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Determination of "Proven Acceptable Independent Range" parameters in a Quality-By-Design approach

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1 Introduction

In pharmaceutical studies, the Quality by Design (QbD) approach [1,2,3] is increasingly being implemented to improve product development. Product quality is tested at each step of the manufacturing process, allowing a better process understanding and a better risk management, thus avoiding manufacturing defects.

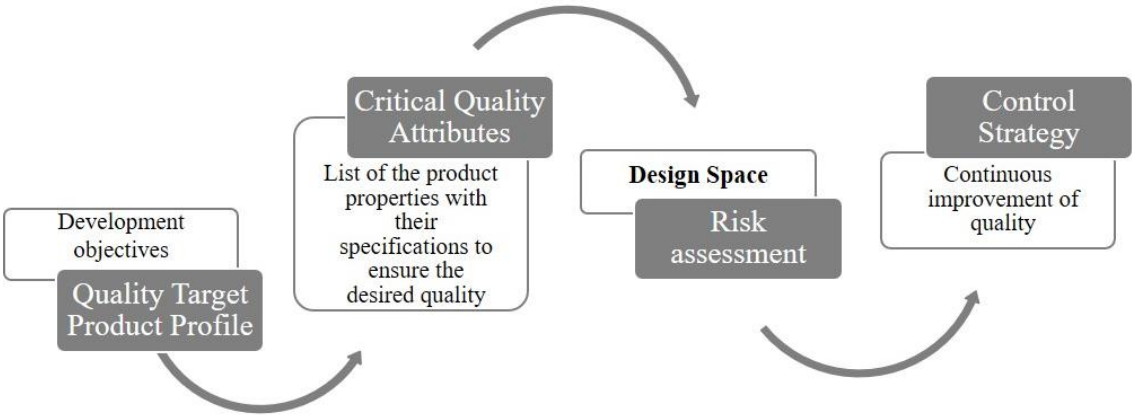

Figure 1: Elements of QbD approach

2 Theory

A key element of QbD is the construction of a Design Space (DS)[4], i.e., a region in which the probability that the specifications on the output parameters will be met is imposed. Among the various possible construction methods, Designs of Experiments (DoE), and more precisely Response Surface Methodology, represent a perfectly adapted tool.

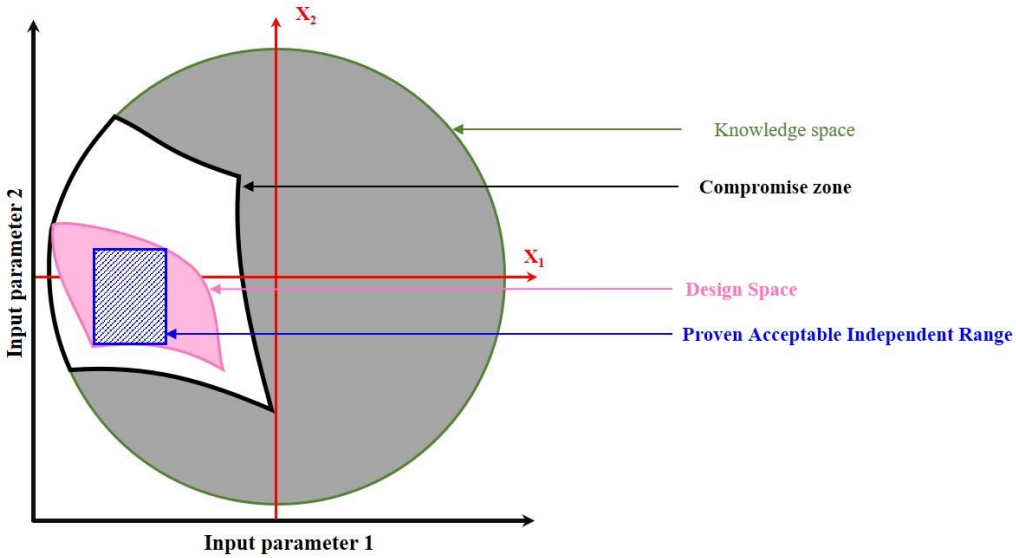

Figure 2: Illustration of QbD concepts in experimental domain - 2D representation

3 Results and discussion

The DS obtained may have any geometrical shape; consequently, the acceptable variation range of an input may depend on the value of other inputs. However, the experimenters would like to directly know the variation range of each input so that their variation domains are independent. In this context, we developed a method to determine the "Proven Acceptable Independent Range" (PAIR). It consists of looking for all the hyper polyhedra included in the multidimensional DS and selecting a hyper polyhedron according to various strategies.

We will illustrate the performance of our method on different DoE cases.

4 References

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