Acceptance criteria for Gauge R&R studies generated from statistical tolerance intervals as per ISO 16269-6

Background

Justification for sampling plans and statistical analysis of results is a requirement for verification and validation in medical devices. Current standards [1] and regulations [2] however, give limited advice or guidance regarding this topic. Several approaches where therefore adopted by the medical device industry.

Purpose

This statement intends to evaluate, if acceptance criteria for Gauge R&R studies [3] could be generated from statistical tolerance intervals calculated as per ISO 16269-6 [4]. It is not intending to question or challenge the approaches as such.

Discussion

Statistical tolerance intervals

The use of statistical tolerance intervals as described in ISO 16269-6 can be found in different regulatory sources like ISO 11608-1 [5] and FDA Guidance for stents [6].

- The basic idea behind the statistical tolerance intervals is to use the average and standard deviation observed within a sample group in order to calculate a tolerance interval.
- The ISO 16269-6 approach is recommended for validation as it makes use of the LTPD (consumer's risk), instead of AQL (producer's risk).
- Usually this is accomplished by a calculation of average +/- k*standard deviation, where the k-value is derived from tables within the standard.
- The k-value considers sample size used as well as the confidence and the probability levels chosen.
- Selection of adequate levels is the responsibility of the manufacturer and must be justified. Some regulatory requirements for applicable confidence and the probability levels are given within the relevant documents [5, 6].

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- The calculated statistical tolerance interval shall then be compared to the given specification of the product under consideration. It is essential to understand, that the individual results must also meet specification.
- Statistical tolerance intervals are therefore a well-accepted way of fulfilling the requirements to justify sampling plans and to analyze results of process validation activities.

Gauge R&R studies

A well-known approach chosen in the field of test method validation are Gauge R&R studies [7]. These studies aim to divide the observed variation into the variation caused by the product and the variation caused by the measurement.

- Gauge R&R is usually calculated using ANOVA methods.
- The acceptance criteria are expressed as “Total Gauge R&R Standard deviation % Tolerance” and is calculated by

  100 * 6 * standard deviation R&R / (USL-LSL), or
  100 * 6 * standard deviation R&R / (2*(average - LSL))

For Gauge R&R, regulatory acceptance criteria are seldom published. Most often it can be observed, that industries just „borrow“ values commonly accepted in automotive industries without further justification. For the discussion in this paper I applied the generally accepted criterion of Total gauge R&R < 30%.

Comparison and evaluation

- It can be seen, that the formula used to calculate Total Gauge R&R is similar to the formula used to calculate Cp and cpk. Remember that
  - cp is calculated by cp= (USL-LSL) / (6* standard deviation)
  - cpk is calculated by cpk=(average – LSL) / (3*standard deviation)
- Both formulas (Total Gauge R&R and cp) can be merged (via USL-LSL).
  - USL-LSL = cp*6*stdev
  - USL-LSL = 100*6*stdev R&R / Total Gauge R&R
  - Cp*6*stdev = 100*6*stdev R&R / Total Gauge R&R
  - Cp*stdev = 100*stdev R&R / Total Gauge R&R
  - Total Gauge R&R = 100*stdev R&R / (cp*stdev)
  - Total gauge R&R = 100/cp *stdevR&R/stdev

- The equation would make sense, given a cpk=1 and given the Total Gauge R&R = 30%, which is used in automotive very often [4]. The portion of the standard variation caused by R&R would be 30% of the total standard deviation.

  In an early paper I explained acceptance criteria for process capability indexes generated from statistical tolerance intervals as per ISO 16269-6 [8]. At that time I concluded:

  > Consequently, one could use the relevant k-value from ISO 16269-6 as a measure for an acceptable Cpk value:
  >
  > - Cpk >= k/3 or k <= 3*Cpk
  >   or in words, Cpk must be equal or larger than the applicable k-value divided by 3,
  >   Cpk >= k(n, C,P) / 3, where n=sample size, C=Confidence level, P = Probability level, selected from applicable standard ISO 16269-6

- As a consequence of the above written, the acceptance criteria of Total Gauge R&R <30% could be aligned to the statistical tolerance intervals as described in ISO 16269-6. Select the relevant k-value from ISO 16269-6 for the sample size selected in the Gauge R&R. The Total Gauge R&R should then be 30/k/3 or easier 90/k.

Plausibility Check

Gauge R&R is often recommended to be done with 3 operators testing 10 products each (i.e. n=10, DF=9).

- When looking into ISO 16269-6, DF=n=9 for a Confidence level 95,0 % and proportion 90,0 % (Table D.4) results in k=2.9861). Calculating 90/k would require a Total Gauge R&R = 30.1% and a cpk = 1.0.
- When looking into ISO 16269-6, DF=n=9 for a Confidence level 95,0 % and proportion 95,0 % (Table D.5) results in k=3.5459). Calculating 90/k would require a Total Gauge R&R = 25.4% and a cpk = 1.18.
- When looking into ISO 16269-6, DF=n=9 for a Confidence level 95,0 % and proportion 99,0 % (Table D.6) results in k=4,6329). Calculating 90/k would require a Total Gauge R&R = 19,4% and a cpk = 1.54.

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Rule-of-thumb

From the above, the following rules of thumb could be concluded:

- Gauge R&R calculated from n=10 samples would satisfy a Confidence/Probability level of 95/99% if the acceptance criteria would be maximum 20%.
- Gauge R&R calculated from n=10 samples would satisfy a Confidence/Probability level of 95/95% if the acceptance criteria would be maximum 26%.
- Gauge R&R calculated from n=10 samples would satisfy a Confidence/Probability level of 95/90% if the acceptance criteria would be maximum 30%.

[1] ISO 13485:2016 Medical devices — Quality management systems — Requirements for regulatory purposes

[2] 21CFR820, Quality system regulation, FDA

[3] AIAG MSA 4th edition, 2010

[4] ISO 16269-6:2014 Statistical interpretation of data Part 6: Determination of statistical tolerance intervals

[5] ISO 11608-1:2014 Needle-based injection systems for medical use – Requirements and test methods –Part 1: Needle-based injection systems

[6] Guidance for Industry and FDA Staff: Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems, April 2010

[7] Dr.Wayne Taylor, Statistical procedures for the medical device industry, 2017

[8] Acceptance criteria for process capability indexes generated from statistical tolerance intervals as per ISO 16269-6, Michael Schäfer, www.quality-on-site.com

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