Application of Parametric Tolerance Interval (PTI) Tests

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4:00-4:45 PM and 4:45-5:30 PM

Application of Parametric Tolerance Interval (PTI) Tests

- **Product quality assessment for the 21st century**
  - **<u>Current State:</u> Many tests motivate minimal testing strategies (example: zero-tolerance counting tests)**
  - **<u>Desired State:</u> No penalty for increased testing to better determine product quality (example: PTI test)**

Concept of Coverage in Defining / Determining Product Quality

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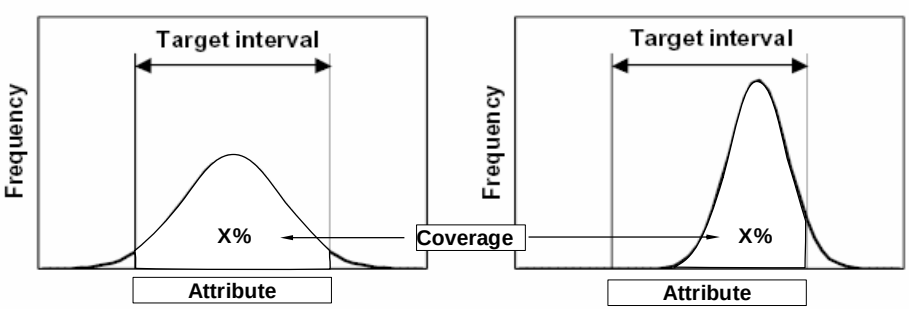
- **Minimum quality standard defined in terms of the proportion of an attribute within a certain range (i.e., "coverage" requirement)**
- **Batches with equal coverage have equal quality**
- **Batch quality determination based on confidence that a certain proportion of an attribute is within a specified range (i.e., minimum coverage requirement met)**
- **Can be estimated using either parametric or non-parametric approach**



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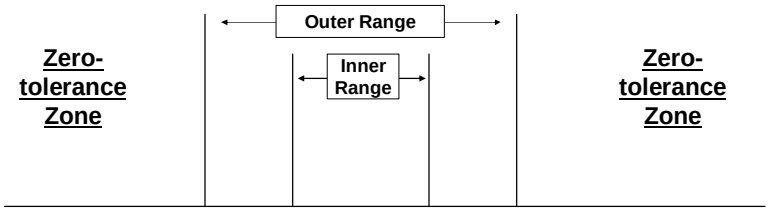
Parametric vs. Non-parametric Approaches

- **Parametric**
  - **uses sample data to estimate parameters of a distribution (e.g., mean, std. dev.)**
  - **must assume underlying distribution**
  - **very effective use of data**
- **Non-parametric**
  - **does not require assumption of underlying distribution**
  - **less effective use of data (less powerful)**

Example: Zero-tolerance Counting Test

- **A non-parametric approach**
- **Coverage (proportion of an attribute within certain ranges) is estimated by counting the number of test results outside inner/outer ranges**
- **Batch quality determination based on how many test results outside inner range, with <u>none</u> allowed outside outer range**



<u>Outcome:</u> ***Increased testing results in increased failures <u>regardless</u> of batch quality (i.e., increased testing = more wrong decisions)***

<u>Consequence:</u> ***Minimal testing strategies pursued to minimize unnecessary failure of acceptable product***

Example: Parametric Tolerance Interval (PTI) Test

- **A parametric approach**
- **Coverage (proportion of an attribute within certain ranges) is estimated using formulas based on sample mean and standard deviation which control:**
  - **within batch variability**
  - **batch mean**
  - **combination of w/in batch variability and batch mean**
- **Batch quality determination based on whether all acceptance limits met**
- **No zero-tolerance limit for individual test results**

<u>Outcome:</u> ***Increased testing results in better determination of batch quality (i.e., increased testing = more correct decisions)***

<u>Consequence:</u> ***Promotes increased testing to help ensure acceptable product to consumer***

Questions to Stimulate Discussion

1. How do we approach testing in QbD in such a way that companies are not penalized for increased testing? PTIT? Other alternatives?
2. When do we need to control only the mean? When do we need to control variability as well as the mean?
3. How do companies control variability now? How are sample sizes selected for this?
4. For what tests is it appropriate to use PTIT? Are there physical, chemical, analytical-method areas when PTIT is not appropriate?
5. When in the product life cycle is it appropriate to start using PTIT? (e.g., phase 1, 2, 3, manufacturing, post-marketing)
6. When is it appropriate to use a zero-tolerance type trigger that would override PTI testing?
7. Questions from the floor…