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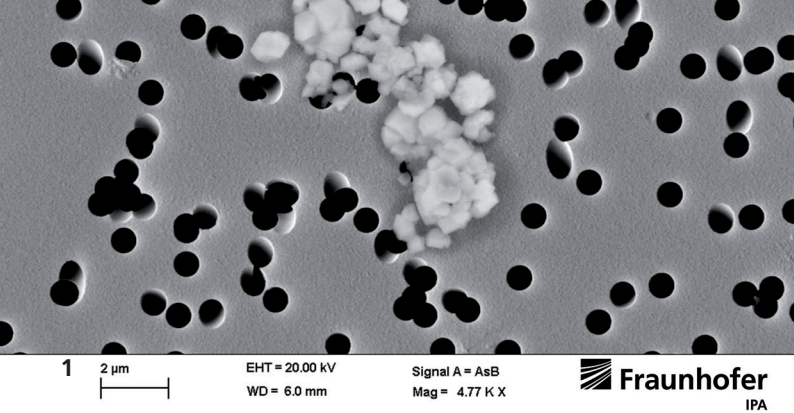
VALIDATING PARTICULATE CLEANLINESS IN MEDICAL TECHNOLOGY

Relevance of cleanliness

Although the issue of cleanliness has been deeply rooted in medical technology since decades and bindingly defined in relevant national and international standards, problems linked to insufficient levels of cleanliness still tend to arise. This has led to approximately 250 medical products being recalled by the Food and Drug Administration (FDA) within the last ten years, with approx. 30 % of them being due to contamination. One explanation for this is inadequate cleaning processes and unreliable procedures for checking the cleanliness of medical products.

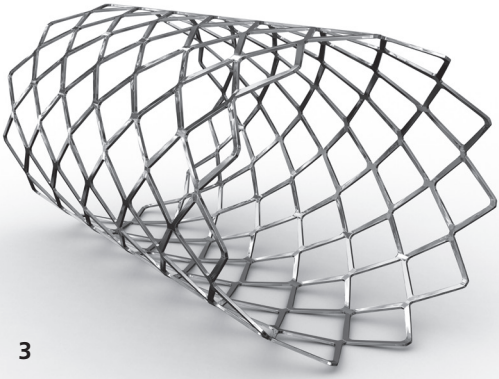
Despite the application of established cleanroom technologies, critical contamination in the manufacture of medical products cannot be fully excluded: staff, process equipment and process media are all capable of introducing contamination into the manufacturing environment and spreading it in an uncontrolled manner. In the same way, medical products can also become contaminated by production processes. As a result, the aspect of particulate cleanliness is becoming more and more important because even particles, for example abrasion particles from metal or rubber, can have a pyrogenic effect similar to dead microorganisms, which can also be considered as particles in this context. Continuous monitoring and the reliable validation of the particulate cleanliness of medical products therefore play a major role in quality control.



Validating cleanliness

In order to achieve reliable results, where possible the entire relevant surface of a product needs to be tested. Due to component geometries and surface characteristics, contamination has to be removed from the surface of products by means of extraction and then transferred to a filter membrane.

At this point, it makes sense to validate the extraction procedure used and its parameters. Although component-specific extraction procedures are carried out to remove contamination from medical products, their efficacy is not investigated. This can be achieved by adapting the procedure described in VDA Volume 19, or ISO 16232 respectively, which is used by the automotive industry to validate suitable component-specific procedures and their parameters. In doing so, a so-called qualification test (also known as declining test) is performed in which the same component is repeatedly tested to assess whether all relevant particles are removed from the component surface using the chosen extraction parameters, e. g. duration, volume flow, ultrasound output. A further advantage of this procedure is that particles can be analyzed fully automatically by light microscopy or scanning electron microscopy depending on the information required (size, material, etc.).



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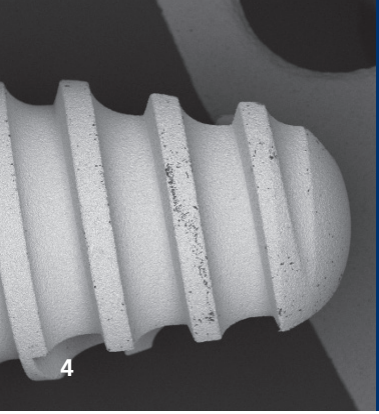
Cleaning techniques

If the cleanliness state of a product is found to be insufficient, a specific cleaning process may be needed to remove the contamination. In order to select an appropriate technique, the efficacy of cleaning processes has to be assessed both quantitatively and comparatively. Methods for validating cleanliness can also be utilized to evaluate cleaning techniques, such as CO_2 snow-jet cleaning or cleaning with hypercritical CO_2. Cleaning efficacy is ascertained by comparing the cleanliness state of a sample that has been contaminated in a defined way both before and after cleaning.

The efficacy of the CO_2 cleaning process is in the nano-range for dead or colony-forming particles and in the ppb-range for filmy contamination, thus enabling both production-related and application-related contamination to be controlled. The CO_2 cleaning technology can be implemented either using simple manually-operated cleaning equipment or automated systems.

1 *Extracted contamination on a filter membrane in a SEM.*
2 *CO_2 snow-jet cleaning.*
3 *Vascular stent.*



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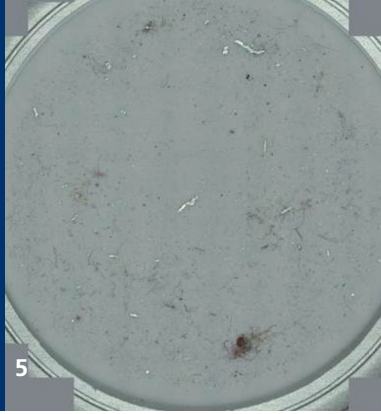

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Infrastructure

In cleanroom laboratories with the highest air cleanliness class (Class 1 according to ISO 14644-1) where tasks can be performed without the risk of cross contamination and thus reliable blank values can be attained, the following analytics are used:

- Automated counting and morphological analysis of particles by means of light microscopy and scanning electron microscopy
- Material and element analysis with x-ray spectral analysis (EDX)
- CO_2 cleaning tools for hypercritical as well as snow-jet cleaning tasks

References (extract)

- European Space Agency ESA
- Uhlmann Pac-Systeme GmbH & Co. KG
- OptiMed Medizinische Instrumente GmbH
- Dentsply Friadent GmbH
- DeepClean, InnoNet project: 16IN0705, BMWi

TITLE *SEM analysis.*

4 *SEM image of a dental implant.*

5 *Filter membrane counted using a light microscope.*

6 *Cleaning a dental implant with hypercritical CO_2.*

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