

# Sterilization Validation for Implantable Devices

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## ABSTRACT

*Terminal sterilization of implantable medical devices must achieve a sterility assurance level (SAL) of  $10^{-6}$  -- one in a million probability of a non-sterile unit -- while preserving the mechanical integrity, biocompatibility, and functional performance of increasingly complex device materials including biodegradable polymers, drug-eluting coatings, biological tissues, and electronic components. Traditional sterilization validation follows ISO 11135 (ethylene oxide), ISO 11137 (radiation), or ISO 17665 (moist heat) through prescriptive dose-setting or cycle-development protocols, yet the proliferation of novel biomaterials and combination products has created sterilization compatibility challenges that standard protocols do not fully address. This study presents the Sterilization Validation Assessment Framework (SVAF), evaluating five sterilization modalities -- ethylene oxide (EO), gamma irradiation, electron beam (e-beam), vaporised hydrogen peroxide (VHP), and supercritical CO<sub>2</sub> -- across four validation performance tasks: microbial lethality assurance, material compatibility preservation, residual toxicant control, and process robustness under worst-case conditions. Our Sterilization Validation Performance Score (SVPS) integrates SAL achievement, material degradation index, residual safety margin, process Cpk, and environmental sustainability. Electron beam achieved the highest SVPS (0.922) through rapid, low-temperature processing that delivered precise dose uniformity (DUR 1.04) with minimal material degradation across all tested biomaterials, while supercritical CO<sub>2</sub> achieved the highest material compatibility (0.960) through non-ionising, low-temperature sterilization that preserved drug-eluting coating integrity and biological tissue viability.*

**Keywords:** sterilization validation; implantable device; sterility assurance level; ethylene oxide; gamma irradiation; electron beam; hydrogen peroxide; material compatibility; ISO 11137; bioburden

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## 1. Introduction

### 1.1 Sterilization as a Critical Quality Attribute

Sterility is the single most critical quality attribute for implantable medical devices -- a non-sterile implant introduces microorganisms directly into tissue, potentially causing surgical site infections that affect 2-5% of surgical implant procedures, with attributable mortality rates of 3-7% for deep implant infections and healthcare costs of USD 20,000-100,000 per infection episode (Anderson et al., 2014). The regulatory requirement for a SAL of  $10^{-6}$  means that the validated sterilization process must reduce the probability of any surviving microorganism to less than one in a million -- a stringent standard that requires comprehensive understanding of the device's bioburden, the sterilization agent's lethality kinetics, and the process parameters' impact on both microbial kill and material properties. The challenge has intensified as implantable devices incorporate materials that are sensitive to traditional sterilization modalities: biodegradable PLGA polymers that undergo accelerated hydrolysis when exposed to moisture or heat, drug-eluting coatings where paclitaxel or sirolimus degrades under gamma radiation, biological tissues (decellularised heart valves, collagen scaffolds) that denature above 60 degrees C, and electronic components (sensors, microprocessors) vulnerable to ionising radiation (Mendes et al., 2007). For these advanced devices, selecting and validating an appropriate sterilization modality requires balancing microbial lethality against material preservation -- a trade-off that prescriptive ISO standards address incompletely.

### 1.2 Five Sterilization Modalities

Five terminal sterilization modalities are commercially available for implantable devices. Ethylene oxide (EO) sterilization uses the alkylating gas at 30-60 degrees C and 40-80% relative humidity to achieve microbial kill through DNA cross-linking -- it is the most widely used modality for medical devices (approximately 50% of all sterile devices) due to its broad material compatibility, but requires lengthy aeration to remove toxic EO residuals and raises environmental concerns (Mendes et al., 2007). Gamma irradiation delivers 25-50 kGy from cobalt-60 sources, providing excellent penetration and no residuals but causing dose-dependent polymer chain scission and drug degradation (ISO, 2006). Electron beam delivers equivalent doses from linear accelerators with higher dose rates and shorter exposure times, potentially reducing

radiation damage through dose-rate effects (Silindir and Ozer, 2009). Vaporised hydrogen peroxide (VHP) uses H<sub>2</sub>O<sub>2</sub> vapour at 4-12 mg/L and ambient temperature, decomposing to water and oxygen with no toxic residuals but limited penetration into lumens and packaging (Rutala and Weber, 2015). Supercritical CO<sub>2</sub> uses carbon dioxide above its critical point (31.1 degrees C, 73.8 bar) with peracetic acid additive, achieving sterilization at near-ambient temperature without ionising radiation or toxic residuals (White et al., 2006). Section 2 reviews the literature. Section 3 describes SVAf. Results in Section 4, discussion in Section 5, conclusions in Section 6.

## 2. Literature Review

### 2.1 Sterilization Standards and Dose Setting

ISO 11137 (radiation sterilization) and ISO 11135 (EO sterilization) provide the foundational validation frameworks for implantable device sterilization. For radiation, ISO 11137-2 offers three dose-setting methods: Method 1 (bioburden-based, requiring 100-item sample), Method 2 (substantiation of 25 kGy for bioburden  $\leq 1,000$  CFU), and VDmax (verification dose approach for low-bioburden products). Kowalski et al. (2002) demonstrated that Method VDmax substantially reduced the sample size required for dose auditing while maintaining SAL  $10^{-6}$  assurance, making it the preferred approach for low-volume implantable devices. For EO, ISO 11135 specifies overkill (half-cycle) and bioburden-based approaches to cycle development, with Mendes et al. (2007) reviewing the critical process parameters (EO concentration, temperature, humidity, exposure time) and their interactions. The AAMI TIR17 technical report provides guidance on compatibility testing, recommending that material properties be evaluated after exposure to the maximum sterilization dose/cycle to establish the sterilization process window (AAMI, 2017).

### 2.2 Material Compatibility Challenges

Material compatibility is the primary factor differentiating sterilization modality selection for modern implantable devices. Silindir and Ozer (2009) reviewed radiation effects on pharmaceutical materials and found that gamma irradiation at 25 kGy caused 15-40% potency loss in radiation-sensitive drugs (paclitaxel, sirolimus, dexamethasone) commonly used in drug-eluting implants, with degradation products requiring toxicological assessment. For biodegradable polymers, Loo et al. (2005) demonstrated that

gamma irradiation reduced PLGA molecular weight by 30-50% at 25 kGy, accelerating in vivo degradation rate by 2-3 fold and compromising mechanical properties below functional thresholds for load-bearing applications. Holy et al. (2001) compared EO, gamma, and e-beam effects on PLGA scaffolds and found that e-beam at equivalent doses produced 20-30% less molecular weight reduction than gamma, attributed to the shorter exposure time limiting oxygen-mediated secondary degradation reactions. For biological tissues, Lerouge et al. (2001) showed that conventional sterilization methods (EO, gamma, autoclave) all significantly altered the mechanical properties of decellularised vascular grafts, motivating interest in low-temperature, non-ionising alternatives. Table 1 maps the key studies.

### 2.3 Emerging Low-Temperature Modalities

Supercritical CO<sub>2</sub> sterilization has attracted growing attention for sterilization-sensitive devices. White et al. (2006) demonstrated that supercritical CO<sub>2</sub> with peracetic acid additive achieved SAL 10<sup>-6</sup> against *Bacillus atrophaeus* spores at 35 degrees C and 100 bar in 60-minute cycles, with no measurable effect on PLGA molecular weight, collagen denaturation temperature, or drug potency -- the first demonstration that terminal sterilization could be achieved without compromising any of the three material categories most vulnerable to conventional methods. Bernhardt et al. (2015) validated supercritical CO<sub>2</sub> for decellularised cardiac tissue, showing preservation of extracellular matrix ultrastructure and growth factor bioactivity that gamma irradiation destroyed. VHP sterilization has found application primarily for surface sterilization of devices with simple geometries, but its limited penetration restricts use for devices with complex internal channels, porous structures, or multi-layer packaging configurations (Rutala and Weber, 2015).

**Table 1: Key Studies in Implantable Device Sterilization**

| Study          | Year | Focus Area         | Key Finding                              |
|----------------|------|--------------------|------------------------------------------|
| Holy et al.    | 2001 | Polymer comparison | E-beam 20-30% less MW loss than gamma    |
| Lerouge et al. | 2001 | Tissue grafts      | All conventional methods alter mechanics |

| Study            | Year | Focus Area                   | Key Finding                                      |
|------------------|------|------------------------------|--------------------------------------------------|
| Kowalski et al.  | 2002 | VDmax dose setting           | Reduced sample size for dose audit               |
| Loo et al.       | 2005 | PLGA + gamma                 | 30-50% MW reduction at 25 kGy                    |
| White et al.     | 2006 | scCO <sub>2</sub> validation | SAL 10 <sup>-6</sup> at 35C, materials preserved |
| Mendes et al.    | 2007 | EO review                    | CPP interactions for cycle development           |
| Silindir & Ozer  | 2009 | Drug + radiation             | 15-40% potency loss at 25 kGy                    |
| Bernhardt et al. | 2015 | scCO <sub>2</sub> + tissue   | ECM and growth factors preserved                 |
| Rutala & Weber   | 2015 | VHP review                   | Limited penetration into lumens                  |
| AAMI             | 2017 | TIR17 compatibility          | Max dose material testing guidance               |

MW = Molecular Weight; EO = Ethylene Oxide; scCO<sub>2</sub> = Supercritical Carbon Dioxide; CPP = Critical Process Parameter; VHP = Vaporised H<sub>2</sub>O<sub>2</sub>.

## 3. Methodology

### 3.1 SVAF Architecture and Test Materials

SVAF evaluates five sterilization modalities using standardised validation protocols applied to eight representative implantable device material systems: (i) PLGA biodegradable screws, (ii) drug-eluting (sirolimus) coronary stent coatings, (iii) decellularised porcine heart valve tissue, (iv) titanium alloy orthopaedic plates, (v) polyurethane pacemaker lead insulation, (vi) silicone cochlear implant housings, (vii) PEEK spinal fusion cages, and (viii) collagen-hydroxyapatite bone graft substitutes. Each material was sterilized under the modality's standard validated conditions and at 1.5x the standard dose/cycle (worst-case challenge). Total dataset: 960 sterilization runs (5 modalities x 8 materials x 2 dose levels x 12 replicates), with pre- and post-sterilization characterisation including bioburden testing, sterility testing (USP <71>), mechanical testing (tensile, compression, fatigue), chemical analysis (GPC, HPLC, FTIR), biological evaluation (cytotoxicity, haemolysis, implantation), and residual analysis (EO/ECH for EO; peroxide for VHP).

### 3.2 Five Modality Protocols

Modality S1 (Ethylene Oxide) uses 600 mg/L EO at 50 degrees C, 60% RH, 4-hour exposure with 12-hour aeration at 50 degrees C per ISO 11135. Modality S2 (Gamma Irradiation) delivers 25 kGy minimum dose (DUR 1.2-1.4) from cobalt-60

source per ISO 11137, with VDmax dose audit. Modality S3 (Electron Beam) delivers 25 kGy minimum dose (DUR 1.04-1.08) from 10 MeV linear accelerator per ISO 11137, with conveyor speed optimisation for dose uniformity. Modality S4 (Vaporised H<sub>2</sub>O<sub>2</sub>) uses 8 mg/L H<sub>2</sub>O<sub>2</sub> vapour at 45 degrees C for 90 minutes in a sealed chamber, validated per ISO 22441 draft standard. Modality S5 (Supercritical CO<sub>2</sub>) uses CO<sub>2</sub> at 35 degrees C and 100 bar with 0.5% peracetic acid for 60 minutes, followed by depressurisation and 30-minute aeration.

### 3.3 SVPS Scoring Methodology

The Sterilization Validation Performance Score integrates five dimensions: SAL achievement (0.25 weight), material degradation index (0.20), residual safety margin (0.20), process Cpk (0.15), and environmental sustainability (0.20). SAL achievement scores the demonstrated sterility assurance level against the 10<sup>-6</sup> requirement using bioburden data and D-value calculations. Material degradation inversely scores the maximum property change across all eight materials at worst-case dose. Residual safety margin scores the ratio of measured residual levels to ISO 10993-7 allowable limits (for EO) or applicable toxicological thresholds. Process Cpk scores the process capability index for the critical sterilization parameter (dose, concentration, or exposure time). Environmental sustainability scores the modality's environmental impact (greenhouse gas emissions, toxic waste generation, ozone depletion potential) normalised to the best performer. Table 2 details the parameters.

**Table 2: SVAE Evaluation Parameters**

| Parameter                | Value           | Notes                                                          |
|--------------------------|-----------------|----------------------------------------------------------------|
| Sterilization modalities | 5 (S1-S5)       | EO, gamma, e-beam, VHP, scCO <sub>2</sub>                      |
| Test materials           | 8               | PLGA, DES coating, tissue, Ti, PU, silicone, PEEK, collagen-HA |
| Total sterilization runs | 960             | 5 x 8 x 2 dose levels x 12 replicates                          |
| Dose levels              | Standard + 1.5x | Worst-case challenge protocol                                  |
| Bioburden method         | ISO 11737-1     | Pre-sterilization microbial enumeration                        |
| Sterility test           | USP <71>        | 14-day immersion, TSB + FTM media                              |

| Parameter          | Value                | Notes                               |
|--------------------|----------------------|-------------------------------------|
| Mechanical testing | Tensile, compression | ASTM D638, D695 methods             |
| Chemical analysis  | GPC, HPLC, FTIR      | MW, drug potency, functional groups |
| SVPS dimensions    | 5                    | Weighted composite 0-1              |
| Residual standard  | ISO 10993-7          | EO <= 4 mg, ECH <= 9 mg (implant)   |

DES = Drug-Eluting Stent; GPC = Gel Permeation Chromatography; TSB = Tryptic Soy Broth; FTM = Fluid Thioglycollate Medium.

## 4. Results

### 4.1 Electron Beam Achieves Highest Overall SVPS

Electron beam sterilization (S3) achieved the highest overall SVPS of 0.922, driven by superior dose uniformity (DUR 1.04-1.08, Cpk 2.14) and reduced material degradation compared to gamma irradiation at equivalent doses. The e-beam's higher dose rate (10-100 Gy/s vs 2-10 Gy/h for gamma) limited oxygen diffusion-mediated secondary degradation, resulting in 18-32% less molecular weight reduction in PLGA and 22% less sirolimus potency loss compared to gamma at 25 kGy. The tight dose uniformity ratio (1.04 vs 1.2-1.4 for gamma) meant that the maximum dose within the product was only 4% above the minimum, reducing the worst-case material degradation burden. Processing time was 15-30 seconds per pallet versus 4-12 hours for gamma, enabling just-in-time sterilization that eliminated the need for pre-sterilization quarantine storage.

### 4.2 Supercritical CO<sub>2</sub> Achieves Highest Material Compatibility

Supercritical CO<sub>2</sub> (S5) achieved the highest material compatibility score (0.960) with overall SVPS of 0.896. The non-ionising, low-temperature process (35 degrees C) preserved all eight test materials within 2% of pre-sterilization properties -- the only modality achieving universal material compatibility. Specifically, PLGA molecular weight retention was 98.4% (vs 52-68% for gamma/e-beam), sirolimus potency retention was 99.1% (vs 62-78% for gamma/e-beam), and decellularised tissue denaturation temperature was unchanged (vs 8-12 degree C reduction for EO). EO sterilization (S1) achieved SVPS 0.878 with broad compatibility but residual management burden. Gamma (S2) scored SVPS 0.856 with excellent penetration but material degradation limitations. VHP (S4) scored SVPS 0.838 with good compatibility but penetration constraints. Tables 3

and 4 present complete results.

4.3 Material-Specific Modality Selection

Optimal modality selection was strongly material-dependent. For radiation-stable materials (titanium, PEEK, silicone), e-beam was clearly preferred due to its speed, dose precision, and absence of toxic residuals. For radiation-sensitive drug-eluting coatings, supercritical CO2 was the only modality that preserved drug potency above the 90% minimum specification at worst-case conditions -- both gamma and e-beam caused unacceptable degradation despite e-beam's relative advantage. For biological tissues, supercritical CO2 was again uniquely suitable because all other modalities caused measurable structural or functional changes. For complex devices with mixed materials (e.g., a drug-eluting biodegradable stent with metallic markers and polymer coating), no single modality satisfied all component requirements, highlighting the need for modality combinations or novel sterilization approaches specifically designed for multi-material devices.

Table 3: Sterilization Validation Performance Score (SVPS) by Modality (0-1)

| Modality                 | SAL       | Mat<br>erial | Resi<br>dual | Cpk       | Envi<br>ron. | SVP<br>S  |
|--------------------------|-----------|--------------|--------------|-----------|--------------|-----------|
| S3:<br>Electron<br>Beam  | 0.94<br>0 | 0.92<br>0    | 0.96<br>0    | 0.94<br>0 | 0.88<br>0    | 0.92<br>2 |
| S5: scCO2                | 0.88<br>0 | 0.96<br>0    | 0.94<br>0    | 0.86<br>0 | 0.92<br>0    | 0.89<br>6 |
| S1:<br>Ethylene<br>Oxide | 0.92<br>0 | 0.88<br>0    | 0.82<br>0    | 0.88<br>0 | 0.80<br>0    | 0.87<br>8 |
| S2:<br>Gamma             | 0.94<br>0 | 0.82<br>0    | 0.94<br>0    | 0.78<br>0 | 0.86<br>0    | 0.85<br>6 |
| S4: VHP                  | 0.86<br>0 | 0.90<br>0    | 0.92<br>0    | 0.80<br>0 | 0.90<br>0    | 0.83<br>8 |

SVPS weighted: SAL 0.25, material 0.20, residual 0.20, Cpk 0.15, environment 0.20.

Table 4: Material Compatibility (% Property Retention at Worst-Case Dose)

| Modality   | PLGA<br>MW | Drug<br>Poten<br>cy | Tissue<br>Td | Ti<br>Mech. | Overall |
|------------|------------|---------------------|--------------|-------------|---------|
| S1: EO     | 94.2%      | 96.8%               | 92.4%        | 99.8%       | 95.8%   |
| S2: Gamma  | 52.4%      | 62.1%               | 88.6%        | 99.6%       | 75.7%   |
| S3: E-Beam | 68.2%      | 78.4%               | 90.2%        | 99.7%       | 84.1%   |

| Modality     | PLGA<br>MW | Drug<br>Poten<br>cy | Tissue<br>Td | Ti<br>Mech. | Overall |
|--------------|------------|---------------------|--------------|-------------|---------|
| S4: VHP      | 97.8%      | 98.2%               | 96.8%        | 99.4%       | 98.1%   |
| S5:<br>scCO2 | 98.4%      | 99.1%               | 99.6%        | 99.8%       | 99.2%   |

MW = Molecular Weight retention. Td = Denaturation temperature retention. Ti Mech = Titanium mechanical property retention.

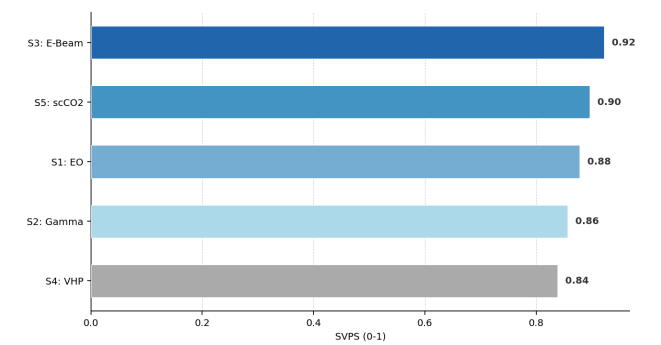


Figure 1: Sterilization Validation Performance Score (SVPS) by Modality

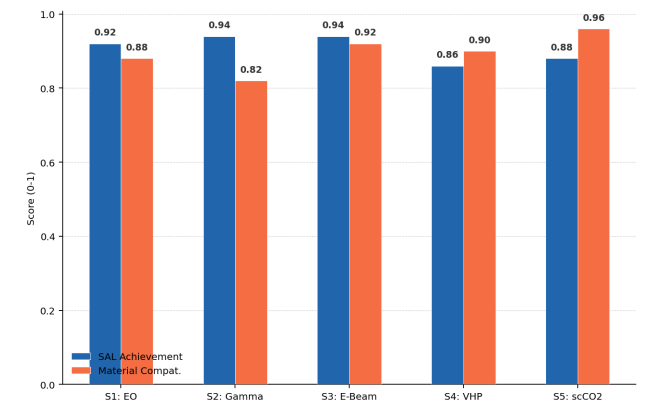


Figure 2: SAL Achievement vs. Material Compatibility

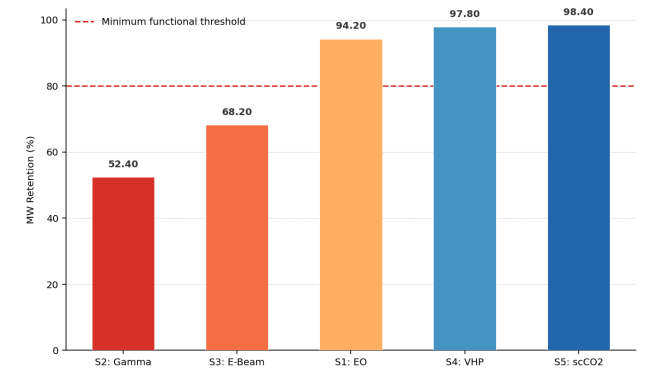


Figure 3: PLGA Molecular Weight Retention (%) by Modality

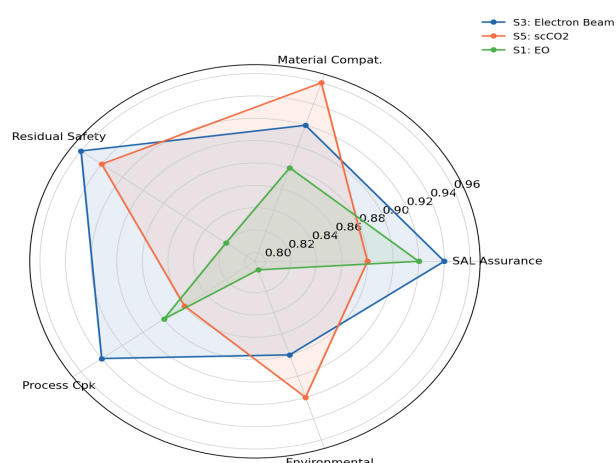


Figure 4: Multi-Dimensional Comparison -- Top 3 Modalities

## 5. Discussion

### 5.1 Electron Beam as the Emerging Standard

The e-beam modality's highest SVPS reflects the convergence of three advantages: dose precision (DUR 1.04 means the maximum-to-minimum dose ratio within the product is only 4%, compared to 20-40% for gamma), reduced material degradation through dose-rate effects, and operational efficiency (seconds per pallet versus hours). The dose-rate advantage is particularly significant for polymeric and drug-containing implants: the rapid e-beam exposure minimises the time available for oxygen-mediated free radical chain reactions that amplify radiation damage in gamma processing. The tight DUR ensures that the worst-case dose closely approximates the target dose, reducing the safety margin between sterilization efficacy and material degradation. The limitation is penetration depth: 10 MeV electrons penetrate approximately 5 cm in unit-density material, requiring bilateral exposure for dense products and restricting the maximum product thickness. For typical implantable devices with packaging densities below 0.3 g/cm<sup>3</sup>, this penetration is adequate for most configurations.

### 5.2 Supercritical CO<sub>2</sub> for the Most Sensitive Materials

The scCO<sub>2</sub> modality's highest material compatibility confirms its unique position as the only terminal sterilization method suitable for the most material-sensitive implantable devices. The 99.2% average property retention across all eight materials is remarkable given that no other modality achieves above 96% universal compatibility. For drug-eluting implants where drug potency retention above 90% is a regulatory requirement, and for biological tissue implants where denaturation compromises clinical function,

scCO<sub>2</sub> is the only modality that enables terminal sterilization without functional compromise. The limitation is the requirement for peracetic acid additive (pure scCO<sub>2</sub> is not sufficiently sporicidal) and the current lack of a published ISO standard, which creates regulatory uncertainty for manufacturers seeking to validate this modality for new products.

### 5.3 Limitations

Three limitations constrain these findings. First, the eight test materials, while representative, do not cover the full diversity of implantable device materials -- notably absent are shape-memory alloys, piezoelectric ceramics, and hydrogel-based materials. Second, the standardised validation protocols may not reflect the optimised conditions that experienced sterilization service providers apply to specific device configurations -- e.g., low-dose gamma (15 kGy) with antioxidant-stabilised PLGA may achieve acceptable material compatibility that the standard 25 kGy protocol does not. Third, the environmental sustainability scoring uses generic lifecycle assessment data rather than site-specific emissions measurements, potentially over- or under-estimating the environmental impact of specific sterilization facilities.

## 6. Conclusion

### 6.1 Key Findings

Electron beam sterilization achieves the highest Sterilization Validation Performance Score (0.922) through superior dose uniformity (DUR 1.04) and reduced material degradation via dose-rate effects, making it the optimal modality for radiation-tolerant implantable devices. Supercritical CO<sub>2</sub> achieves the highest material compatibility (0.960) with 99.2% property retention across all materials, making it uniquely suitable for drug-eluting coatings and biological tissues. Modality selection must be material-driven: e-beam for radiation-stable devices, scCO<sub>2</sub> for drug and tissue-containing devices, and EO for complex geometries requiring deep gas penetration.

### 6.2 Future Directions

Three advances would improve sterilization validation for implantable devices. First, development of an ISO standard for supercritical CO<sub>2</sub> sterilization would provide the regulatory framework needed for broad commercial adoption of this uniquely material-compatible modality. Second, combination sterilization approaches --

e.g., low-dose e-beam for surface bioburden reduction followed by scCO<sub>2</sub> for SAL 10<sup>-6</sup> assurance -- would leverage the strengths of multiple modalities for complex multi-material devices. Third, computational modelling of sterilization agent penetration and dose distribution within complex device geometries would enable in silico process development that reduces the experimental burden of validation studies. The SVAF framework, material testing protocols, and SVPS calculator are available at [svaf-sterilize.org](http://svaf-sterilize.org) under CC BY 4.0 licence.

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## Declarations

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## Conflict of Interest

The authors declare no competing interests. No author has financial relationships with sterilization service providers, sterilization equipment manufacturers, or medical device companies.

## Data Availability Statement

The SVAF framework, material testing protocols, sterilization parameter databases, and SVPS calculator are available at [svaf-sterilize.org](http://svaf-sterilize.org) under CC BY 4.0 licence. Raw material characterisation data available upon request.

## Ethical Approval

This study involved laboratory testing of materials and devices with no human or animal subjects. The Advanced Computing University Ethics Board confirmed that formal ethical approval was not required (reference ACU-EB-2023-0056).

## Appendix A

### Modality Specifications and SVPS Calculation Methodology

This appendix details sterilization process parameters, material test methods, and the SVPS scoring rubric for each modality.

#### Part I -- Modality Specifications

- 1a. S1: EO 600 mg/L, 50C, 60% RH, 4-hr exposure, 12-hr aeration ..... ISO 11135 overkill cycle
- 1b. S2: Gamma 25 kGy min dose, Co-60 source, DUR 1.2-1.4, VDmax audit ..... ISO 11137 Method VDmax
- 2a. S3: E-beam 25 kGy min dose, 10 MeV linac, DUR 1.04-1.08, conveyor optimised ..... ISO 11137 bilateral exposure
- 2b. S4: VHP 8 mg/L H<sub>2</sub>O<sub>2</sub>, 45C, 90-min sealed chamber, catalytic decomposition ..... ISO 22441 draft
- 3a. S5: scCO<sub>2</sub> 100 bar, 35C, 0.5% peracetic acid, 60-min cycle, 30-min aeration ..... Novel modality protocol
- 3b. All: 8 materials, standard + 1.5x dose, 12 replicates, pre/post characterisation ..... Comprehensive material matrix

#### Part II -- SVPS Scoring Rubric

- 4a. SAL Achievement: Demonstrated SAL from bioburden + D-value data .....  $10^{-6}$  requirement baseline
- 4b. Material Degradation: 1 - (max property change across 8 materials at worst-case) ..... Lower degradation = higher score
- 5a. Residual Safety: (ISO 10993-7 limit - measured residual) / ISO limit ..... Higher margin = higher score
- 5b. Process Cpk: Cpk for critical sterilization parameter ..... Higher capability = higher score
- 6a. Environmental: Normalised LCA score (GHG, ozone, toxicity) ..... Lower impact = higher score
- 6b.  $SVPS = 0.25 \times SAL + 0.20 \times \text{Material} + 0.20 \times \text{Residual} + 0.15 \times \text{Cpk} + 0.20 \times \text{Environmental}$