Medtronic

July 30, 2026

Public Comment for the ICCVAM Public Forum

July 29–30, 2026 · NIH Neuroscience Center, Rockville, MD

Submitted by Kelly Coleman, Medtronic; U.S. Expert, ISO/TC 194 Working Group 8

Re: FDA/CDRH recognition of ISO 10993-23:2021

Dear ICCVAM Co-Chairs and Members,

Thank you for the opportunity to provide these oral comments to the ICCVAM Public Forum. I commend the agenda's strong focus on New Approach Methodologies (NAMs), including ORIVA and NICEATM updates and actvities at FDA.
It's time for this momentum to finally reach medical device irritation testing.

The scientific case is settled. A seven-year, ISO/TC 194-sponsored round robin—with 18 laboratories from industry, government, and academia—demonstrated that reconstructed human epidermis (RhE) assays identified irritants and non-irritants with 97.4% accuracy across labs. Follow-up work confirmed RhE models produce results "essentially equivalent" to the in vivo rabbit intracutaneous test and are acceptable replacements for it. Subsequent studies extended applicability to mild irritants and to non-extractable devices. This evidence underpins ISO 10993-23:2021, which specifies that in vitro RhE testing shall be conducted before any in vivo testing is considered.

The method is also robust across independent platforms. Recent "me-too" studies added two RhE models via ISO 10993-23:2021/Amd 1:2025: Japan's LabCyte EPI-MODEL24 (100% sensitivity, 98.9% specificity, 99.5% accuracy across 16 labs) and Korea's KeraSkin (100% within- and between-laboratory concordance, 91.6% accuracy). RhE irritation testing is not tied to any single vendor and continues to gain international qualification.

The regulatory gap—not the science—is now the problem. A 2025 review of all 193 UN Member States found that 191 (99%) directly or indirectly recognize ISO 10993-23:2021 and accept in vitro irritation data; only the United States and Canada do not. Countries accepting these data represent 95% of the world's population and 83% of global GDP (PPP). Meanwhile, Draize rabbit tests conducted by the medical device industry still consume an estimated 50,000 animals annually. FDA/CDRH's non-recognition forces

manufacturers into wasteful dual testing, and ISO/TC 194 and the device community are understandably frustrated.

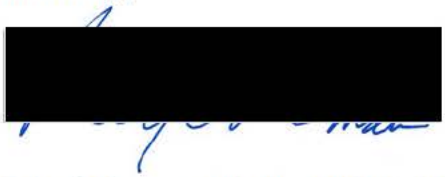
Notably, this position is inconsistent even within FDA. CDER now accepts in vitro dermal irritation data: its list of acceptable NAMs states that “non-animal methods may be used to assess dermal irritation” and that “a 3D reconstructed human epidermis model is accepted for human pharmaceuticals,” referencing OECD 439. If the identical RhE method is acceptable for drugs at CDER, there is no scientific justification for CDRH to reject it for devices.

CDRH professes support for NAMs, yet its Medical Device Development Tools (MDDT) program has never qualified a single in vitro replacement for an animal test since its inception in 2015. CDRH participated in the original validation study and correctly identified 100% of the blinded samples, yet still declines to accept in vitro irritation data. FDA’s 2025 Roadmap commits the agency to reduce animal testing, to leverage ICCVAM for multi-agency validation, and to lead globally in regulatory science. Recognizing an already-validated RhE method would be the fastest, lowest-risk proof of that commitment.

I respectfully urge ICCVAM to encourage FDA/CDRH to work with NIH’s ORIVA and NICEATM to formally recognize ISO 10993-23:2021 and RhE-based in vitro irritation testing. ORIVA’s validation-and-qualification mandate is the ideal vehicle to move this method through MDDT to acceptance, eliminate redundant animal use, and align the U.S. with the rest of the world. Doing so would improve patient safety, reduce cost and animal suffering, and prove that FDA’s NAMs commitments extend to devices, not just drugs.

Thank you for your consideration.

Sincerely,



Kelly Coleman, Ph.D., DABT, ERT, ATS, RAC
Senior Distinguished Toxicologist, Bakken Fellow, Technical Fellow
Medtronic Physiological Research Laboratories
11520 Yellow Pine Street NW
Minneapolis, MN 55448
[redacted]

The views expressed are my own and do not necessarily represent those of Medtronic.