Risk Assessment & Ranking of the SUPAC-IR & MR Guidance

1. Background

The SUPAC Guidance documents for IR and MR dosage forms were finalized in 1995-99. They continue to be used by the pharmaceutical industry and FDA to help assess the impact of changes to products during scale-up and post-NDA/ANDA approval. The use of risk assessment tools in pharmaceutical development and manufacturing has led to a more objective identification of risks, and the current guidance documents would benefit from a systematic risk assessment and ranking which ensures that it is aligned with current QbD expectations. In particular, the principles of QbD call for the use of improved product development approaches including enhanced statistical tools to evaluated the limits of product design space and application of Process Analytical Technologies (PAT) in the on-line and in-line control of identified critical product parameters and quality attributes.

2. Project Objective

The purpose of this project is to align the SUPAC-IR & MR Guidance documents with ICH and QbD concepts by quantifying and ranking risks. While pharmaceutical companies recognize the inherent value in this approach, they nevertheless also see the added time and cost that are imposed by employing QbD in the development of products. The additional costs are a natural result of the fact that QbD principles must be employed from the earliest stages of development in order to be effective. Since many pharmaceutical products will still fail to meet the ultimate safety and efficacy requirements needed for successful registration and approval, there is a continued reluctance to employ the more expensive QbD requirements without some assurance of payback for these costs with downstream “regulatory relief”. Such regulatory relief may be expected in the form of faster and easier post-approval changes to products. Industry is hopeful that a product dossier that includes QbD principles may allow for a simplification of current SUPAC filing requirements. For example, if an updated dossier contains an approved IVIVC, it should remove the regulatory burden of a “pre-approval supplement” and allow filing as a “changes being effected” submission for all changes to formulation and process made within the defined design space of the product. This approach is known as a “biowaiver” provision. Similar provisions would allow what were previously defined as “CBE” submissions to be down-regulated to Annually Reportable (AR) submissions.

This work project will evaluate the changes possible in the following guidance documents if submissions are made using QRM principles that reflect product development practices which include current ICH, PAT, and QbD principles.

- SUPAC-IR: Questions and Answers about SUPAC-IR
- SUPAC-IR/MR: Immediate Release and Modified Release Solid Oral Dosage Forms Manufacturing Equipment Addendum

The resulting Whitepaper will articulate the principles and suggest how, in practice, these can be used to obtain the desired regulatory relief that will be beneficial to both the FDA and the regulated pharmaceutical manufactures (branded and generic). As such the Whitepaper will be a focal point to stimulate discussion that could lead to the desired regulatory relief principles.

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