DHF Impact and Actions Recommendation – ISO 10993-7:2026

Design History File (DHF) Impact Analysis

Gap Assessment: ISO 10993-7:2026 versus ISO 10993-7:2008+A1
Document Type: Design History File (DHF) Impact Analysis
Standard Reference: ISO 10993-7:2026 – Biological evaluation of medical devices – Part 7: Ethylene oxide sterilization residuals
Date: August 18, 2026
Revision: 01

1. Executive Summary

ISO 10993-7:2026 shifts the standard from a largely descriptive, fixed-dose framework to a quantitative, formula-driven risk model for ethylene oxide (EO) and ethylene chlorohydrin (ECH) residuals. The attached gap assessment's consolidated conclusion states that the 2026 edition introduces quantitative formulae, expanded categorization logic, and explicit tolerable intake (TI) and allowable limit (AL) calculations for EO and ECH, emphasizing risk-based assessment, patient population specificity, and structured calculation protocols, moving beyond the descriptive toxicological focus of the 2008/A1 edition.

Key Impact Areas for DHF:

- A new mandatory formula set for allowable limits — TE = TI × mb × CEF and AL = TE × (D/N) — replacing the 2008/A1 edition's fixed adult dose caps for every exposure category.
- Renamed and restructured exposure categories (limited, prolonged, long-term exposure replacing "permanent contact" language), with explicit cumulative-contact thresholds omitted and new provisions added for very brief contact and residual materials.
- Explicit tolerable intake (TI) values defined for EO and ECH across limited, prolonged, and long-term exposure, including separate adult and paediatric worked calculations and defined body-mass assumptions down to very-low-birthweight infants (0.5 kg).
- A largely new set of device-specific special-situation limits (blood cell separators, extracorporeal blood purification, peritoneal dialysis, blood oxygenators/reservoirs, cardiopulmonary bypass devices, loose-skin-contact devices) replacing the single consolidated table in the 2008/A1 edition.
- Two brand-new tolerable contact level (TCL) clauses for EO (10 µg/cm²) and ECH (5 mg/cm²) with an ISO 10993-23 non-irritation alternative pathway.
- New clauses for multi-device systems/convenience kits, aeration-family adoption, and mandatory change evaluation whenever product, packaging, exposure, patient population, device count, or sterilization process changes.
- Expanded analytical method validation requirements and a statistically defined batch-release model using a 95% confidence/prediction limit in place of the 2008/A1 edition's simpler dissipation-curve and no-dissipation-curve release pathways.

This document converts the attached ISO 10993-7:2026 versus 2008+A1 comparison into a DHF impact-and-actions recommendation using the same structured implementation style reflected in prior DHF impact assessments prepared for this program.

2. Key Changes Summary

2.1 General Requirements and Scope (Clause 4.1)

Change: Clause 4.1 clarifies allowable limits (ALs) for EO/ECH, references ISO 10993-1:2025, and exempts devices already tested to the previous edition unless Clause 10 issues arise under ISO 10993-1:2025. The 2008/A1 edition required ISO 10993-3, ISO 10993-10, and an explicit ethylene glycol (EG) risk assessment — all omitted from the 2026 scope. The 2026 edition also adds an Annex A decision flowchart and NIST-based rounding rules, replacing the 2008/A1 edition's detailed EG/tolerable contact level (TCL) annexes.

DHF Impact:

- Biological risk assessment protocols must be updated to reflect the revised reference set (ISO 10993-1:2025) and the removal of the mandatory EG evaluation.
- Legacy-device files need a documented exemption check confirming no Clause 10 issues exist under ISO 10993-1:2025 before relying on prior test data.
- Risk assessment templates and decision trees should incorporate the new Annex A flowchart logic and NIST rounding convention.

Recommended Actions:

Action	Timeline	Owner	Priority
Update biological risk assessment protocols to remove mandatory EG evaluation and add ISO 10993-1:2025 references	3 weeks	Regulatory / Toxicology	**Critical**
Create a legacy-device exemption checklist tied to ISO 10993-1:2025 Clause 10	3 weeks	Quality Systems	High
Embed the Annex A decision flowchart and NIST rounding rule into risk assessment work instructions	4 weeks	Regulatory Affairs	Medium

2.2 Device Categorization (Clause 4.2)

Change: Clause 4.2 renames exposure categories, replacing "permanent exposure" with "long-term exposure," and omits the 2008/A1 edition's explicit cumulative contact-time thresholds (24 hours, 30 days). It expands requirements for repeated-use devices and adds new provisions for very brief contact and residual materials requiring detailed biological evaluation.

DHF Impact:

- Device classification records across the product portfolio must be re-labeled to the new limited/prolonged/long-term terminology and re-verified against the (now qualitative) categorization logic.
- Repeated-use device files need expanded justification since explicit time thresholds no longer anchor the categorization decision.

- New product-risk files must be created for very-brief-contact devices and devices with residual materials requiring detailed biological evaluation — a category not previously addressed.

Recommended Actions:

Action	Timeline	Owner	Priority
Re-map device categorization records to limited/prolonged/long-term terminology	3 weeks	Regulatory Affairs	**Critical**
Draft a justification procedure for repeated-use device categorization absent fixed time thresholds	4 weeks	Quality Systems	High
Create a new risk-assessment pathway for very-brief-contact devices and residual-material evaluation	4 weeks	Toxicology / Regulatory	High

2.3 Allowable Limits — General Formula Framework (Clause 4.3.1)

Change: Clause 4.3.1 introduces explicit exposure formulae — TE = TI × mb × CEF (tolerable exposure) and AL = TE × (D/N) (allowable limit) — mandates documentation of the lowest intended patient population mass, allows risk-based alternative limits, and requires documented intended-population justification for non-device-based exposure (liquids, powders). The 2008/A1 edition only referenced maximum doses by exposure category and suggested, but did not require, concomitant exposure factor (CEF) or patient exposure factor (PEF) use.

DHF Impact:

- Every EO/ECH allowable-limit calculation across the product portfolio must be converted to the TE/AL formula model, with body mass, CEF, device count (N), and exposure duration (D) all individually documented and traceable.
- DHF records must show the lowest intended patient population mass used in each calculation, with explicit justification when risk-based alternative limits are applied instead of default values.
- Non-device-based exposure pathways (liquids, powders) need a new documentation trail establishing intended population assumptions.

Recommended Actions:

Action	Timeline	Owner	Priority
Build a validated TE/AL calculation template implementing TE = TI × mb × CEF and AL = TE × (D/N)	5 weeks	Regulatory / Biostatistics	**Critical**
Update DHF risk files to record lowest intended patient population mass and justification for risk-based alternative limits	4 weeks	Regulatory Affairs	High
Create a documentation procedure for non-device-based (liquid/powder) exposure population assumptions	4 weeks	Toxicology	Medium

2.4 Limited and Prolonged Exposure Devices (Clauses 4.3.2, 4.3.3)

Change: Clause 4.3.2 sets EO TI = 0.3 mg/kg/day and ECH TI = 0.64 mg/kg/day with a default CEF of 0.2 for limited exposure, replacing the 2008/A1 edition's fixed adult limits (4 mg EO, 9 mg ECH on a 70

kg body-mass basis with PEF). Clause 4.3.3 sets EO TI = 0.3 mg/kg/day and ECH TI = 0.27 mg/kg/day (default CEF 0.2) for prolonged exposure up to 30 days, and mandates that prolonged-exposure devices also meet the limited-exposure AL within the first 24 hours. Worked examples are provided in Annex K for both categories.

DHF Impact:

- All limited- and prolonged-exposure device files currently anchored to the fixed 4 mg EO / 9 mg ECH (or equivalent) adult limits must be recalculated using the new TI/CEF formula set.
- Prolonged-exposure product files need a new first-24-hour compliance check against the limited-exposure AL, layered on top of the 30-day cumulative limit.
- Special-population body-mass justification records (previously only loosely required) must now be integrated with the Annex K worked-example format.

Recommended Actions:

Action	Timeline	Owner	Priority
Recalculate all limited- and prolonged-exposure device ALs using the new TI/CEF formulae	6 weeks	Regulatory / Toxicology	**Critical**
Add a mandatory first-24-hour limited-exposure AL check to prolonged-exposure device release protocols	4 weeks	Quality Systems	High
Align special-population body-mass justification records with Annex K worked-example format	5 weeks	Regulatory Affairs	Medium

2.5 Long-Term Exposure — Ethylene Oxide and Ethylene Chlorohydrin (Clauses 4.3.4.1, 4.3.4.2)

Change: Clause 4.3.4.1 sets EO TI = 0.02 mg/kg/day with explicit adult and paediatric worked formulae and requires long-term-exposure devices to also meet the short-term (24-hour/30-day) thresholds. Clause 4.3.4.2 sets ECH TI = 0.029 mg/kg/day, an adult daily tolerable exposure of 0.35 mg, and a recalculated paediatric value of 0.16 mg/day, again layered on top of the limited/prolonged ALs. The 2008/A1 edition (clauses 4.4.1.2/4.4.1.3) only described the toxicological/carcinogenic profile of EO and ECH narratively, without quantitative long-term limits.

DHF Impact:

- Long-term (formerly "permanent") contact device files require entirely new quantitative EO and ECH long-term exposure calculations — no equivalent existed under the 2008/A1 edition.
- Paediatric exposure files must be created or updated with the recalculated 0.16 mg/day ECH value and corresponding EO paediatric worked example.
- Layered-compliance verification (long-term AND limited/prolonged AND short-term thresholds) must be documented as a single traceable chain per device.

Recommended Actions:

Action	Timeline	Owner	Priority
Develop new long-term EO/ECH TE/AL calculations for all long-term-contact devices (adult and paediatric)	6 weeks	Regulatory / Toxicology	**Critical**