Sterilization of Pharmaceutical Formulations with Polymers for Aseptic Filling
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**Purpose**
Determining the sterilization method for pharmaceutical solutions/suspensions containing polymers is one of the first critical decision points to be considered. Polymers commonly used are HEC, CMC, Xanthan gum, guar gum, gelatin, agar, and HPMC. Often in product formulations, sterile filtration is not an option and terminal sterilization of the final formulation may not be possible due to the thermal lability of the API or excipients. Steam/thermal sterilization of polymeric solutions is generally the method of choice; however, depending on the methodology, steam sterilization can have a deleterious effect on the rheological properties of the polymer.

**Methods**
Consideration should be given to the following sterilization methods for polymer sterilization/formulations:

a) Radiation sterilization of dry polymer followed by aseptic formulation in an aseptic isolator with sterile transfer to a sterile final formulation vessel

b) Bulk tank (steam) sterilization in a pressure vessel allowing the polymeric solution to boil followed by sterile addition of heat labile components

c) Bulk tank sterilization (steam) in a pressure vessel with steam overpressure to prevent the polymeric solution from boiling followed by sterile addition of heat labile components

d) Ultra High Temperature (UHT) sterilization with indirect heating or direct steam injection heating with sterile transfer to the final formulation vessel.

**Results**
The rheological specifications of the polymeric solution in the final formulation must consistently meet the final product specifications. The method of sterilization can then be selected based on the risks imposed to final product formulation which are as follows:

1. Viscosity changes or gradients within the formulation
2. Gel strength loss due to thermal degradation
3. Polymer agglomeration/“fish eyes” causing fill nozzles to plug or clarifying filters to block.
4. Polymer “fouling/burn-on” or concentration of polymer on the heat transfer surface of the process sterilization vessel causing viscosity reduction/gradients and cleaning issues
5. Extraneous substances or “unknowns” from polymer breakdown due to excessive thermal exposure.

**Conclusion**
The sterilization method is determined by selecting the least complex yet most efficacious process to meet the desired final polymer characteristics. For heat stable and for low concentrations of polymeric solutions, a steam sterilization cycle in a processing vessel with boiling to provide the overpressure may be acceptable. For solutions where the viscosity/gel strength is critical or where accumulation of hydrated polymer on the heat exchange surfaces of the processing vessel is deleterious to the final product, then a steam overpressure cycle is required. If the polymer is heat labile and sensitive to sterilization temperatures which can cause changes to the polymer and subsequently undesirable rheological changes, a UHT system should be considered.