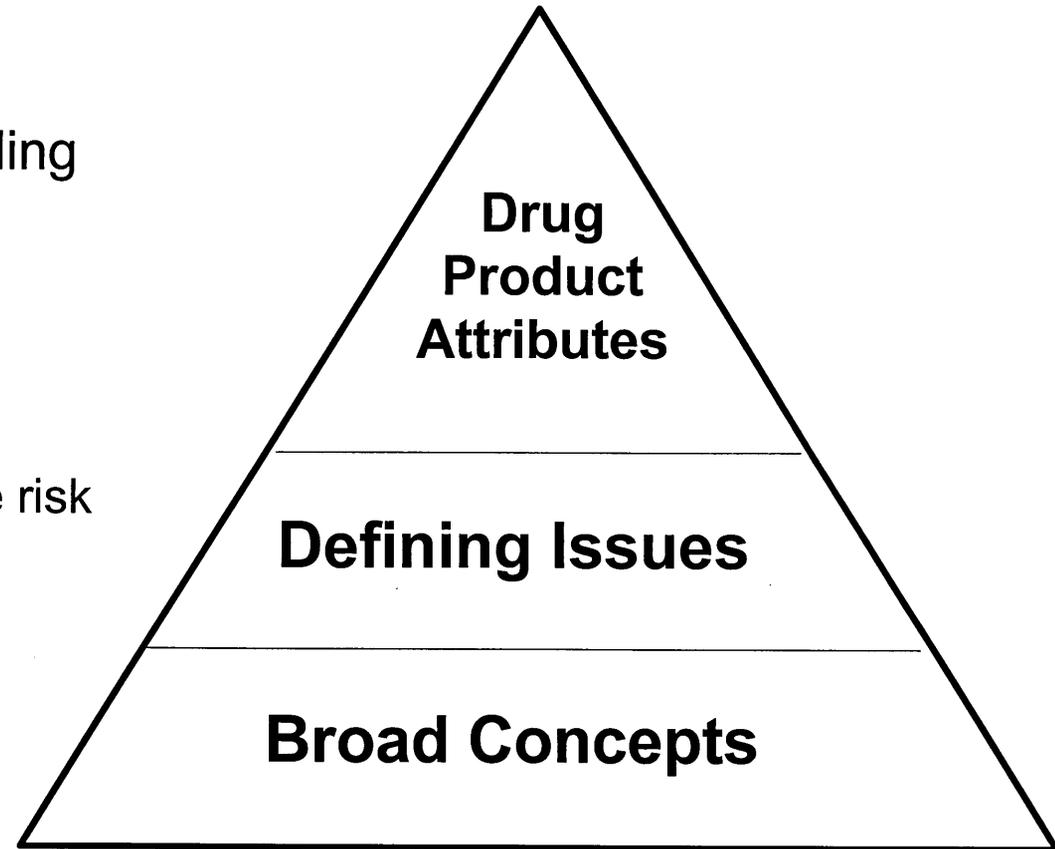
- Is there a spectrum of risk regarding quality?

•**Defining Issues**

- Non-technical aspects that influence risk assessment (not to be discussed)

•**Drug Product Attributes**

- Manufacturing
- Specifications
- Stability



Day 2-Drug Product Breakouts

◆ Broad Concepts

- *All dosage forms may be viewed as low risk*
- *Some dosage forms may take more work to get to understand them, but once knowledge established, little if any distinction of risk*
- *For implementation, may choose to move cautiously including limited dosage forms (e.g., IR solid orals) but this limitation is not due to technical concerns*
- *Strength is not a consideration for definition of risk from a quality perspective*
- *Combination products (two actives) should not be excluded from consideration as high risk*

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◆ Drug Product Attributes

● Manufacturing

- Is demonstration of multiple process capability a determinant of risk?

Multiple suppliers do not suggest a lower risk of product or process, nor does only a single supplier confer a higher perception of risk.

- What type of controls indicate high risk? *Nothing specific.*

- *The process does not inherently contribute to a consideration of risk*

- *The overall consensus is that sufficient understanding of your product, formulation, manufacturing process, and the demonstration of its robustness, is critical for defining a low risk. However, a manufacture's proficiency with a given process across a broad product range may be indicative of their ability to address appropriate quality attributes to confer a low risk. Other manufactures' products' experience is unlikely to be relevant.*

- *That understanding may be demonstrated by a combination of product development, historic experience, and tolerance of a broad range of processing conditions*

Day 2-Drug Product Breakouts

◆ Drug Product Attributes

● Specifications

- Means of describing comparative quality
- Suitability to serve as a benchmark
- Relationship to current compendial monograph and specific parameters in monograph
- Need for updates to contemporary standards
- *Need to update to contemporary specifications in order to adequately assess risk, and also to be able to gauge impact of changes in the future*
- *Compendia typically DO NOT provide those contemporary standards*
- *Burden to contemporize is often great, so must make the benefit commensurate and possibly may need to provide incentive. Additionally, must not penalize manufacturer for observations obtained when updating (e.g. “new” impurities)*

Day 2-Drug Product Breakouts

- ◆ Drug Product Attributes

- Stability

- Evaluation of physical and chemical attributes as it relates to risk

- Reproducible and predictable profile

- Development studies

- Commercial Stability experience

- Predictable behavior is key, NOT an arbitrary threshold of degradation*

- Should also demonstrate a knowledge of the pathway and mechanism of degradation. This may be done with old data sets and need not be ICH. Should define some level of shelf-life storage data (Time and # of batches) to confirm predictability.*

- Products that qualify for Controlled Room Temperature storage

- All storage conditions are acceptable as low risk so long as the behavior at that condition is understood and predictable*

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- ◆ Drug Product Attributes

- Packaging

- e.g. New packaging material for oral product vs. LVP

- *Little if any inherent characteristics of a packaging define risk*

- *Might be a consideration in the context of the product and its stability behavior*

- *Probably need to exclude functional packaging and delivery systems from low risk*

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◆ Miscellaneous Comments

- The concept of establishing a risk profile is more than just a list of drugs and quality attributes. Risk assessment requires an evaluation of the integration of the risk profile of the drug product and the manufacturer's profile.
- A process probably needs to be established for submission and review of an "application" for low risk
- Quality attributes are difficult to evaluate without a knowledge of the process to establish low risk
- Industry should establish a Task Force to make recommendations to FDA, as well as share historic product experiences with FDA