Sterilization & Chemical Resistance of Healthcare Polymers

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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 (HAI's)

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

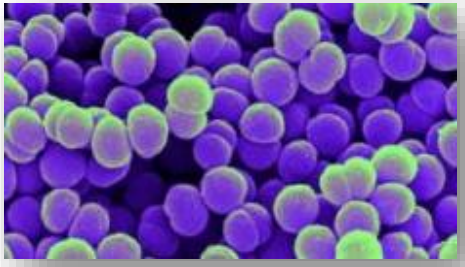
Sterilization

Techniques designed to kills 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

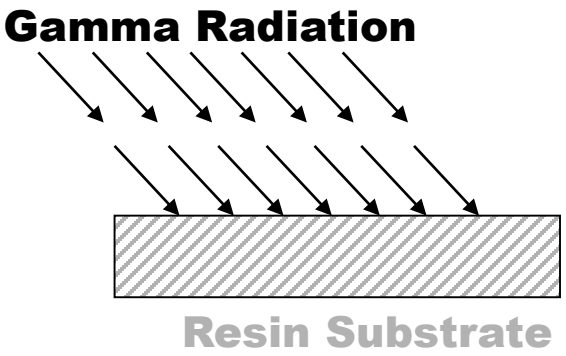
Gamma Sterilization

Sterilization technique that uses gamma radiation to kill micro-organisms 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

- Cleaner, no heat, leaves no chemical residue
- Can be sterilized with packaging
- Irradiation is generally recommended single use applications
- Significant improvements in cycle time, inventory and overall systems cost
- Photo-bleaching can occur
- 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

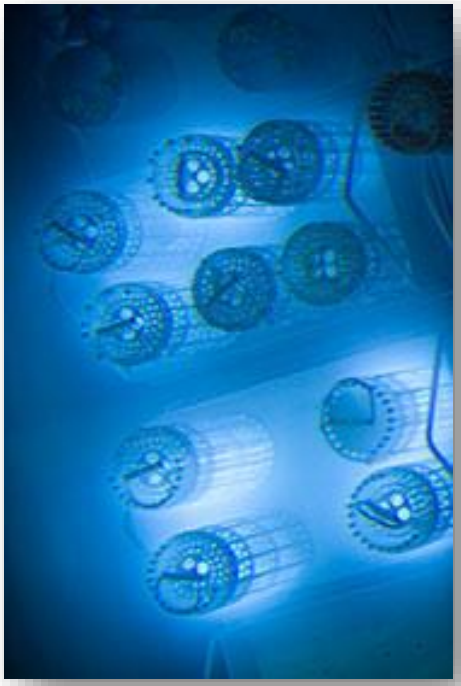
Polymer Compatibility to Gamma Radiation

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)

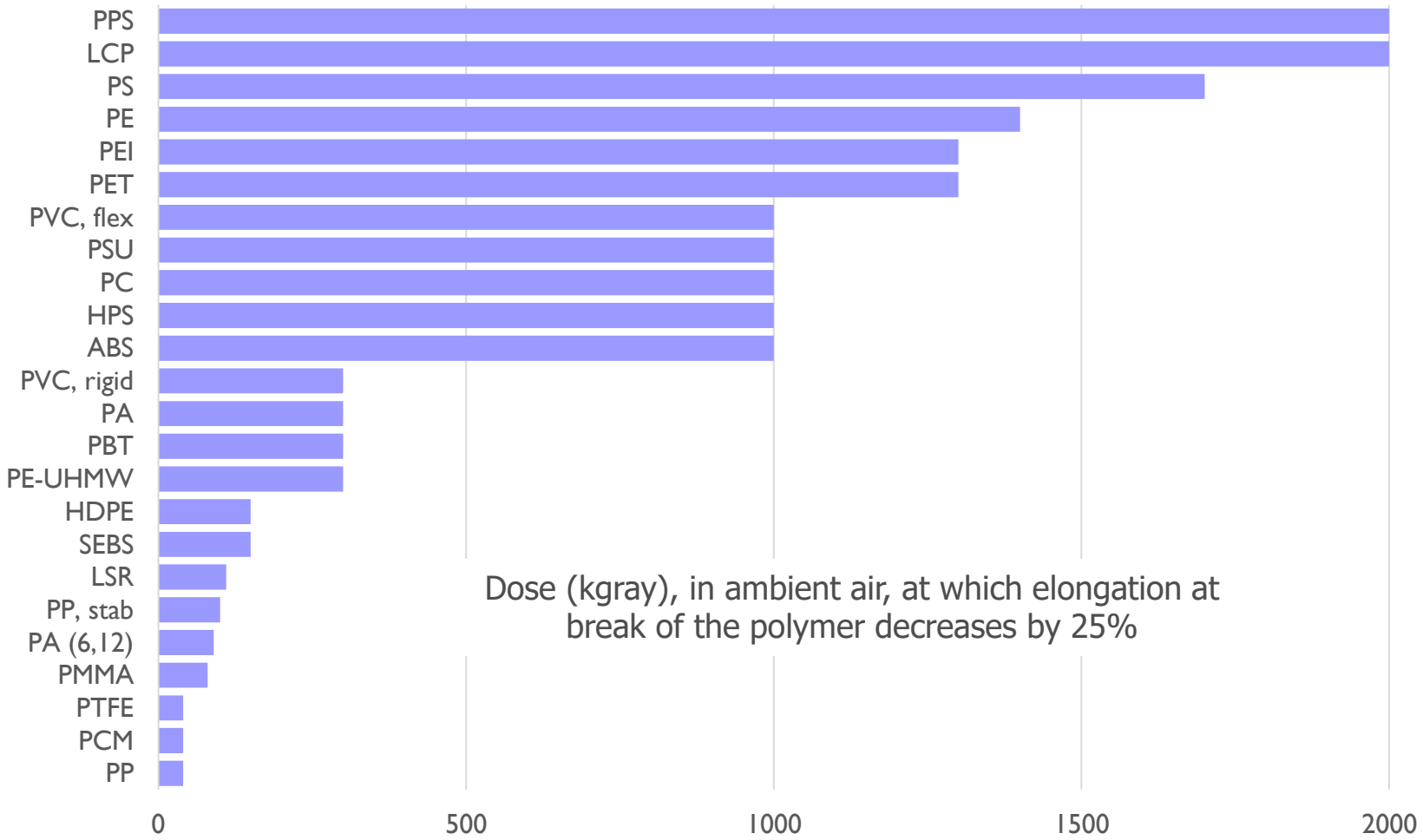
Recombination - no change in properties

Crosslinking - increased strength, decreased elongation

Chain scission - loss of strength & elongation

Polymer Exposure to Gamma Radiation

Elongation Retention



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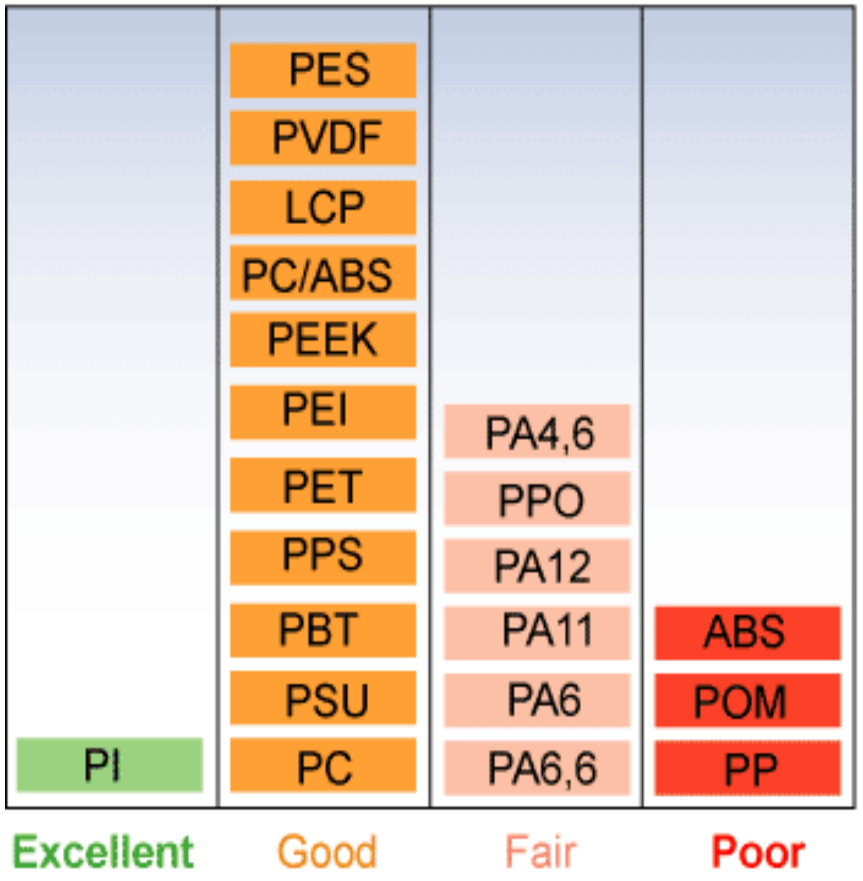
Polymer Suitability to Gamma Radiation



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Electron Beam (E-Beam) Sterilization

Only 5% of market (but growing)

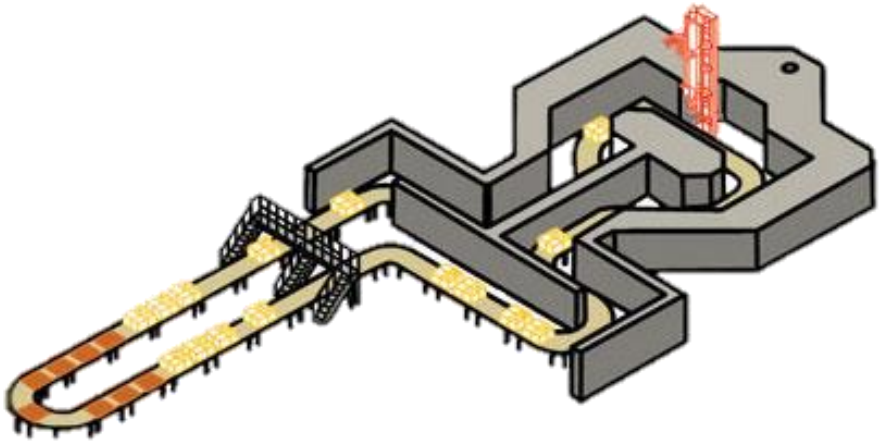
Limited penetration vs. gamma (requires multiple cycles from different angles)

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



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Critical Radiation Doses for Polymers

Polymer	Critical Dose (kGy)
PET	1000
Polysulfone	700
Polystyrene	600
EPDM	400
Polyamides	300
Rigid PVC	300
Polyurethanes	300
Polycarbonate	250
Polyethylene	100
Silicone rubber	40
Polypropylene	10
PTFE	4

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Ethylene Oxide Sterilization Gas (EtO)

Colorless, flammable, poison gas that kills micro-organisms 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

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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

	Gravity Displacement Steam Sterilization				Dynamic Air Removal Steam	
Item	Exposure Time at 121C	Exposure Time at 132C	Exposure Time at 135C		Exposure Time at 132C	Exposure Time at 135C
Wrapped Instruments	30 minutes	15 minutes	10 minutes		4 minutes	3 minutes
Textile Packs	30 minutes	25 minutes	10 minutes		4 minutes	3 minutes
Wrappped Utensiles	30 minutes	15 minutes	10 minutes		4 minutes	3 minutes
Unwrapped Non-porous Items		3 minutes	3 minutes		3 minutes	3 minutes
Unwrapped non -porous and porous items in mixed load		10 minutes	10 minutes		4 minutes	3 minutes

Source: Pacific BioLabs

Un-modified PC can withstand limited exposures to 121C,
High heat PC can withstand limited exposure to 132C

Steam Sterilization Compatible Materials and Temperatures

121 °C

Polypropylene

PPO/PPE

Polyamides

Polycarbonate

134 °C

LCP

PEI

PPS

PSY

High Heat Polycarbonate

PEEK

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

Source: Steris

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 e 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

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

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

http://www.namsa.com/Portals/0/Documents/Making_Sure_Its_Sterile%20July%202006.pdf

http://www.bioreliance.com/bioburdentesting.aspx