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A Word about Sample Sizes for Validation

23 September 2008

Default sample sizes for validation are not recommended or advised. Any and all sample sizes require justification and rationale.

The most current thinking by industry and FDA is that N=3 sample sizes are not acceptable default sample sizes. If such defaults are used, they should be accompanied by a prospective written justification.

Sample sizes for validation need to be a statistically valid determination based on the following:

- (1) Engineering run or commissioning data
- (2) Previous experience with similar systems, processes, etc.
- (3) Estimates of variability – this almost always being the standard deviation – based on (1), (2), and other available data
- (4) Documented risk assessments
- (5) Expected and required acceptance criteria

When doing validation, it is also important to define what is actually being validated with respect to higher level systems and related sub-systems. Depending on how the equipment, process, etc. is designed to operate, there may be inherent robustness and margins-of-safety associated with the design. This robustness is usually fleshed out in the risk assessment process and effectively lowers the criticality of any one parameter or sub-system. Lowering the criticality effectively lowers the burden of the sampling plan and is a good way to keep sample sizes small. This whole concept is essentially "Quality by Design" which is the systematic effort to design robustness and quality into the overall process.

Attribute or pass-fail data are particularly troublesome with respect to statistics and associated validation. Whenever possible, assays should be quantitative in nature to avoid sample plans that are ten times greater (or more) than their quantitative-based counterparts. The decision to use quantifiable assays should be made early in the product development process as changes to approved products are difficult and the return-on-investment may not be favorable.

Regards,

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For an electronic copy of today's presentation titled "Leveraging Statistical Methods and Analysis for Validation," please send a request email to stephen.perry@kymanox.com.