The PhRMA report on microbiological monitoring in nonsterile pharmaceutical manufacturing areas (1997) recommended that depending on the product type, cleaning validation should include microbial sampling to ensure microbiological quality.

The ICH Q7A Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients states "Equipment cleaning/sanitization studies should address microbiological and endotoxin contamination for those processes where there is a need to reduce total microbiological count or endotoxins in the API, or other processes where such contamination could be of concern (e.g., non-sterile APIs used to manufacture sterile products).

The Canadian Health Products and Food Branch Inspectorate on Cleaning Validation Guidelines further states "There should be some documented evidence that routine cleaning and storage of equipment does not allow microbial proliferation. These studies are designed to demonstrate and document that cleaning procedures are effective and do not contribute to conditions favorable for the proliferation of microorganisms."

Risk assessment has become an acceptable approach in cleaning validation. A documented and approved risk assessment is recommended for microbial testing of non-sterile equipment and for affirming the proposed acceptability limits. One of the considerations of a risk assessment is whether the final rinse of the clean equipment is performed using an organic solvent or water.

Recommended Methodology

If it is determined that microbiological testing is needed, where possible, it is recommended that bioburden samples be collected via rinse sampling. A known quantity of Purified Water or Water for Injection (dependent on the final rinsing type prescribed by the cleaning procedure) sufficient to completely rinse the product contact surfaces of the equipment is used. A sample of the effluent rinse is collected in a sterile container and microbiologically evaluated.

Sampling should be conducted according to a sampling plan which does not either contribute to the potential contamination of the samples or impacts the integrity of subsequent samples. If surface sampling is needed, sterile swabs saturated with a sterile diluent such as Sterile Water for Injection or Sterile Saline Solution are used. Alternatively, RODAC® plates may be employed for sample sites in which the entire surface of the RODAC® plate is able to be in contact with the equipment surface. If RODAC® plates are used; the sampled surface should be cleaned by a qualified cleaning procedure prior to use of the equipment for production (e.g. wiped with a sterile saturated 70% isopropyl alcohol wipe).

The following sampling guidelines and associated limits are recommended. They should be applied at the completion of the cleaning cycle.

A. For manufacturing equipment for sterile drug products and the final stage of sterile drug substances where applicable (except where cleaning is followed by a validated overkill sterilization cycle):

