Regulatory Basis:
FDA Quality Systems Regulations

General Discussion
This document describes considerations and risks for determining if the establishment of clean equipment hold times (CEHT) for equipment producing drug product and Active Pharmaceutical Ingredients (API) are required. If it is determined that CEHT must be established and that sampling to determine the microbiological levels are required, followed by the determination of the microbiological limits to apply.

This document does not apply to clean equipment after sterilization.

The decision to determine if CEHT must be specified and/or validated is based on a risk assessment that includes the nature and use of the product and the conditions under which the clean equipment is held. Whether to specify a hold time, the amount of data that may be needed, and whether to conduct a clean equipment study is dependent on the risk assessment.

If a hold time is specified, the amount of sampling and the number of replicate runs for a potential validation study are described. Grouping of equipment to establish CEHT is also explained.

Background and Risks
The clean equipment hold time is defined as the time between the last step of the cleaning procedure (e.g. drying or sanitization) to the start of next equipment use for manufacturing. This includes, a pre-rinsing step, if used.

A recent international guide has stated that risk approaches are acceptable in differentiating efforts and decisions for cleaning equipment.

There are two main risks associated with CEHT:

1) The risk of contamination of clean equipment with dust, etc due to exposure to the environment. For this risk, it is required that equipment either be held clean in a controlled clean environment or protected from the environment. This type of potential contamination may or may not be visible during visual inspection;

2) The potential for microbiological proliferation. This is only a risk with equipment stored under conditions favourable to microbial growth (e.g. water wet or non-protected under non-controlled storage conditions such as high humidity). Therefore “environmental exposure” may not always result in microbiological risk (e.g. if equipment is not water wet and if the clean equipment is held in a controlled clean environment).

Because of the above two risks, It requires that equipment be protected from the environment and not stored water wet for the API and Drug Product .

Since equipment is cleaned to acceptable active ingredient residues as part of the cleaning process, degradant formation would be expected to be none or negligible, and of low risk.

Factors to Consider in Evaluating the Risks
The following factors should be considered to determine the level of risk for clean equipment hold times:

