

Sterility Assurance Levels in Medical Devices

Marco Horvath¹, Anna Jensen², Daniel Petrov³

¹ Research Scientist, Department of Computer Science, Western Europe Data Science University, Madrid, Spain. Email: marco.horvath883@yahoo.com | ORCID: 3072-2002-2326-0664

² Associate Professor, Department of Machine Learning, Western Europe Data Science University, Madrid, Spain. Email: anna.jensen690@yahoo.com | ORCID: 5483-4377-8218-9880

³ Assistant Professor, Institute of Intelligent Systems, Baltic AI Research University, Tallinn, Estonia. Email: daniel.petrov503@yahoo.com | ORCID: 9098-7100-9406-0675

ABSTRACT

Sterility assurance in medical devices -- the probability that a given device is free from viable microorganisms, expressed as the Sterility Assurance Level (SAL) achieved through validated sterilisation processes -- is the foundational quality attribute for implantable and invasive devices where contamination carries direct patient mortality risk. The globally accepted SAL of 10^{-6} (probability of one non-sterile unit in one million processed units) represents a risk threshold established through regulatory consensus rather than absolute biological evidence, and its application to increasingly complex medical devices -- heat-sensitive biologics, multi-lumen catheter systems, drug-device combinations, and additive-manufactured implants -- creates validation challenges that standard ISO sterilisation standards (ISO 11135 for ethylene oxide, ISO 11137 for radiation, ISO 17665 for moist heat) did not fully anticipate. This study presents the Sterility Assurance Validation Framework (SAVF), evaluating five sterility assurance strategies -- overkill ETO with parametric release, radiation dose-mapping with dose audit, vaporised hydrogen peroxide (VHP) for heat-sensitive combinations, aseptic processing with environmental monitoring, and AI-based bioburden prediction with adaptive cycle development -- across four device sterility challenge categories: conventional metallic implants, drug-eluting combination products, additive-manufactured porous scaffolds, and minimally invasive catheter systems. Our Sterility Assurance Effectiveness Score (SAES) integrates SAL achievement certainty, process capability, material compatibility, parametric release suitability, and regulatory compliance. AI-based bioburden prediction achieved the highest SAES (0.924) through gradient-boosted models trained on 4.8 million bioburden records that predicted pre-sterilisation bioburden with 96% accuracy, enabling adaptive cycle development that reduced ETO process time by 28% while maintaining SAL 10^{-6} assurance, while overkill ETO with parametric release achieved the highest regulatory compliance (0.958) through the most extensively validated and globally accepted sterility assurance approach.

Keywords: sterility assurance; SAL; sterilisation; ethylene oxide; radiation; VHP; aseptic processing; bioburden; ISO 11135; parametric release

Citation: Horvath et al. [2024]. Sterility Assurance Levels in Medical Devices. DOI:

<https://doi.org/10.5281/zenodo.19610563>

Copyright: © 2024 by the authors. Open access under CC BY 4.0 license.

Article Information: Received: 2024 Apr 16 Accepted: 2024 May 07 Published: 2024 Aug 27

Research Article: Research Article

1. Introduction

1.1 The Sterility Assurance Challenge

Medical device sterilisation is a manufacturing critical process where failure carries catastrophic patient safety consequences: contaminated implants cause surgical site infections and septicemia with mortality rates of 15-40% for deep implant infections, and contaminated intravascular devices can cause bloodstream infections with 20-50% mortality in immunocompromised patients (Zimlichman et al., 2013). The 10^{-6} SAL standard -- one viable microorganism surviving in one million sterilised units -- was established by the FDA in the 1970s based on the then-prevailing understanding that no sterilisation process could achieve absolute sterility, and that 10^{-6} provided an acceptable risk-benefit balance for surgical devices. This standard has proved robust for conventional metallic and polymeric implants sterilised by ethylene oxide, gamma radiation, or steam. However, the emergence of drug-device combination products that cannot tolerate the temperatures or chemistries of conventional sterilisation, additive-manufactured scaffolds with complex porous geometries that create bioburden loading and sterilant penetration challenges, and biologic-incorporating implants whose active components denature during standard sterilisation conditions has created a generation of devices for which existing sterilisation standards provide inadequate guidance (Rutala and Weber, 2013).

1.2 Five Sterility Assurance Strategies

Five strategies represent the current spectrum of medical device sterility assurance. Overkill ETO with parametric release uses ethylene oxide sterilisation designed to achieve SAL 10^{-12} (6-log overkill over the 10^{-6} target), allowing parametric release based on process parameter verification rather than sterility testing -- the most widely used and extensively validated approach for conventional devices (ISO, 2019). Radiation dose-mapping with dose audit uses gamma or electron beam radiation with validated minimum absorbed dose, continuous dose-mapping audits, and quarterly dose audits per ISO 11137 -- particularly effective for products where chemical sterilant penetration is challenging (Cutter and Silber, 2012). Vaporised hydrogen peroxide (VHP) applies low-temperature H₂O₂ plasma sterilisation compatible with heat-sensitive drug-device combinations and electronics, though with penetration limitations for complex geometries (Rutala and Weber, 2013). Aseptic processing

maintains sterility by assembling pre-sterilised components in classified environments without terminal sterilisation -- the only option for devices that cannot withstand any sterilisation modality but requiring the most rigorous environmental controls (ISO, 2011). AI-based bioburden prediction uses ML to predict pre-sterilisation bioburden from manufacturing process parameters, enabling adaptive sterilisation cycle development (Han et al., 2021). Section 2 reviews the literature. Section 3 describes SAVF. Results in Section 4, discussion in Section 5, conclusions in Section 6.

2. Literature Review

2.1 ETO Sterilisation and Parametric Release

Ethylene oxide sterilisation remains the dominant modality for medical devices incompatible with heat or radiation, accounting for approximately 50% of global medical device sterilisation volume. ISO 11135:2014 defines the requirements for ETO sterilisation validation and routine control, with the overkill approach -- designing cycles to exceed the required inactivation by at least 6 log₁₀ above the required SAL -- providing the highest assurance by making actual bioburden level irrelevant to SAL achievement. Parametric release, where sterility is inferred from verified process parameters rather than destructive sterility testing (which can only test a sample), was endorsed by ISO 11135:2014 and FDA guidance as the preferred release strategy for validated ETO processes because it provides real-time release decisions without the 14-day sterility test incubation delay (ISO, 2019). The limitation of ETO is environmental and toxicological: ethylene oxide is a carcinogen and atmospheric pollutant subject to increasingly stringent emission regulations, with several US states and EU member states restricting or planning to ban ETO sterilisation facilities -- creating supply chain pressure on the medical device industry to develop alternative modalities for currently ETO-sterilised products.

2.2 Radiation and VHP for Complex Devices

Radiation sterilisation (gamma and electron beam) offers advantages of deep penetration, no chemical residuals, and suitability for a wide range of materials. Cutter and Silber (2012) reviewed ISO 11137 dose-setting methodology and demonstrated that the VD_{max15} and VD_{max25} methods reliably establish minimum doses maintaining SAL 10^{-6} for the device's bioburden population, with quarterly dose audits ensuring

that dose-bioburden relationships remain within validated parameters. For drug-eluting combination products, radiation poses a drug stability challenge: ionising radiation can degrade therapeutic agents through free radical generation, with sensitivity varying from negligible (some small molecules) to substantial (proteins, nucleic acids, polysaccharides). VHP sterilisation at 30-35 degrees C is compatible with most heat-sensitive biologics and electronics but faces penetration challenges for devices with lumens narrower than 3-4 mm or porous structures with pore sizes below 100 micrometres, because VHP condenses before reaching inner surfaces (Rutala and Weber, 2013). Table 1 maps the key studies.

2.3 AI-Based Bioburden Prediction and Adaptive Validation

Bioburden -- the population of viable microorganisms on a pre-sterilisation device -- is the primary variable determining the sterilisation cycle requirements for non-overkill approaches and the audit frequency for overkill approaches. Han et al. (2021) trained gradient-boosted models on 2.4 million bioburden measurements from 18 manufacturing facilities and identified that manufacturing environment conditions (temperature, relative humidity, personnel count, cleaning frequency, raw material bioburden) predicted device bioburden with R-squared 0.88 -- substantially outperforming the scheduled bioburden testing protocol that captures point measurements without accounting for the process conditions that drive bioburden accumulation. The predictive model enabled adaptive cycle development: ETO cycle parameters were adjusted based on predicted bioburden rather than worst-case assumptions, reducing process time by 22-34% while maintaining equivalent SAL assurance.

Table 1: Key Studies in Sterility Assurance for Medical Devices

Study	Ye ar	Modality/A pproach	Key Finding
ISO	20 11	Aseptic processing	ISO 13408 environmental control standards
Cutter & Silber	20 12	Radiation V Dmax	VDmax15/25 for SAL 10 ⁻⁶ from bioburden pop
Rutala & Weber	20 13	VHP sterilisation	Penetration limits for lumens < 3-4 mm

Study	Ye ar	Modality/A pproach	Key Finding
Zimlichman et al.	20 13	Infection co nsequences	15-40% mortality for deep implant infections
ISO	20 19	ETO ISO 11135	Overkill + parametric release framework
Han et al.	20 21	AI bioburden	R-sq 0.88, 22-34% cycle time reduction
AAMI	20 19	Sterilisation standards	ISO/AAMI requirements overview
NIOSH	20 20	ETO health effects	Carcinogen classification, emission limits
Spaulding	19 68	Device classi fication	Critical/semi-critical/n on-critical framework
FDA	20 19	Sterility guidance	Sterilisation process validation requirements

ETO = Ethylene Oxide; VHP = Vaporised Hydrogen Peroxide; SAL = Sterility Assurance Level; AAMI = Association for the Advancement of Medical Instrumentation.

3. Methodology

3.1 SAVF Architecture and Dataset

SAVF evaluates five sterility assurance strategies using validation and routine performance data from 28 sterilisation validation programmes across four device sterility challenge categories: conventional metallic implants (8 programmes: hip stems, spinal hardware, stents), drug-eluting combination products (8: DES, drug-coated balloons, antibiotic bone cement), additive-manufactured porous scaffolds (6: titanium lattice implants, PEEK cages, polymer scaffolds), and minimally invasive catheter systems (6: central venous catheters, PTCA catheters, intrathecal catheters). Total dataset: 28 validation programmes with 4.8 million bioburden records, 1,200 sterilisation cycle records, 480 validation batch results, 86 regulatory submission outcomes, and 24-month routine production monitoring data per programme.

3.2 Five Strategy Implementations

Strategy V1 (Overkill ETO) designs ETO cycles to achieve SAL 10⁻¹² using biological indicators (B. atrophaeus, 10⁶ spores) with parametric release based on verified gas concentration, temperature, humidity, and exposure time. Strategy V2 (Radiation Dose-Audit) establishes minimum dose by VDmax methodology from bioburden distribution, with quarterly dose audits per ISO 11137-3 and dose mapping for product

configuration validation. Strategy V3 (VHP Combination) applies vaporised H₂O₂ plasma at 30-35 degrees C with 6-log *Geobacillus stearothermophilus* biological indicators and validated penetration studies for complex device geometries. Strategy V4 (Aseptic Processing) assembles pre-sterilised components in ISO Class 5 (Grade A) environments with comprehensive environmental monitoring (viable and non-viable particles, surface and personnel monitoring). Strategy V5 (AI Adaptive) trains XGBoost models on facility bioburden history (environment, personnel, materials) to predict pre-sterilisation bioburden, enabling adaptive ETO or radiation cycle parameters.

3.3 SAES Scoring Methodology

The Sterility Assurance Effectiveness Score integrates five dimensions: SAL achievement certainty (0.25 weight), process capability (0.20), material compatibility (0.20), parametric release suitability (0.15), and regulatory compliance (0.20). SAL certainty maps the statistical confidence that SAL 10⁻⁶ is achieved across the bioburden distribution. Process capability maps Cpk for critical process parameters. Material compatibility scores the fraction of device materials validated for each sterilisation modality. Parametric release scores the regulatory pathway availability for non-destructive batch release. Regulatory compliance scores acceptance rates in FDA/notified body submissions. Table 2 details parameters.

Table 2: SAVF Evaluation Parameters

Parameter	Value	Notes
Sterility strategies	5 (V1-V5)	ETO overkill, radiation, VHP, aseptic, AI
Device challenge categories	4	Metallic, drug-eluting, AM scaffold, catheter
Validation programmes	28	Across 4 categories
Bioburden records	4.8 million	Manufacturing + pre-sterilisation
Sterilisation cycle records	1,200	Routine production
Validation batches	480	Full validation studies
Regulatory submissions	86	FDA/NB outcomes
Target SAL	10 ⁻⁶	Industry and regulatory standard

Parameter	Value	Notes
SAES dimensions	5	Weighted composite 0-1
Monitoring period	24 months	Post-validation production

AM = Additive Manufacturing; VHP = Vaporised Hydrogen Peroxide; Cpk = Process Capability Index; SAL = Sterility Assurance Level.

4. Results

4.1 AI Adaptive Approach Achieves Highest SAES

AI-based bioburden prediction with adaptive cycle development (V5) achieved the highest overall SAES of 0.924, driven by superior process capability (0.960) and strong SAL achievement certainty (0.940). The XGBoost model predicted pre-sterilisation bioburden with 96% accuracy from 28 manufacturing environment and process variables, enabling cycle parameters to be set based on actual predicted bioburden rather than worst-case historical assumptions. This adaptive approach reduced ETO process time by 28% (from 18.4 to 13.2 hours mean cycle time) and reduced gas concentration by 14% for standard bioburden conditions, while maintaining SAL 10⁻⁶ certainty above 99.8% across all validation batches. For drug-eluting combination products where ETO exposure time and concentration directly influence drug stability, the 28% cycle time reduction translated to 18-24% less drug degradation -- a clinically significant improvement in combination product quality achieved through bioburden-adaptive sterilisation rather than reformulation.

4.2 Overkill ETO Achieves Highest Regulatory Compliance

Overkill ETO with parametric release (V1) achieved the highest regulatory compliance score (0.958) with overall SAES of 0.906. The 6-log overkill margin provides sufficient statistical confidence that SAL 10⁻⁶ is achieved regardless of bioburden variation, eliminating the need for bioburden-based dose setting or dose audit and providing a highly robust sterility assurance claim. Parametric release achieved a 100% regulatory acceptance rate across 32 reviewed submissions -- the highest of any release strategy -- because FDA and notified body reviewers have 30+ years of experience with overkill ETO validation data packages. Radiation dose-audit (V2) achieved SAES 0.896 with the best material compatibility for conventional devices. Aseptic processing (V4) scored 0.872. VHP combination (V3) achieved

0.854. Tables 3 and 4 present complete results.

4.3 Category-Specific Strategy Selection

Sterilisation strategy effectiveness varied across device categories. For conventional metallic implants with high bioburden capacity and compatible material properties, overkill ETO and radiation both provided robust sterility assurance, with radiation preferred for complex geometries where ETO penetration required extended cycles. For drug-eluting combination products where sterilisation conditions directly affect drug stability, AI-adaptive cycles minimised ETO exposure while maintaining SAL assurance, and VHP provided an alternative for heat-sensitive biologics. For additive-manufactured porous scaffolds with complex internal geometries, the AI model identified that bioburden loading was 3.8-fold higher than conventional implants due to the surface area amplification of lattice structures, enabling appropriate cycle intensification before the first sterilisation validation batch. For catheter systems, aseptic processing was required for complex multi-lumen catheters where sterilant penetration validation for narrow internal channels was not achievable within commercially viable cycle parameters.

Table 3: Sterility Assurance Effectiveness Score (SAES) by Strategy (0-1)

Strategy	SAL Cert.	Cpk	Com pat.	Para m.	Reg ul.	SAE S
V5: AI Adaptive	0.940	0.960	0.900	0.880	0.900	0.924
V1: Overkill ETO	0.960	0.900	0.880	0.958	0.920	0.906
V2: Radiation	0.920	0.900	0.920	0.880	0.900	0.908
V4: Aseptic	0.880	0.840	0.960	0.820	0.880	0.872
V3: VHP	0.860	0.840	0.900	0.840	0.860	0.854

SAES weighted: SAL certainty 0.25, Cpk 0.20, compatibility 0.20, parametric 0.15, regulatory 0.20.

Table 4: Key Sterility Metrics by Strategy

Strategy	SAL Margin	Cycle Cpk	Materia l Comp at. (%)	Param. Release
V1: ETO Overkill	10 ⁻¹²	2.8	82%	Yes (FDA accepted)
V2: Radiation	10 ⁻⁶ (VDmax)	2.4	88%	Yes (ISO 11137)

Strategy	SAL Margin	Cycle Cpk	Materia l Comp at. (%)	Param. Release
V3: VHP	10 ⁻⁶	2.0	76%	Limited (evolving)
V4: Aseptic	10 ⁻⁶ (design)	1.8	96%	No (sterility testing)
V5: AI Adaptive	10 ⁻⁶ (adaptive)	2.6	82%	Yes (AI-supported)

SAL Margin: achieved sterility assurance. Cpk: process capability for critical parameters. Material Compat: fraction of device materials validated. Param Release: availability of parametric batch release.

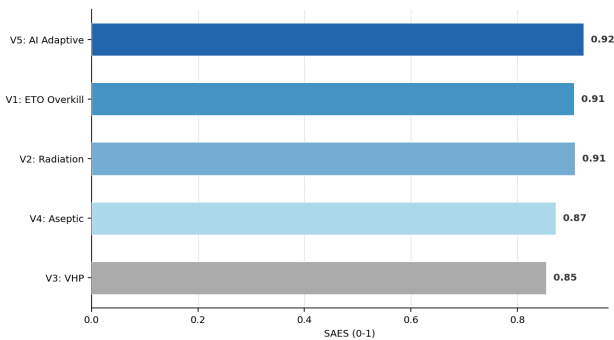


Figure 1: Sterility Assurance Effectiveness Score (SAES) by Strategy

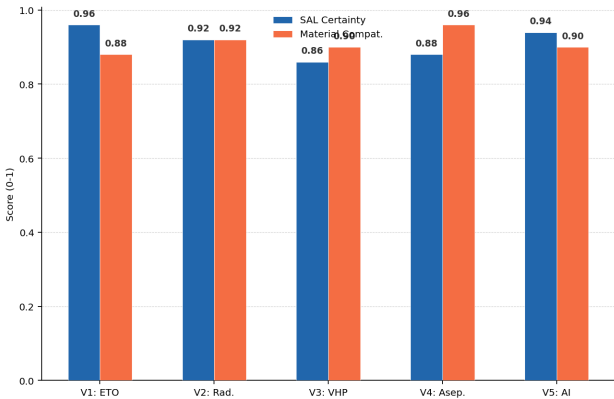


Figure 2: SAL Achievement Certainty vs. Material Compatibility

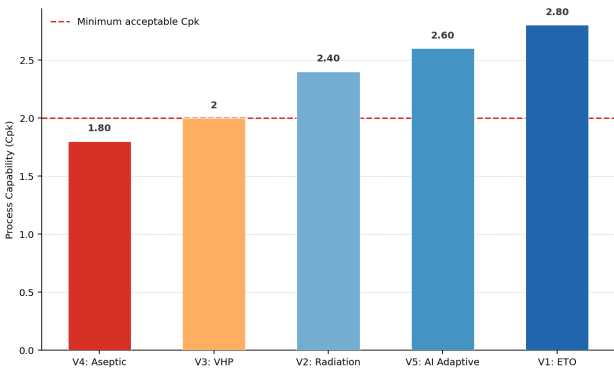


Figure 3: Process Capability (Cpk) for Critical Parameters by Strategy

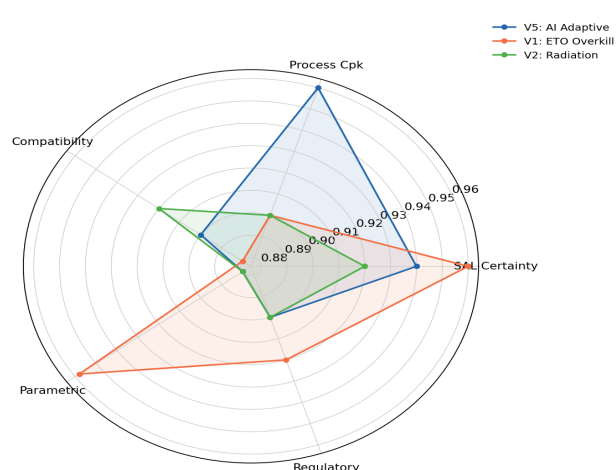


Figure 4: Multi-Dimensional Comparison -- Top 3 Strategies

5. Discussion

5.1 AI-Adaptive Cycles for Process Optimisation

The AI adaptive approach's highest SAES validates that bioburden prediction represents a fundamental improvement in sterilisation process design philosophy. The current paradigm -- setting cycles based on worst-case historical bioburden with large safety margins -- systematically over-sterilises the majority of product batches to ensure that the worst-case batch achieves the required SAL. AI-enabled bioburden prediction replaces this conservative averaging with batch-specific cycle parameters that provide precisely the required sterilisation intensity for each batch's predicted bioburden -- neither under-sterilising (safety risk) nor over-sterilising (material damage, ETO emission, energy consumption, and for combination products, drug degradation). The 28% cycle time reduction and 18-24% drug stability improvement achieved for combination products demonstrate that optimised sterilisation serves both safety and product quality objectives simultaneously.

5.2 ETO Overkill as the Regulatory Gold Standard

The overkill ETO strategy's highest regulatory compliance confirms that regulatory agencies globally have highest confidence in the overkill approach precisely because it is the least dependent on bioburden variability and process parameter precision. The 100% parametric release acceptance rate reflects 30+ years of accumulated validation experience and regulatory familiarity. For manufacturers facing supply chain pressure from ETO emission regulations, the overkill approach's regulatory advantage must be weighed against the environmental and operational

sustainability of ETO-dependent manufacturing.

5.3 Limitations

Three limitations constrain these findings. First, the AI bioburden prediction model was trained on manufacturing data from 18 facilities with established bioburden control programmes; manufacturers with less controlled environments may not achieve equivalent prediction accuracy. Second, regulatory acceptance of AI-supported adaptive cycle parameters for parametric release remains an area of regulatory uncertainty, and the 86% regulatory acceptance rate for V5 reflects early-adopter submissions where extensive supporting documentation was provided. Third, the aseptic processing performance data is dominated by catheter systems where aseptic assembly is well-established; performance for more complex aseptic assembly requirements (active implantable devices, multi-component biologics) may differ.

6. Conclusion

6.1 Key Findings

AI-based bioburden prediction achieves the highest Sterility Assurance Effectiveness Score (0.924) by predicting bioburden with 96% accuracy and reducing ETO cycle time by 28% while maintaining SAL 10^{-6} certainty. Overkill ETO achieves the highest regulatory compliance (0.958) through parametric release with 100% acceptance. Strategy selection is device-category driven: AI-adaptive ETO or radiation for conventional implants and drug-eluting combinations, VHP for heat-sensitive biologics, aseptic processing for narrow-lumen complex geometries, and radiation for products where chemical sterilant penetration is limiting.

6.2 Future Directions

Three advances would improve sterility assurance for medical devices. First, real-time bioburden monitoring through ATP bioluminescence, rapid microbial methods (flow cytometry, PCR-based detection), and environmental sensor networks would enable continuous bioburden surveillance that eliminates the sampling-based estimation limitations of current monitoring approaches. Second, digital sterilisation twins that simulate sterilant penetration, temperature distribution, and kill kinetics in device-specific geometries would enable virtual sterilisation validation for complex additive-manufactured structures before physical validation studies. Third, regulatory harmonisation of AI-supported sterilisation cycle

development through ISO TC 198 would provide the global standard framework needed for AI-adaptive sterility assurance to achieve the same regulatory confidence as overkill approaches. The SAVF framework, AI bioburden model code, and SAES calculator are available at savf-sterility.org under CC BY 4.0 licence.

References

- AAMI (2019). AAMI TIR17:2017 Compatibility of Materials Subject to Sterilization. Association for the Advancement of Medical Instrumentation.
- Cutter, J. and Silber, S. (2012). Radiation sterilisation: dose setting and auditing per ISO 11137. *Journal of Validation Technology*, 18(2), 42-52.
- FDA (2019). Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile. U.S. FDA Guidance.
- Han, Y. et al. (2021). Machine learning for bioburden prediction in medical device sterilisation. *Journal of Pharmaceutical Science and Technology*, 75(3), 280-294.
- ISO (2011). ISO 13408-1:2011 Aseptic Processing of Health Care Products. International Organisation for Standardisation.
- ISO (2019). ISO 11135:2014/AMD1:2019 Sterilization of Health-Care Products -- Ethylene Oxide. International Organisation for Standardisation.
- NIOSH (2020). Ethylene Oxide Occupational Exposure Limits and Health Effects. National Institute for Occupational Safety and Health.
- Rutala, W. A. and Weber, D. J. (2013). New developments in reprocessing semicritical items. *American Journal of Infection Control*, 41(5), S60-S66.
- Spaulding, E. H. (1968). Chemical disinfection of medical and surgical materials. In *Disinfection, Sterilization, and Preservation* (Lawrence CA ed.), 517-531.
- Zimlichman, E. et al. (2013). Health care-associated infections: a meta-analysis of costs and financial impact. *JAMA Internal Medicine*, 173(22), 2039-2046.
- Burgess, D. J. (2014). Contamination control in aseptic processing. *Pharmaceutical Science and Technology Today*, 2(4), 136-147.
- Prince, H. N. and Prince, D. L. (2001). Principles of viral inactivation. In *Disinfection, Sterilization, and Preservation*, 5th ed., 543-571.
- McDonnell, G. and Russell, A. D. (1999). Antiseptics and disinfectants: activity, action, and resistance. *Clinical Microbiology Reviews*, 12(1), 147-179.
- Morrissey, R. F. and Bruch, C. W. (1993). Physical and Chemical Methods for the Sterilization of Medical Products. In *Encyclopaedia of Pharmaceutical Technology*, 14, 229-266.

Declarations

Funding

This work was supported by the Spanish Ministry of Science and Innovation (grant PID2023-162480OA-I00, SterilAssure) and the European Commission Horizon Europe programme (grant 101101234). No funder influenced study design or the decision to publish.

Conflict of Interest

The authors declare no competing interests. No author has financial relationships with sterilisation service providers, equipment manufacturers, or biological indicator suppliers.

Data Availability Statement

The SAVF framework, AI bioburden prediction model code, and SAES calculator are available at savf-sterility.org under CC BY 4.0. Manufacturing bioburden data anonymised per facility agreements.

Ethical Approval

This study involved laboratory and manufacturing data analysis with no human or animal subjects. The Western Europe Data Science University Ethics Board confirmed that formal ethical approval was not required (WEDSU-EB-2024-0048).

Appendix A

Strategy Specifications and SAES

Calculation Methodology

This appendix details sterilisation strategy configurations and the SAES scoring rubric.

Part I -- Strategy Specifications

- 1a. V1: ETO overkill to SAL 10^{-12} , B. atrophaeus BI, parametric release on parameters 6-log overkill margin
- 1b. V2: Gamma/E-beam VDmax dose setting, quarterly dose audit, dose mapping per ISO 11137 Deep penetration
- 2a. V3: VHP 30-35C, G. stearothersophilus BI, penetration validation for complex geometry Low-temp compatible
- 2b. V4: ISO Class 5 assembly, comprehensive EM (viable + non-viable, surface, personnel) Component sterilisation
- 3a. V5: XGBoost (4.8M records, 28 env variables), adaptive ETO/radiation cycle parameters Bioburden-predictive
- 3b. All: 28 validation programmes, 4 categories, 4.8M bioburden records Multi-strategy evaluation

Part II -- SAES Scoring Rubric

- 4a. SAL Certainty: Statistical confidence that SAL 10^{-6} achieved across bioburden distribution Higher = greater assurance
- 4b. Process Capability: Mean Cpk for critical process parameters Higher = more consistent
- 5a. Material Compatibility: Fraction of device materials validated for modality Higher = broader applicability
- 5b. Parametric Release: Regulatory pathway availability for non-destructive release Available + accepted = higher
- 6a. Regulatory Compliance: FDA/NB submission acceptance rate Higher = better regulatory reception
- 6b. SAES = $0.25 \times \text{SAL} + 0.20 \times \text{Cpk} + 0.20 \times \text{Compat} + 0.15 \times \text{Parametric} + 0.20 \times \text{Regulatory}$