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Assessment of Organic Residues on Medical Devices

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Introduction

1. **Important steps for cleanliness assessment**
2. **Overview of test methods and evaluation**
3. **FTIR method for organic residues at low levels**
4. **Identification of residues by GC-MS**

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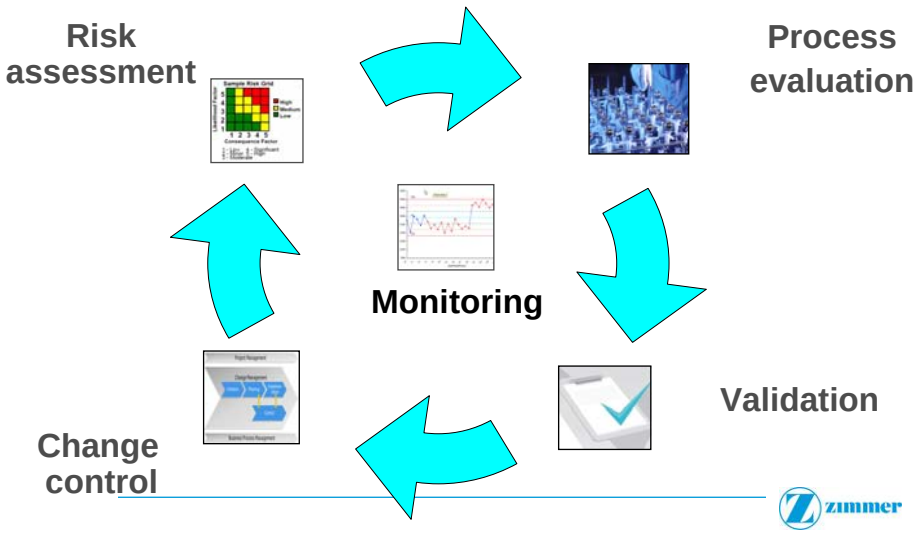
Cleanliness Assessment



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Which Test Method ?

Only 1 test method (ASTM 2459) for non bio residues has been published

According to WK15532 more specific methods are required

No standard for non water-soluble organics (e.g. oil residues)

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Different strategies, methods and specifications to assess cleanliness additional ASTM standards required

⇓

Which test method is best?

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Evaluation of Test Method

- Detectability of all potential residues
- Detection limit below specified cleanliness
- Compatibility of device with the method
- Quantitative (comparison with alarm / limit values)
- Accepted by authorities / standardized
- Costs and throughput time

Test Methods for cleanliness control I

	Technique	+	-
Direct Analysis (Surface)	**Visual examination**	• Rapid • Inexpensive • No extraction	• Only large visible spots detectable • limited for complex surfaces
	SEM/EDX XPS TOF-SIMS	• Rapid identification • No extraction	• no quant. of total MD surface • limited for complex surfaces
Indirect Specific Analysis (Extraction)	**GC-MS ICP-MS**	• Identification of mixtures • Low LOD: ng/device	• Not universal • Expensive • Complex

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Test Methods for cleanliness control II

	Technique	+	-
Indirect Universal Analysis (Extraction)	**TOC** USP 643	• low LOD: 0.03 mg • all water-soluble organics	• no nonpolar organics • recovery valid.
	FTIR ASTM JAI13391	• low LOD: 0.03 mg • nonpolar organics	• polymer lachables • recovery valid.
	Conductivity USP 645	• inorganic and organic ions • inexpensive	• limited to ions • recovery valid.
	Gravimetry e.g. ASTM F2459	• most universal: all nonvolatiles • Inexpensive	• high LOD: 0.3 mg/device • recovery valid.
	Particle count USP 788	• low LOD: a few particles	• no solubles • recovery valid.

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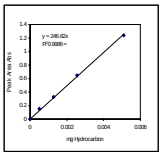
Principle of Cleanliness Testing with Extraction


Complete immersion in a (non) polar solvent


Ultrasonic extraction of polar, non polar or particulate residues


Analysis with sensitive techniques


Quantification with a reference compound calibration

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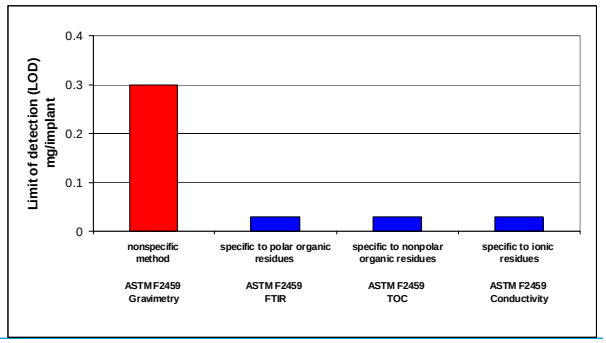
Limitation of ASTM F2459 / Gravimetry

- LOD of 0.3 mg not low enough for cleanliness assessment
- Differentiation between (inorganic / organic) not possible
- long-term experience for reproducible analysis required
- More sensitive methods (e.g. FTIR) 10 x lower LOD required



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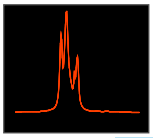
FTIR Method for Organic Residues

Extraction acc. ASTM F2459 with carbon tetrachloride (CCl_4)

polymers:	1-10 min Ultrasonic (US) at room temperature (RT)
metals:	US / RT structure dependent
ceramics:	US / RT
Hydroxyapatite	US / RT

Measurement of IR spectra by FTIR based on ASTM F1374-92[1]

- direct measurement of extract in transmission (1 cm cuvette)
- recording spectra in the range from 2500 – 4000 cm^{-1}
- covers all extractable hydrocarbons (oil, cooling agents etc.)



Quantification

- integration of hydrocarbon peak (C-H) in the range from 2800 – 3000 cm^{-1}
- quantification against a reference hydrocarbon (hexadecane or reference oil)
- results in mg/implant or mg/area

1) ASTM F1374-92 Standard Test Method for Ionic/Organic Extractables of Internal Surfaces-IC/GC/FTIR for Gas Distribution System Components (Ultra-High-Purity Gas Distribution Systems)

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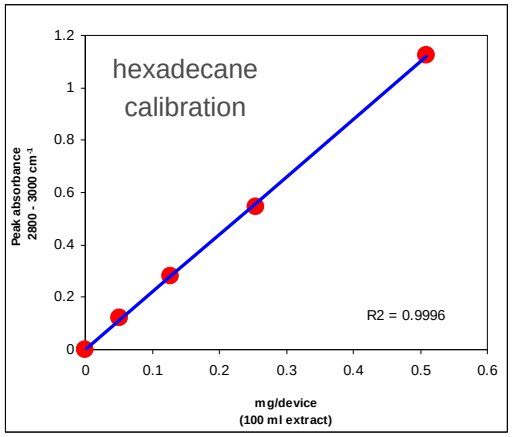
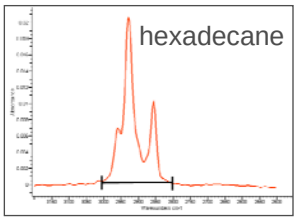
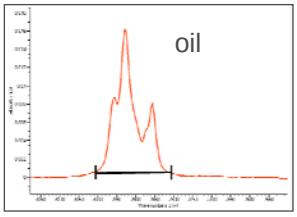
Quantification by FTIR







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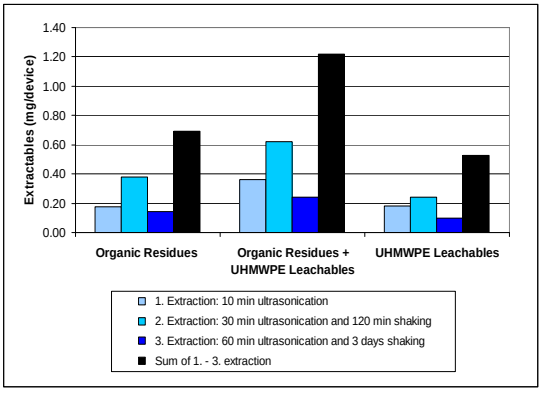
Organic Residues / Polymer Leachables

Extraction of polymers can release polymer leachables
Differentiation residues / leachables if possible



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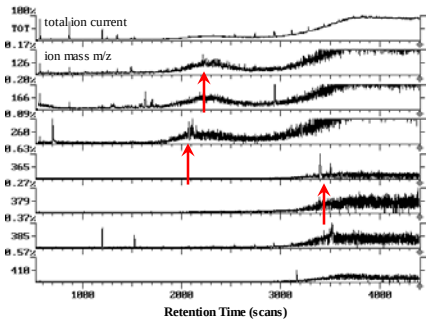
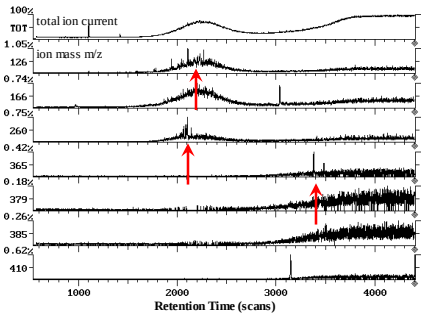
Identification of Residues by GC-MS



Extract of machined UHMWPE test device



Reference processing aid
(mineral oil-based cooling agent)

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Conclusions

- ASTM F2459 can be used for polymeric implants
- Gravimetry alone may not be sensitive enough for cleanliness assessment, therefore it should be used in combination with other analytical techniques.
- Extraction ASTM F2459 with FTIR
  - Sensitive enough with LOD of 0.03 mg/implant
  - Good recovery also at low levels > 80 %
  - Specific to extractable hydrocarbons, such as oils
- Publication of ASTM standards with FTIR specific for MD
- Highly specific methods (GC-MS) only for identification required

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Thank you for your attention