Title:	Non-Sterile Active Pharmaceutical Ingredient (API) Manufacturing Area Environmental Control				
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Non-Sterile Active Pharmaceutical Ingredient (API) Manufacturing Area Environmental Control

Introduction

This guidance is to address environmental control for existing, new, and modified non-sterile API processing areas used for the manufacture of commercial materials. This includes non-sterile API manufacturing areas where the API will subsequently be used to produce sterile Drug Product.

Sterile and aseptic API manufacturing areas are outside the scope of this guidance.

This guidance applies to those areas where the API molecule is formed and subsequent manufacturing steps. In accordance with ICH Q7a, it is expected that there be increasing environmental control from the early steps of the API manufacturing process (e.g., from the introduction of the API starting material for small molecule chemical synthesis), through to the final API steps.

Recommendations and Discussion

Environmental Control Risk Assessment

For each API product, a risk-based assessment of environmental control requirements should be performed, documented, and approved by the Site Quality and Production Teams.

The risk assessment may be conducted on a product or facility-centric basis. This risk assessment should include consideration of at least the following:

- Type of API manufactured (e.g., small molecule API via chemical synthesis or classical fermentation);
- For APIs produced by chemical synthesis or classical fermentation, the risk assessment should be conducted to include the step where the API molecule is formed and on each of the subsequent step(s) of manufacture, including an evaluation on whether or not there is further purification of the API;
- For APIs exposed to the environment, the subsequent Drug Product dosage form (e.g., oral, parenteral, topical, inhalant) should be considered during the risk assessment. For APIs subsequently used in multiple dosage forms, it is recommended that the most conservative dosage form with respect to patient safety (e.g., parenteral) is considered in the risk assessment;
- Microbial risk associated with the API process (e.g., high water activity, water-wet cake for Final API, inhibitory nature of the process for microbial growth), that may have an effect on the bioburden of the drug product;

