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The industrial perspective through the eyes of consultants

ISO 10993-:2025

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Overview

01 Why ISO 10993-1:2025 Matters

02 How companies are responding

03 Main industries hurdles with industry examples

04 Lessons Learned & Key Takeaways

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Why ISO 10993-1:2025 matters

- Lifecycle approach reinforced
- Stronger integration with ISO 14971 risk management
- Greater emphasis on material, process, and historical knowledge
- Closer alignment with chemistry and toxicology
- Risk-based decision making expected
- Increased scientific justification expectations



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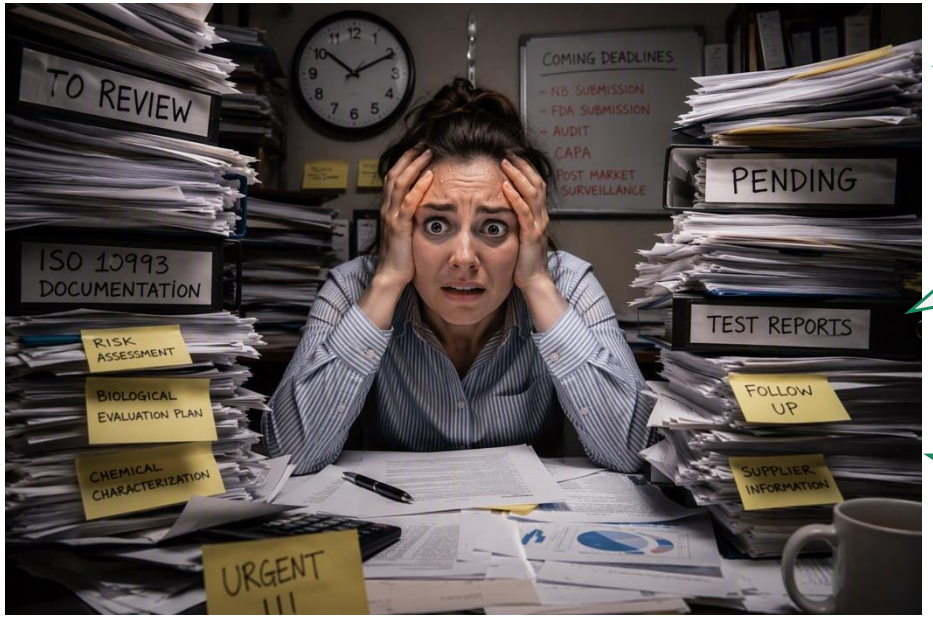
The update is raising urgent questions

- Manufacturers are overwhelmed by the breadth of ISO 10993-1:2025
- Companies struggle with identifying where information exists, understanding how it supports biological safety, and coordinating across departments.
- Initial impact often underestimated

What are Notified Bodies or FDA expecting?

Do legacy products need reassessment?

How should bioaccumulation be evaluated?



How should risk estimation be implemented?

What constitutes systemic reasonably foreseeable misuse?

and many more ???

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How companies are responding

- Larger manufacturers
  - Portfolio-wide gap assessments
  - Prioritization strategies
  - Resource and budget planning
- Smaller manufacturers
  - Direct updates to BRAs/BERs
  - Product-by-product approach
  - Focus on immediate compliance needs
- Wait-and-see approach
  - Monitoring Notified Body expectations
  - Updating primarily new projects

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Main industries hurdles

- Device categorization challenges
- Systemic reasonably foreseeable misuse
- Risk estimation
- Different expectation for Europe and US



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Device categorization challenges

- Intermittent contact devices
  Challenge: Repeated intermittent contacts are counted as one-day exposure events rather than exposure time being cumulated over time.

- Bioaccumulation
  Challenge: Assessing long-term accumulation when supporting data are limited.

→ Could this lead to up-categorization of the device?

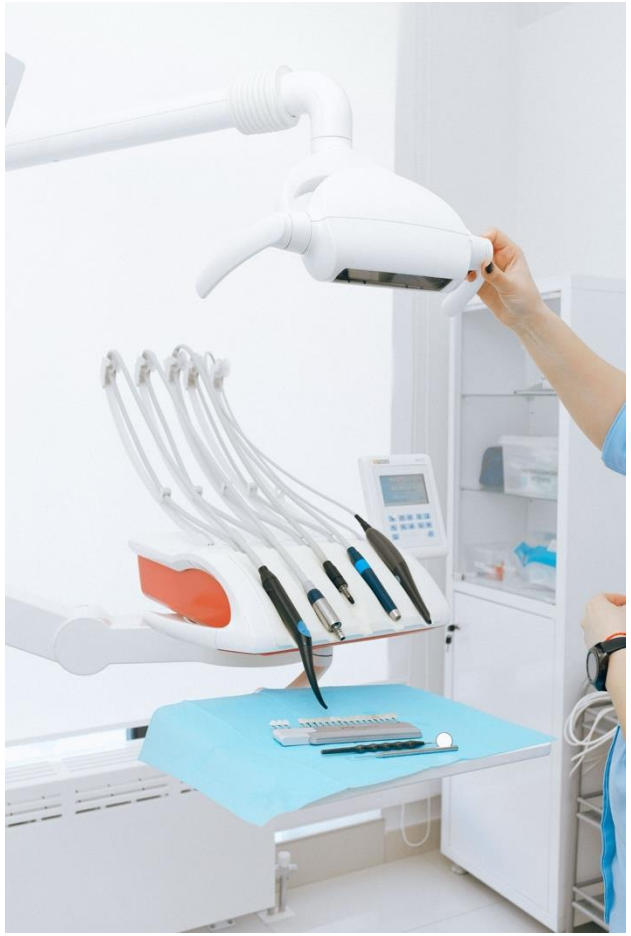


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Industry example

Device Categorization Challenges – Dental devices used for endodontic treatment

- Intermittent contact devices previously categorized as limited contact, based on ISO 10993-1:2025 as prolonged or long-term contact
  - Dental devices used for endodontic treatment, used for a few minutes each time
    - Challenge: Impact on chemical characterization testing and toxicological risk assessment, additional biological effects to evaluate.
    - Potential implications: The standard update allows justification of limited exposure despite repeated contacts, provided body clearance occurs between uses.



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Industry example

Bioaccumulation – Wound dressing

- Devices containing bioaccumulative constituents may be categorized as long-term contact under ISO 10993-1:2025, irrespective of the nominal contact duration, due to the potential for accumulation within the body.
  - Wound dressing
    - Challenge: Siloxanes in raw materials of wound dressing and no chemical characterization testing has been performed, uncertainty on leaching of siloxanes: longer term classification or chemical characterization testing
    - Potential implications: Higher focus on CC testing if bioaccumulation substance is present also for FDA, higher requirement from supplier documents/interaction



Consultant perspective: New hurdles, but flexibility through risk-based justifications.

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Systemic reasonably foreseeable misuse challenge

- Systemic reasonably foreseeable misuse
  - in accordance with ISO 14971,
  - where there is information available (e.g. post-market surveillance data, clinical literature) to suggest that the device can be used outside of its intended use,
  - and this misuse is identified as being systematic

  Challenge: What qualifies as systemic reasonably foreseeable misuse?

→ How to deal with it for new devices? When does it qualify as systemic?

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Industry example

Systemic reasonably foreseeable misuse – Eye Drops

- The introduction of systematic consideration of reasonably foreseeable misuse may influence the biological evaluation strategy by affecting the identified patient population, tissue(s) in contact, nature and duration of exposure, and overall device categorization.
    - Eye drops
        - Challenge: Based on PMS data device is used in patients, that are not intended by the manufacturer (children, pregnant/breast-feeding women)
        - Potential implications: Adaptation of toxicological risk assessment, addition of addressing reproductive and developmental toxicity



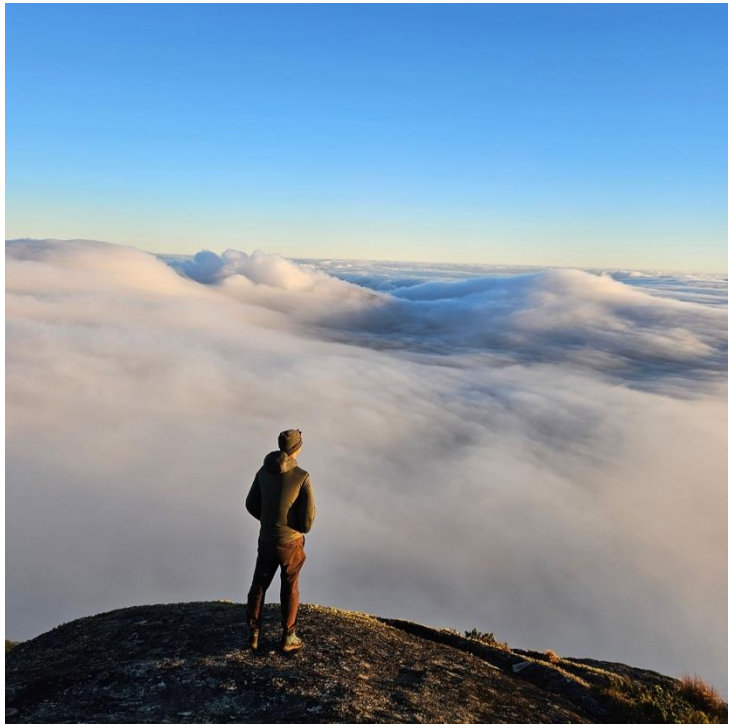
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Risk estimation challenge

- Increased integration of biological evaluation into risk management process
- Biological risk can be estimated by assigning qualitative or quantitative values to the severity and probability of occurrence of biological harm
- Used approach for biological risk estimation shall be documented

Challenge: No clear guideline yet and it seems very flexible, but what will be accepted?

→ How to set severity or probability of occurrence of a biological harm?



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Industry example

Risk estimation

- Risk estimation requires consideration of severity and probability of occurrence of harm.
- General industry example
    - Challenge: How to assign qualitative or quantitative values to the severity and probability of occurrence of biological harm? Further guidance is lacking.
    - Potential implications: Greater collaboration required between biocompatibility and risk management teams.

Consultant perspective: A guidance is necessary to align on how to perform biological risk estimation.

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Notified body/FDA misalignment challenge

Same standard, different reviewer expectations (FDA partial recognition):

- Evidence expectations
- Chemical characterization requirements
- Acceptance of biological justifications
- Risk estimation approaches
- Endpoint-specific requirements (e.g., genotoxicity)

Challenge: How do approach for different markets?

→ Are we reducing testing or simply increasing documentation?

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Industry example

Notified Body/FDA Misalignment -Dialyzer

- CE-marked dialyzer seeking FDA approval
  - Challenge: Biological evaluation was developed to support MDR compliance. Can the same evaluation be used for FDA submission despite differences in reviewer expectations and endpoint-specific requirements (e.g., genotoxicity)?
  - Potential implications: Region-specific biological evaluation updates may be required and biological justification acceptance could trigger additional data requests or testing despite an existing CE mark.



Consultant perspective: Global harmonization aims to minimize duplicate assessments and testing, but differing regional interpretations increasingly challenge this goal.

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Lessons learned & key takeaways

- Start early considerations to understand the gaps
- Many companies expect minor updates but discover significant impacts on existing biological evaluations
- Checkbox approach cannot be used any longer
- Companies are realizing that biocompatibility cannot be managed by biocompatibility teams alone. Collaborate with different departments is necessary.
- Does the revision raises more questions?
  - When is a reasonably foreseeable misuse systemic and how to approach it for new devices?
  - How should biological risk be estimated? What constitutes an acceptable method for assigning severity and probability?
  - Can the BER remain a standalone document? Who should own biological risk management? ISO 14971 risk managers?
  - What is expected and will be accepted by Notified Bodies and FDA?

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Panel discussion

How to be brave?