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Products & CTDMO Services

Application Note

When do you need to consider revalidating the performance of your sterilizing-grade filter?

Introduction

Any product or process change that could potentially affect the GMP compliance of a validated process or system should be evaluated and a risk assessment should be performed to evaluate the impact of the change. Here are some key points to consider for changes related to the sterilizing-grade filter.

Which change might require revalidation?

Filter validation assesses the filter performance for a given product and process. Therefore, a change in any of these three variables must be examined.

- **Product change**
  - Changes to product formulation e.g. Active Pharmaceutical Ingredients (API), excipients, list of ingredients, concentration or pH
  - Changes to product posology affecting the maximum drug dosage per day, increasing the frequency and duration of treatment, or changing the target population
- **Filter change**
  - Changes to device type, e.g. from a cartridge to a capsule
  - Changes to filter membrane type from one material of construction to another
  - Changes to filter pore size
  - Changes to filter size and thus to filtration surface area
- **Process change**
  - Increase in key process parameters such as flux (flow rate/surface area), pressure, filter/product contact time, or volume/surface area
  - Changes to filtration temperature
  - Changes to sterilization method or increase of the sterilization conditions such as time, temperature or number of cycles
  - Decrease of the filtered volume including flush amount, minimum tank volume or batch size
  - Implementation of PUPSIT (Pre-Use Post Sterilization Integrity Test) in the process line, triggers a risk assessment to determine if revalidation is required

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The following chart provides indications on the tests which might have to be re-validated depending on the changes made.

Changes to Consider		Bacterial Retention	Product Bubble Point	Product Diffusion	Compatibility	Extractables/ Leachables & Patient Safety
Product	**Change in product formulation** (concentration, pH, etc.)	✔	✔	✔	✔	✔
	Change in posology (dosage, frequency)					✔
Filter	**Change in filter membrane** (type / materials of construction)	✔	✔	✔	✔	✔
	Same membrane - Change in device type (capsule / cartridge)			✔*	✔	✔
	Same membrane - Change in pore size	✔	✔	✔	✔*	✔*
	Same membrane - Change in filtration surface area	✔ If filtered volume/ surface area is increased		✔		✔*
Process	**Increase in flux** i.e., increased flow rate per surface area	✔				
	Increase in total filter/ product contact time	✔			✔ If it exceeds contact time achieved during testing	✔ If it exceeds the time provided in original report
	Increase in control pressure	✔				
	Increase in batch volume without a scaled increase in filter surface area	✔				
	PUPSIT implementation	✔ Based on risk assessment				
	Change in sterilization method (steam/irradiation) **or** conditions (increase in time, temperature, or number of cycles)	✔ If the new conditions exceed/method differs from those in the original report			✔ If the new conditions exceed/method differs from those in the original report	✔ If the new conditions exceed/method differs from those in the original report
	Change in filtration temperature	✔	✔	✔	✔ If temperature is increased	✔ If temperature is increased

*May need documentation update.

Methodology

Each manufacturer should have a change control program which triggers a review of validation documentation.

- Risk assement should be performed on all aspects of the process
- Identify the critical systems and processes that affect safety of the drug
- Identify changes in those systems and process that would trigger revalidation

Critical equipment should be on a routine revalidation schedule or, at a minimum, a routine revalidation review. This review or revalidation will be highly dependent on the equipment. For example, autoclaves are typically revalidated annually while sterilizing-grade filters may be validated once. However, changes to a filtration operation could result in new operating conditions outside the limits defined in the filter validation. Consequently, it is important to periodically review validation conditions of sterilizing-grade filters to confirm the current process is within the operating window defined in the validation.

The following are suggestions on how to evaluate your current filter validation status:

- Identify all currently manufactured products.
- Have they been validated? If so:
  - Review older validations against the current process conditions.
  - Have there been process changes on the sterilizing-grade filter?
  - Has the product formulation changed since the validation?
  - Is there a change in posology? Does a new dosage exist?
- Have all filtration processes been validated?
- Is there a change in regulator expectation since the time of validation?

Unparalleled support

Our expert validation services team is here to help you assess the impact of product, filter or process changes on filter validation reports and ensure process continuity by meeting regulatory expectations.

Merck KGaA
Frankfurter Strasse 250
64293 Darmstadt, Germany

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MK_AN6306EN Ver. 1.0
62096
03/2025