Elastomers in bioprocessing
EPDM gaskets – What debate?

A technical presentation
by
James Walker & Co Ltd
(First presented at the International Society of Pharmaceutical Engineering conference November 2011)
Outline

BioPharm Sealing Issues

Rubber Technology

Seal Manufacture

Material Development and Testing

Seal Performance
Concerns of Biopharm

Process, economic and regulatory conditions require a high level of demand for:

- Full Traceability
- Repeatability
- Consistent Quality

Pressures to reduce Cost of Goods Sold creating a greater demand for:

- Increased preventative maintenance intervals.
- Increasing throughput or yield.
- Reducing failures and deviations.
Elastomeric Seals in Biopharm

Widely used in conventional bioprocess systems.

- Provides means of connecting a variety of process components.
- Often defines the sterile boundary of the process.
- Prevents environmental contamination.

Common Elastomeric Seals

- Hygienic clamp gaskets (i.e. TriClamp®) for pipe connections.
- Orings on tank manways, pumps and other process components.
- Diaphragms in weir style valves.
Common Issues with Seals

• Typically the *weak link* compared to stainless steel in most processes.

  • Loss of process integrity due to seal failure, sometimes managed through retightening practices.
  • Difficulty cleaning due to excessive intrusion into the bore and surface roughness.
  • Excessive adhesion to stainless steel often resulting in equipment damage, operator injury or tedious change out practices.
  • Marginal performance in common industry fluids and clean steam.
  • Industrial manufacturing process often without robust systems, inspections and change control procedures.
    • Inconsistent service life.
    • Lack of process and ingredient traceability.
    • Potential contamination of drug product or process utilities.
Root Cause of Elastomer Issues

• Seal design and materials are based on requirements for Food & Dairy or Chemical Process Industry (CPI).
  • Lower demands on purity.
  • Lower or no requirements for traceability.
  • Less rigorous sanitization and sterilizing requirements.

• Economics working against the true need.
  • Relative low volume of elastomer requires most seal manufacturers to acquire “off the shelf” compounds optimized for molding throughput and wide range of sealing applications.
  • Commodity status of seals requires constant lowering of price to maintain competitiveness often at the expense of performance.
To properly understand effective solutions, a basic knowledge of elastomers is required.

A rough guide …
EPDM Compounding

Polymer
Fillers
  (black and non-black)
Plasticisers
Processing Aids
Cure System
Antioxidants
UV stabilisers
Ozone resistance
Mixing: An Internal Mixer

- Feed
- Casing - cored for heating/cooling
- Ram
- Rotors
- Mixing chamber
- Discharge door
Infinite Possibilities

Hardness 40 to 90 IRHD

Tensile strength <5 to >15 MPa

Compression set (24 hrs at 100°C) 5 to 40%
All EPDM Materials are not the same!!
Extrusion
Compression Moulding
Injection Moulding

Vertical and Horizontal
Rubber Cure

James Walker

Rheometer Test

<table>
<thead>
<tr>
<th>Instrument Type</th>
<th>Compound</th>
<th>Method</th>
<th>Test Length</th>
<th>Temperature</th>
<th>Arc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Instrument3</td>
<td>ELASTOMER EPDM BLACK</td>
<td>Method</td>
<td>6.00 mins</td>
<td>185.00°C</td>
<td>0.5°</td>
</tr>
</tbody>
</table>

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Clean Room

Cleanroom validated to ISO Class 7 (Class 10,000)
Testing of Elastomers

Hardness
Tensile strength / E at B / modulus
Tear resistance
Compressive stress / strain properties
Compression set or compression stress relaxation (CSR) testing at various temperatures
Immersion testing over wide temperature range
Low temperature flexibility
Abrasion testing
Performance of the final compound depends on selection of the specific type and grade of all ingredients as well as the compounding and moulding process.
Customer Specification

“Black EPDM – USP Class VI Compliant”
What does this tell us?

Biocompatibility

NO indication of how elastomer will function as a seal
Seal Requirements

USP Class VI compliant

FDA compliant

Animal Derived Ingredients Free (ADIF)

Application Specific
Elastomer Selection

Temperature

Media

Mechanical operating conditions

‘Special’ requirements

Cost
A 75 hardness EPDM elastomer specifically designed for the bioprocessing industry

“Clean” ingredients only, all ADIF

Full traceability of all ingredients
### EPDM

<table>
<thead>
<tr>
<th>Property</th>
<th>Unit</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hardness</td>
<td>IRHD</td>
<td>76</td>
</tr>
<tr>
<td>Tensile Strength</td>
<td>psi (MPa)</td>
<td>2378 (16.4)</td>
</tr>
<tr>
<td>Elongation at break</td>
<td>%</td>
<td>130</td>
</tr>
<tr>
<td>Compression Set 168 hours at 100°C</td>
<td>%</td>
<td>6.0</td>
</tr>
<tr>
<td>Compression Set 168 hours at 125°C</td>
<td>%</td>
<td>11.4</td>
</tr>
</tbody>
</table>
Compression Stress Relaxation

- Minimal intrusion
- No re-torque
# Total Organic Carbon USP <381>

<table>
<thead>
<tr>
<th>Sample</th>
<th>TOC (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPDM A</td>
<td>61.2</td>
</tr>
<tr>
<td>EPDM B</td>
<td>119</td>
</tr>
<tr>
<td>EPDM C</td>
<td>138</td>
</tr>
<tr>
<td>EPDM D</td>
<td>139</td>
</tr>
</tbody>
</table>
## CIP 100*

<table>
<thead>
<tr>
<th></th>
<th>4 Weeks at 140 F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume Change (%)</td>
<td>+ 2.6</td>
</tr>
<tr>
<td>Change in Tensile Strength (%)</td>
<td>- 9.7</td>
</tr>
<tr>
<td>Change in Elongation at break (%)</td>
<td>- 7</td>
</tr>
<tr>
<td>Change in hardness (IRHD)</td>
<td>- 2</td>
</tr>
</tbody>
</table>

(* Manufactured by Steris — based on potassium hydroxide. CIP 100® is a registered trademark of Steris Corporation.)
EPDM

50% less TOC extractables than typical EPDM.

Low adhesion to stainless steel after thermal cycling.

Biocompatibility tested via USP Class VI <87> and <88>.

Compatibility tested with common industry chemicals.

Extremely low compression set (~6%) for long term sealability without retightening.
Intrusion
Intrusion for 1” Hygienic Seal

Intrusion (mm)

Applied Load (Nm)
Intrusion for 1" Hygienic Seal

Position

1
2
3
4

Intrusion (mm)

Clamp Number

0
1
2
3
4

-0.18
-0.14
-0.1
-0.06
-0.02
0.02
0.06
Intrusion

![Graph showing intrusion (mm) vs applied load (Nm)]
Claiming and Proving Performance

Steam cycle tested per ASME BPE-2009, Appendix J

- Steam Hold
  - Saturated Clean Steam, >130 C for 1 hour
  - Cool to <25 C with CDA and repeat.

- Analysis
  - Pressure hold before/after required cycles.
  - Visual Inspection - Damage, adhesion, etc.
  - Intrusion Measurement
  - Measurement of weight change.
Intrusion

- Pressure hold passed before and after each round of testing.
  - 45 PSIG, 1 hr, <0.5 PSI loss.
- No cracks, tears or other deformation observed.
- Clean removal from all ferules with minimal adhesion.
- Intrusion
  - All sizes Cat I compliant initially.
  - Excellent performance over time.
- Negligible change in weight.

<table>
<thead>
<tr>
<th>Size</th>
<th>Initial</th>
<th>100 Cycles</th>
<th>500 Cycles</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Intrusion</td>
<td></td>
</tr>
<tr>
<td>1/2</td>
<td>0.11 mm</td>
<td>0.29 mm</td>
<td>Not Tested</td>
</tr>
<tr>
<td>3/4</td>
<td>0.14 mm</td>
<td>0.45 mm</td>
<td>Not Tested</td>
</tr>
<tr>
<td>1&quot;</td>
<td>-0.17 mm</td>
<td>0.49 mm</td>
<td>0.60 mm</td>
</tr>
<tr>
<td>1-1/2</td>
<td>-0.36 mm</td>
<td>-0.57 mm</td>
<td>Not Tested</td>
</tr>
<tr>
<td>2</td>
<td>-0.54 mm</td>
<td>-0.67 mm</td>
<td>Not Tested</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Weight Change (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1&quot;</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>-0.10%</td>
</tr>
<tr>
<td></td>
<td>-0.17%</td>
</tr>
</tbody>
</table>
Summary

- Material designed to meet the needs for the industry and fully tested to confirm desired results.
  - Longer service life allowing for extended PM cycles.
  - Minimal adhesion to stainless steel for easier, safer change outs.
  - Low intrusion for predictable cleanability over time.
  - Engineered compatibility with common cleaning materials, process fluids and steam.
  - High purity material with lower TOC.

- Highly controlled manufacturing process with well identified chain of custody.
  - Reduced risk of failure due to consistent product quality.
  - Data and expertise to support deviation investigations.
  - Full traceability to the raw ingredients and manufacturing process.

- Biopharmaceutical industry concerns and issues addressed.
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