Sterilization & Chemical Resistance of Healthcare Polymers
Key Terms & Definitions

**Sterilization** - A process that eliminates or kills all forms of life, including transmissible agents, on a medical device; used to prevent Hospital acquired infections (HAIs)

**Sterile** - Free from micro-organisms; 100% freedom from micro-organisms cannot be proven

**Bioburden Testing** - Measures the number of bacteria living on a surface that has not been sterilized

**Sterility Assurance Level (SAL)** - Probability of a viable micro-organism on a product after it has been sterilized normally expressed as $10^{-n}$

**Biological Indicators** - Tests used by medical device manufacturers and healthcare providers to monitor the efficacy of different sterilization processes

**Sterilization Validation** - A designed protocol for evaluating the effectiveness of a sterilization process

**Sterility Testing** - Required during the sterilization validation process as well as for process control

**Pathogen** - Infectious agents which is a microorganism

**Efficacy** - Ability of a sterilization process to achieve a desired result

**Terminal Sterilization** - Process whereby a device is sterilized in its final container; The FDA requires terminal sterilization of medical devices
Sterilization

Techniques designed to kill microorganisms/pathogens that may cause infection

Variety of technologies used

Primary technologies for sterilizing medical plastic parts:
- Radiation – gamma, electron beam (E-Beam)
- Ethylene Oxide (EtO)
- Steam Autoclave
Determining Factors for Sterilization Effectiveness

**Type of micro-organism present** - Some micro-organisms are very difficult to kill, some very easy to kill

**Number of micro-organisms present** - Determined by Bioburden testing

**Amount and type of organic material protecting the micro-organism**

**Medical device design** - Cracks, crevices where micro-organisms can hide and collect in
Gamma Sterilization

Sterilization technique that uses gamma radiation to kill microorganisms present on a medical device
- Compatible with most plastics
- Dosage rate must be limited according to the material
- Used on disposable devices

Validation method(s)
- ANSI/AAMI/ISO 11137-2
- AAMI TIR 33
- ANSI/AAMI/ISO 11137-2 VDmax
- AAMI/ISO 15844
Application of Gamma Radiation

Gamma Radiation is a viable alternative to EtO Sterilization and become the industry standard
  o Cleaner, no heat, leaves no chemical residue
  o Can be sterilized with packaging
  o Irradiation is generally recommended single use applications
  o Significant improvements in cycle time, inventory and overall systems cost
  o Photo-bleaching can occur
  o Typical dosage at 2.5 mega-rads is the same as 25 kilo-grays (Kgy)

Ionizing rays of gamma radiation can cause thermoplastics to discolor or yellow; however, the effect on mechanical properties varies by material
Polymer Compatibility to Gamma Radiation

Recommend using polymers with highest molecular weight and narrow molecular weight distribution.

Amorphous polymers are more radiation resistant than semi-crystalline.

Aromatic polymers are more radiation resistant than aliphatic.
Potential Affects of Gamma Sterilization on Polymers

- Physical properties of many thermoplastics change
- Color shift after exposure (i.e., yellowing effect)
- Recombination - no change in properties
- Crosslinking - increased strength, decreased elongation
- Chain scission - loss of strength & elongation
Polymer Exposure to Gamma Radiation

Elongation Retention

Dose (kgray), in ambient air, at which elongation at break of the polymer decreases by 25%
## Polymer Suitability to Gamma Radiation

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Suitability</th>
</tr>
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<tbody>
<tr>
<td>PI</td>
<td>Excellent</td>
</tr>
<tr>
<td>PC</td>
<td>Good</td>
</tr>
<tr>
<td>PES</td>
<td>Fair</td>
</tr>
<tr>
<td>PVDF</td>
<td>Poor</td>
</tr>
<tr>
<td>LCP</td>
<td>Poor</td>
</tr>
<tr>
<td>PC/ABS</td>
<td>Poor</td>
</tr>
<tr>
<td>PEEK</td>
<td>Poor</td>
</tr>
<tr>
<td>PEI</td>
<td>Poor</td>
</tr>
<tr>
<td>PET</td>
<td>Poor</td>
</tr>
<tr>
<td>PPS</td>
<td>Poor</td>
</tr>
<tr>
<td>PBT</td>
<td>Poor</td>
</tr>
<tr>
<td>PSU</td>
<td>Poor</td>
</tr>
<tr>
<td>PC</td>
<td>Poor</td>
</tr>
<tr>
<td>PA4,6</td>
<td>Poor</td>
</tr>
<tr>
<td>PPO</td>
<td>Poor</td>
</tr>
<tr>
<td>PA12</td>
<td>Poor</td>
</tr>
<tr>
<td>PA11</td>
<td>Poor</td>
</tr>
<tr>
<td>ABS</td>
<td>Poor</td>
</tr>
<tr>
<td>POM</td>
<td>Poor</td>
</tr>
<tr>
<td>PP</td>
<td>Poor</td>
</tr>
</tbody>
</table>

Confidential
Electron Beam (E-Beam) Sterilization

Only 5% of market (but growing)

Limited penetration vs. gamma (requires multiple cycles from different angles)

Less degradation to plastics than gamma (color and physical properties)

Lowest energy to radiation ratio

Shorter exposure time than gamma (minutes vs. hours and/or days)

Limited data available on effects to polymer properties and color
# Critical Radiation Doses for Polymers

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Critical Dose (kGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PET</td>
<td>1000</td>
</tr>
<tr>
<td>Polysulfone</td>
<td>700</td>
</tr>
<tr>
<td>Polystyrene</td>
<td>600</td>
</tr>
<tr>
<td>EPDM</td>
<td>400</td>
</tr>
<tr>
<td>Polyamides</td>
<td>300</td>
</tr>
<tr>
<td>Rigid PVC</td>
<td>300</td>
</tr>
<tr>
<td>Polyurethanes</td>
<td>300</td>
</tr>
<tr>
<td>Polycarbonate</td>
<td>250</td>
</tr>
<tr>
<td>Polyethylene</td>
<td>100</td>
</tr>
<tr>
<td>Silicone rubber</td>
<td>40</td>
</tr>
<tr>
<td>Polypropylene</td>
<td>10</td>
</tr>
<tr>
<td>PTFE</td>
<td>4</td>
</tr>
</tbody>
</table>
Ethylene Oxide Sterilization Gas (EtO)

Colorless, flammable, poison gas that kills microorganisms on a medical device
  - Highly compatible with most plastics
  - Used on disposable devices

Causes Sterilization by chemical reaction

Validation method
  - AAMI/ISO 11135 Method C
Applications for EtO Sterilization

Traditionally most widely method for disposable devices; trend is changing to gamma
  - Exposure to high levels of EtO recognized as a health hazard
  - 6 required stages of EtO (preconditioning, humidification, gassing, exposure, evacuation, post vacuum) – extensive cycle times vs. other processes

Main benefits:
  - Sterilizes at low temperatures
  - Little to no effect on thermoplastics

The major concern is the dissipation of residuals during post sterilization process for medical devices maintaining contact with skin, mucous and short-term implants
Steam Sterilization

Utilizes moist heat to kill micro-organisms on a medical device
- Used on reusable devices
- Most plastics cannot withstand repeated steam sterilization
- Two common exposure conditions
  - 121°C for 30 minutes
  - 134°C for 20 minutes

Validation method
- ISO 17665-1: 2006
Autoclave Steam Sterilization

A popular sterilization method for reusable devices

The autoclave’s pressure vessel saturates steam that damage the cell’s structure

Time and temperature is determined by the part, packaging, types of materials used

Two commonly used exposure conditions include:

“Basic” = 121°C for 30 Minutes
“Mid” = 134°C for 20 Minutes

Few thermoplastic materials are compatible with various temperatures of autoclaving
# Steam Sterilization: Recommended Validated Exposure Times

<table>
<thead>
<tr>
<th>Item</th>
<th>Gravity Displacement Steam Sterilization</th>
<th>Dynamic Air Removal Steam</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Exposure Time at 121C</td>
<td>Exposure Time at 132C</td>
</tr>
<tr>
<td>Wrapped Instruments</td>
<td>30 minutes</td>
<td>15 minutes</td>
</tr>
<tr>
<td>Textile Packs</td>
<td>30 minutes</td>
<td>25 minutes</td>
</tr>
<tr>
<td>Wrapped Utensiles</td>
<td>30 minutes</td>
<td>15 minutes</td>
</tr>
<tr>
<td>Unwrapped Non-porous Items</td>
<td>3 minutes</td>
<td>3 minutes</td>
</tr>
<tr>
<td>Unwrapped non-porous and porous items in mixed load</td>
<td>10 minutes</td>
<td>10 minutes</td>
</tr>
</tbody>
</table>

Source: Pacific BioLabs

*Un-modified PC can withstand limited exposures to 121°C, High heat PC can withstand limited exposure to 132°C*
# Steam Sterilization Compatible Materials and Temperatures

<table>
<thead>
<tr>
<th>Temperature</th>
<th>Materials</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>121 °C</strong></td>
<td>Polypropylene, PPO/PPE, Polyamides, Polycarbonate</td>
</tr>
<tr>
<td><strong>134 °C</strong></td>
<td>LCP, PEI, PPS, PSY, High Heat Polycarbonate, PEEK</td>
</tr>
</tbody>
</table>
Specific Materials and Sterilization

There is no sterilization pass/fail for specific materials used in a medical devices

- Terminally sterilized devices can contain many plastic (and metal) components that are made of different plastic materials
- Different plastic materials withstand certain sterilization techniques differently
- In determining the efficacy of a sterilization process the entire device is considered for pass/fail
- The determining factor for pass/fail is the sterility assurance level (SAL) determined for the device
Sterility Assurance Levels (SAL)

Used to describe the killing efficacy of a sterilization process

Expressed in log reduction ($10^{-n}$)

*Example: $10^{-1}$ equals a 90% reduction in microbial population*

Recommended sterility levels of terminally sterilized products are typically $10^{-3}$ or $10^{-6}$ depending on the item
SAL For Terminally Sterilized Devices

10^{-3} SAL Examples

*Products not intended to come in contact with breached skin or compromised tissue*

- Specimen collection or transfer devices
- Topical devices
- Mucosal containing devices
- Products that cannot withstand higher SAL (e.g., porcine heart valves, biological wound dressings)

10^{-6} SAL Examples

*Products intended to come in contact with breached skin or compromised tissue*

- Cardiac catheters
- Wound dressings
- Prefilled syringes
- Invasive devices that enter normally sterile tissue
- Products with claims of sterile fluid pathways (e.g., fluid pathways of IV sets)
- Surgically implanted devices (e.g., Joint replacements, pacemakers, sutures)
- Components used in aseptic processing
Sterilization & The FDA

The FDA’s Center for Devices and Radiological Health (CDRH) is responsible for medical device sterilization regulation.

Sterility of disposable medical devices is sited under FDA GMP.

Sterilization method and process must be put in place for any medical device must be described in a device 510k document (FDA sterility review guidance document K-90-1 (2002)).

The FDA considers hospitals and third party sterilizers as medical device manufacturers and regulates them as such.
# Comparison of Sterilization Methods

<table>
<thead>
<tr>
<th>Considerations</th>
<th>Ethylene Oxide (EtO)</th>
<th>Gamma Radiation</th>
<th>Autoclave (Steam)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product &amp; Package Design</td>
<td>Packaging and product must be designed to allow gas penetration</td>
<td>Density of the product load must be considered to ensure adequate gamma penetration</td>
<td>Packaging must be designed to resist moisture damage</td>
</tr>
<tr>
<td>Component Material</td>
<td>Most materials are satisfactory</td>
<td>Discoloration (yellow), cross-link, physical property degradation post exposure</td>
<td>DNA for materials with low HDT and hygroscopic. Morpoline will require chemical compatibility</td>
</tr>
<tr>
<td>Reliability of Sterilization Process</td>
<td>Process variable must be carefully monitored and controlled</td>
<td>Bioburden control and frequent testing is critical for long-term reliability</td>
<td>Very reliable</td>
</tr>
<tr>
<td>Sterilization Release</td>
<td>Release dictated by biological indicator tests or parametric testing results</td>
<td>Release dependent of dose measured/results</td>
<td>Release dictated by parametric testing results</td>
</tr>
<tr>
<td>Quarantine Period</td>
<td>Quarantined until aeration is complete. Testing requires between 3 and 7 days</td>
<td>Product may be release immediately</td>
<td>Product may be released immediately, although drying may be considered</td>
</tr>
<tr>
<td>Chemical Residuals</td>
<td>Quarantine time must remove</td>
<td>Results pending</td>
<td>None</td>
</tr>
<tr>
<td>Economics</td>
<td>Good on all volumes and load sizes</td>
<td>Good in large volumes</td>
<td>Good on all volumes</td>
</tr>
<tr>
<td>Common Applications</td>
<td>Blood and renal care components. Applications with embedded electronics</td>
<td>Fluid delivery. Pre-packaged components</td>
<td>Lab ware. Instruments and trays</td>
</tr>
<tr>
<td>Usage</td>
<td>52% (decreasing)</td>
<td>46% (increasing)</td>
<td>2%</td>
</tr>
</tbody>
</table>
Chemical Resistance

Can be a difficult problem to predict - many new chemicals and cleaners; Must test to truly predict

In general, crystalline materials have better chemical resistance than amorphous materials

Heat adds to the problem by aging materials

Medical parts are commonly exposed to the following:
- Lipids and fat emulsion (typically used as blood and drug carriers)
- Alcohols
  - Isopropyl Alcohol
  - Ethyl Alcohol
- Hospital cleaners and other chemicals…can be nasty
- Bleach, hydrogen peroxide, saline solution, Cirex, Virex
- Bodily fluids
- Vesicants (blistering agent) in chemotherapy
Data Sources

http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm072783.htm

http://www.isomedix.com/techtips/sterility-assurance-levels-sals-irradiationtechtip-19/

http://www.pacificbiolabs.com/sterilization_intro.asp
