Provantage® Services

Particle Shedding Validation Services

Mitigate your particulate risk to anticipate regulatory requirements

Introduction

The pharmaceutical industry emphasizes the need to evaluate particulate contamination from filters. Additionally, while particulate quality of process equipment is not specified, drug manufacturers must ensure that process equipment does not adversely impact the quality of the final drug product. Normally, Single-Use assemblies will not shed any particles into the final formulation unless the product or processing conditions are not compatible. More important, however, is to investigate the production line after the filter, because both the EU and US Pharmacopoeia look for particles in the final container, not only for the filter downstream and/or process line. Any plastic material used after the filter (e.g., silicone tubing, connector) could release particles and thus add to the total particle content in the final container.

The employment of closed single-use systems manufactured with a wide array of component materials further highlights the need for studying particle shedding as part of an overall qualification plan.

Particulate contamination can be assessed by conducting a validation and process qualification, based on risk management. This demonstrates that all potential risks have been identified, taken into account, evaluated for impact and mitigated or prevented in order to ensure the integrity of the final drug product.

Sources of Particulate Contamination

1) Particle release from filters
2) Particle release from disposable components
3) Crystallization of the drug product and/or in process material

Risks Related to Particulate Contamination

1) Compromised product quality and patient safety
2) Not complying with release specifications
3) Loss of product / Supply issues
4) Costly investigations

Unparalleled Support from Our Lab to Yours

Provantage® Services provide shedding validation testing to assess the particle release from filters and disposable assemblies. Our validation project coordinators will work with you to understand your process, and then by using our in-depth knowledge of our products, help you assess the risk of your application and recommend the appropriate level of testing to mitigate this threat.

Your process will be adapted to a laboratory scale designed to get reliable results. A simulation is performed to quantify the amount of particles at various stages of the process, following worst-case parameter recommendations published in regulatory documents:

- **Higher flow rate** to pull out more particles from the filter or device
- **Temperature** at which the customer product is more viscous
- Filter/device **sterilization** (stress) has to be performed following the strongest sterilization parameters we recommend. The number of customer sterilization cycles must also be applied.

The sampling procedure is usually performed at the beginning, during the middle and at the end of the run. The particle analysis procedure from USP 35 <788> is followed.

The particle results given are compared to specifications given by Pharmacopeia.

Approach and Procedure

A validation project coordinator will be assigned and dedicated to your project from initiation to completion. A standard test protocol is customized for the needs of your specific process and submitted for your review. Once it is approved, testing begins. A standard report summarizing the test results is submitted to the client at the completion of testing. In the event that the study provides evidence that the process fluid or conditions are not compatible with the tested filter/device, we will recommend an alternative solution.

Your validation project coordinator will request the following information in order to customize our standard test protocol for your specific service:

- An MSDS for your test solution, if available
- A classification and code, if it is a controlled drug
- Product incompatibilities
- Exact filter/product catalogue number.
- Flow rate, batch size, time

"We work hand-in-hand with you, exchanging information and defining the most efficient validation strategy."

Worldwide Services

Our teams of process validation experts are available around the globe to help you with your processing challenges.

The current recommendations from industry and regulatory authorities advise that any validation or qualification project should begin with a risk assessment. We are available to help you assess such risks to your drug product and production process.

Our services demonstrate that our products and technologies used with your drug product within your specific process conditions are reliable, robust, efficient, and provide the highest level of performance.

Achieving this objective is a joint effort – we work hand-in-hand with you, exchanging information and defining the most efficient validation strategy.

Coupling our technologies with a wide range of validation and qualification expertise, we can solve your business challenges from upstream through downstream to final fill and finish.

What's more, we can also adapt our Validation and Compliance Services offering to the needs and constraints of your current drug development step. Our experts can advise you on the Validation and Qualification scope to meet regulatory requirements, while mitigating your production process risks.

Provantage® Services global network and capabilities allows us to share information and experiences with more than 70 of our experts, providing consistent, best in class services for global customer projects.

References

1. EurPh, 5.0, 2.9.19 "Particulate Contamination: Sub-Visible Particles" (EDQM, Strasbourg, France, 2005), 253–255.
2. USP 34–NF 29 General Chapter <788>, "Particulate Matter in Injections."
3. Japan Pharmacopoeia XV, 6.06, "Foreign Insoluble Matter Test for Injectables," in General Tests, Processes, and Apparatuses Section, p. 110–113
4. ICH, Q4B, Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions – Annex 3 Test for Particulate Contamination: Subvisible Particles, General Chapter (Jan. 2009).
5. PDA Non-fiber releasing Technical report N°26 Sterilizing filtration of liquids 2008 supplement Volume 62.
6. Code of Federal Regulations, Title 21, Food and Drugs (Government Printing Office, Washington DC), Part 211.65, "Equipment."
7. Code of Federal Regulations, Title 21, Food and Drugs (Government Printing Office, Washington DC), Part 211.72 "Filters."

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