

Stability analysis of censored and over-rounded data

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Abstract

According to ICH Q1E guideline, stability analysis shall be performed by fitting (linear) regression models to stability data and shelf-life shall be determined as the intersection of the 95% confidence interval of the regression line with the specification limit(s). Quite frequently, measurements – in particular at earlier time points – are reported as below the limit of quantification (LOQ). In addition, sometimes one might be facing the situation that the reported data is “over-rounded” such that the data at hand is rather discrete even though the underlying measured values are from a continuous scale. In such cases fitting regression models is challenging. Performing the analysis from rounded values introduces additional imprecision and - depending on how data below the LOQ is treated – results might be biased, in addition. All one can actually conclude from the reported data is that the measured values lie within certain intervals. In this presentation, approaches how to fit regression models and compute shelf-life from censored and/or interval data will be presented. Simulation studies will be conducted to assess the appropriateness of these approaches and to compare them to analyzing over-rounded data and different strategies to replace values below the LOQ by one fixed value.