- Risk of microbiological contamination of Intermediates and APIs, that have an established microbiological limit (e.g. from gowning, sanitization practices or open drains);
- The extent of exposure of the final API to the surrounding environment (if any);
- The extent of exposure of API product contact Packaging Materials to the environment, if any; and
- Dedicated versus multipurpose production areas/facilities and the risk of potential Cross Contamination.

The risk assessment should be documented and include rationales and conclusions. The documentation may be in one of several forms (e.g., validation plan, protocol, separate evaluation/rationale document, system level impact assessment). The assessment results and conclusions should be approved by Site Production Team and Quality Team.

Environmental Control Strategy
Final API steps include where the API molecule is formed and any subsequent manufacturing steps where there is no further purification of the API. The environmental control strategy for these areas should include consideration of the following:

- Design of the applicable API areas to meet the criteria for the drug product manufacturing area where the API is first exposed in drug product manufacturing [e.g., design of these API areas to meet the comparable ISO 14644 Non-Viable Particulate levels];
- Temperature and humidity requirements, where specified for the product;
- Potential for microbial contamination from the environment, if critical to product quality;
- Pressure Differentials between adjacent areas to avoid contamination of the API product;
- Cleaning, and where applicable Sanitization, of product contact Facilities;
- Equipment surfaces;
- Personnel practices (e.g., gowning/de-gowning and training) and
- Other product specific requirements as applicable (e.g. sensitivity to light).

If API, API-product-contact packaging materials, or clean product-contact equipment are exposed to an environment, protective measures should be implemented or the environment should be controlled to eliminate or reduce the exposure to the environment. The protective measures can include consideration of the following:

- Protection of product contact packaging materials (e.g., drum liners, super-sacks) from the environment (e.g., keeping them covered);
- Protection of product contact equipment from the environment (e.g., by keeping equipment closed or covered);
- Elimination or reduction of the exposure to the environment (e.g., with use of

