A Bayesian model for optimizing the filling of a product to reduce risk of being OOS in presence of uncertainty.

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When it is envisaged to proceed to the filling of final products such as syringes, the bulk material must usually be diluted to achieve a desired concentration. The dilution factor to be applied is determined based on the estimate of concentration in the bulk or drug substance. In addition, the release of the final product requires that the estimated average content or reportable result being greater or equal to a lower specification limit LSL.

The first challenge arises from the fact that the estimates of concentration values before and after the dilution is based on bioassays providing estimates with uncertainty while the aim of the filling is to be as close as possible above the specification limit. Given the estimate of the content of the bulk material is obtained with uncertainty, there is a risk that the dilution factor derived from the point estimate lead to under dose the final product. The closer from the target value, the higher the risk to reject the production batch.

The second challenge come from the fact that most products are blend of several substances and that each of them should be above the release limits after dilution. The joint modeling of the estimates is then at the center of the strategy.

The talk will present a Bayesian model that will integrate the prior information about the uncertainties of the assays to derive a safe dilution factors based on the predictive distribution to ensure limited risk of being below specifications for each substance while maximizing the yield of the production.