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ISO 10993-1 FDIS Updates: **FAQ from the Panel Q&A**

ISO 10993-1 guides the biological evaluation of medical devices. With the Final Draft International Standard (FDIS) approved, this update is one of the most significant in recent years.

The panel covered what is changing and how to prepare. This FAQ material was developed based on the feedback from the discussion.

Frequently Asked Questions

1. What does the stronger risk-based approach mean in practice? Can I rely more on materials history and less on new testing? Where do cleaning and passivation fit?

You can lean more on a documented, knowledge-based comprehensive risk assessment when the supporting data are sufficient and relevant to your device and process. The approach considers that risk assessments may replace testing for certain biological effects or process changes. Historical materials data, process knowledge, comparison to predicate devices, and prior testing can support conclusions, but reviewers may still favor objective evidence when uncertainty remains. Cleaning and passivation belong in the risk assessment and lifecycle change-control strategy. If processing chemicals are demonstrably removed or neutralized, you may not need to test for their residuals, but any process change can reopen the assessment.

2. How are particulates treated under the revision?

Particulates are addressed through a risk lens that considers generation and persistence in the body. For example, devices used in the cardiovascular system or other critical pathways can present higher risk if particles can circulate in the vasculature causing mechanical disruption, deposit or accumulation. For skin and mucosal contact, the risk may be lower, but still requires justification based on use, materials, and wear mechanisms. Separate consideration needs to be made for particulates that are residuals based from manufacturing as well as those formed during mechanical wear or degradation. Particulates that can bioaccumulate may extend the duration of exposure of the device to the body thus increasing risk and biological effects requiring evaluation.

3. Can ISO 10993-1 be applied outside medical devices?

Remember, the scope is the scope. The scope for 10993-1 is medical devices. Its concepts can inform toxicological risk assessments in other contexts, but the document is intended for medical device evaluations.

4. How far should I go in evaluating foreseeable misuse?

Consider a realistic, practical misuse that a knowledgeable person would anticipate in clinical settings. You may not need to chase one-in-a-million scenarios, but you should certainly demonstrate a level of due diligence. Make certain you evaluate all credible off-label uses that could change tissues contacted, duration of exposure, or cleaning agents encountered. Consider discussions with clinicians, reprocessing, and human factors experts.

5. Do currently marketed devices need new testing because of the update?

No. The update is not intended to require retrospective application of gaps or new concepts. If you change the device or process, apply the new standard to the modified product and justify your approach.

6. What will FDA recognize, and when?

FDA recognition will follow FDA's internal process and related updates to their recognized consensus standards and "Use of International Standard ISO 10993-1..." guidance document. Partial recognition is possible, but timing and scope are not yet known. Expect FDA to clarify how it wants information presented.

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7. What changes for Biological Evaluation Plans and expertise expectations? Who should author the BEP and gap assessment?

Expect greater emphasis on qualified authorship. Teams should demonstrate relevant education and experience across biocompatibility standards, guidance documents, varying device types, regulatory regions, chemistry, toxicology, in vitro methods, materials, and device use. Plan to include CVs for key contributors. A thin protocol with minimal rationale is unlikely to satisfy reviewers. A team approach and peer review are always advised, and under the guidance will be expected.

8. For absorbable devices, is chemical characterization required?

Not automatically. Use a risk-based rationale tied to materials, degradation products, and clinical use. Chemistry can be challenging for absorbables due to breakdown during extraction. If other data can answer the relevant safety questions, you can justify alternatives.

9. How should I address end of life for single-use and reusable devices?

For single-use devices, assess biocompatibility at labeled shelf life, and consider which materials are more prone to change over time. For reusable devices, validate the intended life and reprocessing cycles. Show that soils can be removed, demonstrate the disinfection or sterilization effectiveness, and evaluate chemical and physical material changes and residuals at the end of the claimed life.

10. What changed in device categorization and contact time?

Contact time determination has changed significantly in how we measure it for repeat use and absorbable devices. We now consider a single exposure, no matter how short, as a day of exposure rather than minutes/hours within a day. If a device is used every three days, we include the time in between uses, not just the days it's used. If foreseeable misuse could reasonably extend exposure across multiple days, categorize accordingly. Consider persistence/bioaccumulation in the body, not only time at its local site. Some devices previously considered limited contact may need prolonged or long-term contact assessments.

11. Why the increased emphasis on genotoxicity, and how should I respond?

Any device can leach compounds that contribute to systemic risk. The revision elevates attention to potential long-term effects including potential genotoxicity. Consider genotoxicity within the biological effects when chemistry, materials, and use indicate a credible risk.

12. How do I choose the right cytotoxicity method and parameters?

Match the method to the device materials and contact nature. There is no one-size approach. Consult your test laboratory to align extraction conditions, cell lines, endpoints, and acceptance criteria with current best practice for your device type.

13. What applies to non-patient contacting devices, including IVDs?

First, confirm that the device truly has no direct or indirect patient or user contact. Consult experts and past precedent to ensure that your device is truly non-patient-contacting. Some IVD systems interact with the body through fluids, gases, or accessories. If any pathway reaches the patient or user, evaluate that risk.

14. If my device is up-categorized, can I rationalize out of additional testing?

Possibly. If you are up-categorized, the standard states you do not need to retrospectively address any new biological effects or concepts. It depends on the effect and your justification. Some effects are harder to waive than others, such as implantation where geometry, surface texture, and crevices can influence risk. Make sure your rationale is clear and thoroughly risk-based.

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15. Is there a grace period after publication?

There is no formal grace period for certain regulatory regions. If you are mid-project, reassess your strategy, especially for European submissions where adoption is expected first as being state of the art. FDA on their recognized consensus standards website will note a grace period although individual reviewers may expect an earlier adoption. Align your approach with submission dates and target markets.

16. Do I need cytotoxicity testing for cleaning validation?

Not necessarily. Many teams run cytotoxicity as a screen for residual cleaners or material changes after cleaning, but chemistry-based approaches or spectroscopic screens can also address residues. Choose methods that best answer the risk question.

17. How does the update affect shelf life and aging studies?

It reinforces end-of-life and lifecycle evaluation. Consider physical and chemical changes over time, and confirm that the device remains biologically safe at the labeled shelf life or after the validated number of reprocessing cycles.

18. Is material-mediated pyrogen testing going away?

The revision notes that pyrogenic reactions from well-known, historically non-pyrogenic materials are unlikely, which can support foregoing the associated testing. Novel materials or uncertain risk will still require evaluation so plan accordingly.

19. What are common pitfalls of a risk-based approach under ISO 14971?

As with most things, we don't know what we don't know. Subjectivity can quickly creep in if the evidence is thin. Risk estimation and completeness of the review are frequent weaknesses. Bridge data gaps with testing when needed, involve qualified experts, and document clear rationales that will persuade a reviewer.

20. When will related TIRs and Technical Specifications be published?

Drafts exist within the working group, but they require significant review and comment resolution. Timelines for publication are yet to be set.

21. For reprocessed devices, what chemistry issues matter most at end of life?

Focus on material degradation and residual chemistry after repeated use and cleaning. Your analysis should demonstrate an understanding of how byproducts interact with other materials, cleaners, and disinfectants at the end of the validated life.

Other Questions?

Have additional questions or need a plan for ISO 10993-1? Nelson Labs Expert Advisory Services helps device and pharmaceutical teams turn requirements into clear, defensible strategies. Our specialists track regulatory trends and serve on standards committees.

For a review of your approach or a roadmap to approval, email:
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