MediTECH Product Line – implantable grade
UHMW-PE

Stefan Willing, QUADRANT
Medical grade UHMW-PE manufactured and supplied by Quadrant MediTECH as shapes (plate, rod, preforms) to be used in Orthopedics Implants.
QUADRANT MediTECH: Medical grade UHMW-PE

GUR 1020 and GUR 1050 resin (powder)

CHIRULEN® 1020 and 1050
EXTRULEN® 1020 and 1050
Shapes (plates, rods, preforms)
QUADRANT MediTECH: Medical grade UHMW-PE

Primary Conversion & Resin Conditioning

Post-sintering and Annealing Processes

Cross-linking Expertise

Blending & Mixing Technology
Compression molding technology: 3 dedicated presses
Cleanroom operations (ISO 14644-1, class 8, note: Vreden only)
Special mold surface allows elimination of release agent

QUADRANT MediTECH: Medical grade UHMW-PE
MediTECH Conversion Technology

- Fort Wayne Pressing Operation
Product range of CHIRULEN® and EXTRULEN®

- **CHIRULEN® 1020**
- **CHIRULEN® 1050**

  **standard sizes:**
  - sheet size: 1000 mm x 500 mm
  - sheet thickness: 20 mm to 80 mm
  - rod diameter: 20 mm to 80 mm
  - rod length: 500 mm, 1000 mm

- **EXTRULEN® 1020**
- **EXTRULEN® 1050**

  **standard diameter:**
  - 12 mm to 100 mm
  - length: 500 mm, 1000 mm, 3000 mm

Special sizes, cut-to-size, fabricated preforms upon request
QUADRANT – Engineering Plastic Products

MediTECH Product Line – Typical applications
[Orthopedics - Total Joint Replacement]

[Application: artificial hip and knee components]

<table>
<thead>
<tr>
<th>Material</th>
<th>[CHIRULEN® 1020 and 1050]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Processes</td>
<td>[Compression Molding, Stabilization under N₂]</td>
</tr>
</tbody>
</table>

**Properties and benefits:**

- Stabilized / annealed under inert atmosphere (N₂)
- High dimensional stability
- Very high impact strength, excellent sliding properties, very high wear resistance
- Full traceability for 30 years
- GMP - Validated Processes
- Biocompatible, per ISO 5834, ASTM F 648 and USP Class VI requirements
- Long-term record in Orthopedics (e.g. hip, knee, elbow joint replacements)
[Orthopedics - Total Joint Replacement]

[Application: artificial hip and knee components]

Material: [Crosslinked CHIRULEN® 1020/1050]
Processes: [Compression Molding, Stabilization under N₂, Crosslinking process, secondary stabilization process under N₂]

Properties and benefits:
- Improved wear resistance
- Manufactured according to customer specifications
- Cross-linking and stabilizing expertise with MediTECH, irradiation process performed by outside vendor(s)
- GMP - Validated Processes
[Orthopedics – Spinal Implant]

**Application: discs in spinal implants**

- **Material**: [CHIRULEN® 1020]
- **Processes**: [Compression Molding, Stabilization under N₂]

**Properties and benefits:**

- High dimensional stability
- Very high toughness and wear resistance
- Full traceability for 30 years
- GMP - Validated Processes
- Biocompatible per USP Class VI requirements
[Medical Devices]

[Application: cutting block for medical device]

Material [CHIRULEN® 1020]
Processes [Compression Molding, Stabilization under N₂]

Properties and benefits:
- High dimensional stability
- Very high toughness and wear resistance
- Full traceability for 30 years
- GMP - Validated Processes
- Biocompatible per USP Class VI requirements
MediTECH® - Quality Management

- Quality Guidelines: ASTM F 648 and ISO 5834, customer’s specification
- Resin lot qualification process
- Cross-check for physical/mechanical properties with Ticona (raw material supplier) and MediTECH U.S.
- Monthly resin lot verification and cross-check
- Dedicated MediTECH press operation since 1994
- 100 % press cycle verification
- Validated compression molding process
- Validated annealing cycles (nitrogen atmosphere)
- AQL10 - visual inspection
- ISO 9001 certified
- ISO 14001 certified
- ISO 13485 certified
Lot Qualification Process

TICONA

1250 kg per lot for testing and qualification purposes

Converting of sheets (pressing)

Annealing

Planing

Sawing

Visual check

MediTECH USA Check of physical properties

Certificate acc. to EN 10204-3.1.

Investigation:
- PHS USA
- OFG
- Ticona

Pressing?

Reason?

YES

NO

YES

O.K.?

NO

Release

Documentation in Database

YES
- Process parameters are visualized and filed during the entire process
- Quality Manuals available in the Intranet for medical personnel
- Traceability System based on Electronic Database
MediTECH® - Technology

- Annealing Technology using Nitrogen Atmosphere
  - Tight implant tolerances
  - Preventing material oxidation
  - Quenching free radicals after cross linking

4 Programmierung des Ofens

Temperprogramme Chirurgie; Abkühlung des Ofens mit 5°C/h

<table>
<thead>
<tr>
<th>Schritt 1</th>
<th>Schritt 2</th>
<th>Schritt 3</th>
<th>Schritt 4</th>
<th>Schritt 5</th>
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<td>halten</td>
<td>Steigung</td>
<td>auf Temp</td>
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<td>Schritt 4</td>
<td>Schritt 5</td>
<td>Schritt 6</td>
<td>Schritt 7</td>
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</table>

Ziel: 120°C
How does MediTECH Division ensure the extremely high quality standard necessary for CHIRULEN® and EXTRULEN®?

CHIRULEN® and EXTRULEN® products undergo intensive visual inspection to make sure requirements of ISO 5834 and ASTM F 648 are by far exceeded.
Test per ISO 5834-1 and ASTM F-648 at Ticona

7.1.2.1 A 300 g sample is divided into four 75 g samples. Place a 75 g sample in each of four 1000 mL Erlenmeyer flasks, add 400 mL isopropyl alcohol, shake 5 min. and let settle for 5 min. Count the total number of particles of extraneous matter in the four flasks.
Shape “Cleanliness”

Test per ISO 5834 -2 and ASTM F-648 at QEPP MediTECH

8.8 Sample area for extraneous matter

A total machined surface area of \((500 \times 10^3) \text{ mm}^2\) shall be taken from locations within the fabricated form. The area examined shall include both transverse and longitudinal samples or may be produced by repeated sectioning through the thickness of fabricated form.

Chirulen Pressenposition - Stippenzahl

Prese: 12
von: 01.01.1988 bis: 21.04.2010
MediTECH® - Technology

State of the art machining operations
- CNC lathe without cooling agent (for preforms only – no final implant component!)
- Optical and mechanical measurement device
- AQL10 optical inspection
Quality standards achieved by:  
-> continuous process improvements and well trained people

<table>
<thead>
<tr>
<th>resin</th>
<th>pressing</th>
<th>annealing</th>
<th>Machining (preforms)</th>
</tr>
</thead>
</table>
| • Resin lot qualification and Cross-check process  
  • Reduced contamination by training the operators  
  • Validated resin conditioning | • Dedicated press  
  • Small scale press  
  • High pressure operations  
  • No release agents  
  • Validated in the manner of GMP | • Cycle for dimensional stability, low stress  
  • Unique inert process, prevent oxidation | • No cooling agents  
  • Special tooling and machining parameters  
  • Optical inspection of surface quality |

Validated in the manner of GMP
Process/Product Innovation
Proven Research and Development capabilities

MediTECH® conversion evolution
- Next generation pressing technology for product and process improvement
- Improved homogeneity through optimized resin handling

Radiation processing (Crosslinking)
- Developed jointly with our customers’ R&D / Technical Departments
- Leading supplier of Crosslinked UHMWPE in bulk form

Stabilized PE-UHMW
- Blend PE-UHMW with additives, to improve oxidation behavior
- Developed jointly with our customers’ R&D / Technical Departments
Jointly developed Medical Polymers: UHMW-PE with Vitamin E

Start

Feasibility, material and process development, investment, Supplier-Join-In, trials, validation ...

Take off

Phase 1 Phase 3 Phase 3

Process feasibility & structure development

Scale up & optimization, PFMEA

Validation, Operation & Performance Qualification (IQ, OQ, PQ)

DEVELOPPERS
DESIGNERS
ENABLERS
Highly cross-linked medical grade PE-UHMW

Latest development in the orthopedic implant industry with regard to Polyethylene:

- Highly cross-linked PE-UHMW with improved tribological properties.
- Highly cross-linking achieved through either electron beam or gamma irradiation and subsequent, specially designed, annealing process to eliminate free radicals.
- ...to markedly improve the wear resistance of UHMWPE
- ...to significantly reduce the number of wear particles generated in vivo.
Cross-linking of medical grade PE-UHMW

Radiation Chemistry
– Gamma Irradiation
– E-Beam Irradiation

Conventional Chemistry
– Peroxide Chemistry
– Silane Chemistry

Radiation Units: 10 kGy = 1 Mrad
Typical sterilization dose levels: 25-40 kGy = 2.5-4 Mrad

Highly cross-linking: above typical dose level of sterilization.
E-beam and gamma irradiation

**E-beam irradiation**

1 - penetration depth of electrons
2 - primary electrons (source)
3 - secondary electrons
4 - irradiated material

**Gamma irradiation**

5 - Co-60 irradiation source
6 - γ-quanta
Cross-linking of medical grade PE-UHMW

What can MediTECH contribute to develop highly cross-linked PE-UHMW for orthopedic implants?

✓ MediTECH has several years experience developing highly cross-linked PE-UHMW for orthopedic implants in close cooperation with leading orthopedic implant manufacturers

✓ MediTECH currently provides significant commercial quantities of radiation cross-linked PE-UHMW to the orthopedic industry

✓ MediTECH understands the radiation process with respect to PE-UHMW closely cooperating with radiation vendors

✓ MediTECH knows how radiation and subsequent annealing affects PE-UHMW

✓ MediTECH has more than 20 years experience heat treating PE-UHMW for stabilization on large scale
Supply chain for highly cross-linked premium PE-UHMW

1. MediTECH produces semi-finished PE-UHMW products (CHIRULEN® and EXTRULEN®)
2. Irradition of PE-UHMW semi-finished products at irradiation vendor at specified dose range (note: the dose range is to be specified by the OIM)
3. Specially designed annealing process at MediTECH to eliminate residual free radicals and to complete cross-linking process (note: annealing temperature and process is to be specified by the OIM)
4. Machine finish of highly cross-linked PE-UHMW products (planed sheets, rods, preforms etc.) at MediTECH
5. Delivery to customer, machine finish, packaging, sterilization
Options for highly cross-linked premium PE-UHMW

Example for a process specification to be devised by the Impant Manufacturer

<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>base material</td>
<td>Chirulen 1020/1050 CHIRULEN 1020</td>
</tr>
<tr>
<td>2</td>
<td>shape initial size</td>
<td>sheet 1000x500 [mm] x [mm]</td>
</tr>
<tr>
<td></td>
<td>at irradiation</td>
<td>rod 1000 [mm] x 70 [mm]</td>
</tr>
<tr>
<td>3</td>
<td>irradiation</td>
<td>gamma, dose rate 75 [kGy], Tolerance: +/- 10 %</td>
</tr>
<tr>
<td></td>
<td>e-beam, dose rate</td>
<td>kGy</td>
</tr>
<tr>
<td></td>
<td>Temperature</td>
<td>room temperature [°C]</td>
</tr>
<tr>
<td></td>
<td>Atmosphere (Air/Inert)</td>
<td>Air</td>
</tr>
<tr>
<td>4</td>
<td>quenching</td>
<td>MediTECH cycle 150 [°C]</td>
</tr>
<tr>
<td></td>
<td>110° / 150 °</td>
<td>Atmosphere (Air/Inert) Inert (= Nitrogen)</td>
</tr>
<tr>
<td>5</td>
<td>remove surface</td>
<td>final shape</td>
</tr>
<tr>
<td></td>
<td>after irradiation and annealing/ quenching</td>
<td>sheet 1000x500 [mm] x [mm]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>rod 1000 [mm] x 60 [mm]</td>
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<td>packaging</td>
<td>standard/ black PE film black PE film</td>
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