Using measurement uncertainty to assess the fitness for purpose of analytical procedures used in pharmaceutical industries

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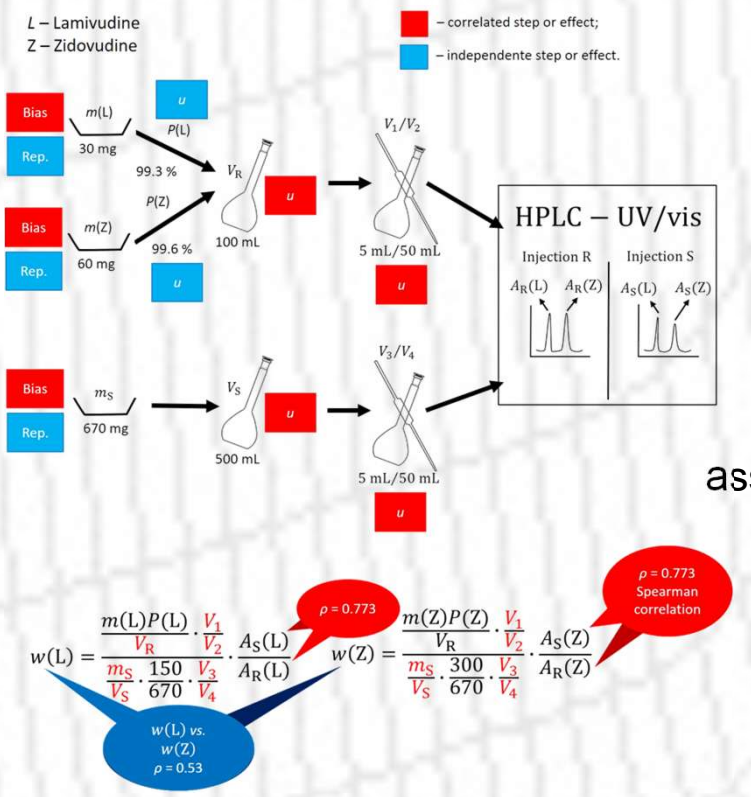
Problem: The assessment of the conformity of some medicines with specification limits involves the determination of various parameters using the same chromatographic run from the analysis of the same sample solution. Since the measured quantity values of the various components become correlated due to the sharing of analytical steps and effects, this correlation should be considered in the management of wrong compliance decisions.

Objective: Development and validation of tools to estimated the metrological correlation of data and to quantify the impact of this correlation in conformity decisions.

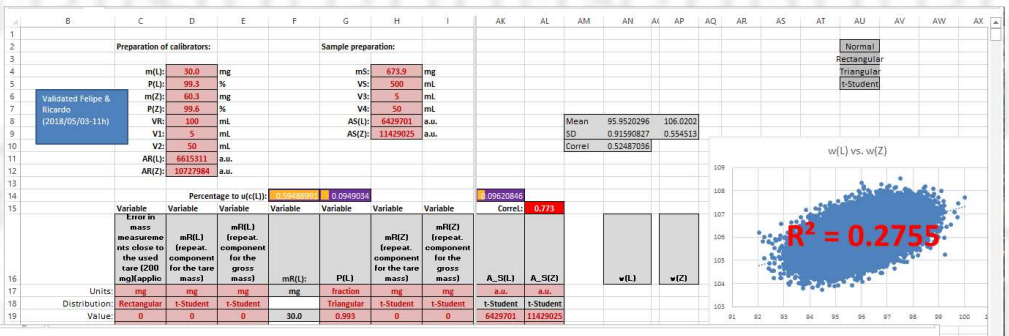
Methodology: 1) The use of the Monte Carlo Method (MCM) to estimate the correlation of measured quantity values produced by measurements procedures that share analytical steps and effects; **2)** The use of MCM to estimate the frequentist risk of false conformity decisions.

Measurement procedure:

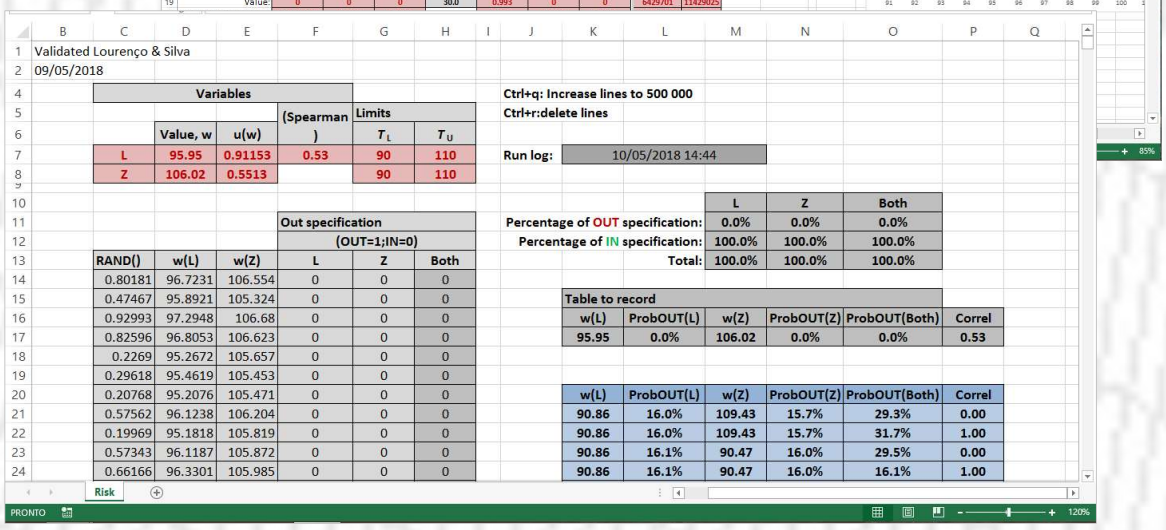


Monte Carlo Method:

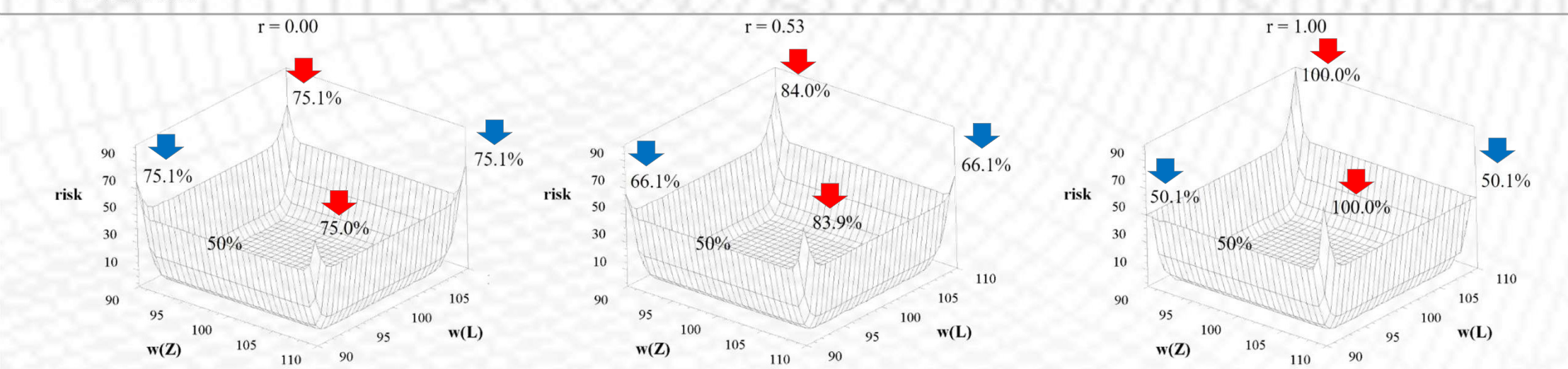
Metrological correlation:



Risk assessment:



Results:



risk: 'total specific consumer's risk'

Conclusions:

The observed METROLOGICAL correlation between two components of the studied medicines affects, significantly, the risk of false conformity decisions. The correlation decreases the 'total specific consumer's risk' if the mass fractions of both components are close to the upper or lower tolerance limits (↓). When the value of one of the components is positioned close to the upper tolerance limit while the other is positioned next to the lower limit, the metrological correlation of data increases the risk (↓).

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