How Will Proposed ISO 10993-1 Change Impact Your Biocompatibility Plans?

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Document UCM348890 (FDA's April 2013 proposal to change the guidance document for ISO 10993-1) seems pretty straight forward—with things like testing details associated with genotoxicity and how to go about labeling your device as "Not made with BPA" instead of "BPA-free" clarified.

Many of these updates are geared towards test houses—and will become familiar to reputable ones. However, Appendix A has financial ramifications for additional testing in specific device categories that may not be familiar to medical device developers but has an impact.

Some of the proposed changes make sense. For example, external communicating devices contacting tissue/bone/dentin could require additional testing. I can think of a few applications on which I would want to see systemic toxicity be conducted for my peace of mind. However, requiring an implantation study for a temporary nasogastric intubation (mucosal contact for >24h) seems extreme. The footnote change in the proposed standard "provide rationale for its omission" allows subjectivity for both the applicant and the FDA auditor to skip conducting these additional tests. If the device is being applied for as part of a 510(k) submission, and does not utilize novel materials, does this constitute acceptance that the "new" tests do not need to be conducted? Perhaps inclusion or exclusion of all tests can be determined through the Risk Management File?

Draft – Not for Implementation

1131 **Attachment A:**

1132 **Table 1 – Initial Evaluation Tests for Consideration**

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Device categorization by			Biologic effect							
nature of body contact (see 5.2)		Contact duration (see 5.3) A – limited (≤ 24 h) B- prolonged (>24 h to 30 d) C – permanent (> 30 d)	Cytotoxicity	Sensitization	Irritation or Intracutaneous reactivity	Systemic toxicity (acute)	Subchronic toxicity (subacute toxicity)	Genotoxicity	Implantation	Haemocompatibility
Category	Contact									
Surface device	Intact skin	A	X	X	X					
		B	X	X	X					
		C	X	X	X					
	Mucosal membrane	A	X	X	X					
		B	X	X	X	O	O		O	
		C	X	X	X	O	X	X	O	
	Breached or compromised surface	A	X	X	X	O				
		B	X	X	X	O	O		O	
		C	X	X	X	O	X	X	O	
External communicating device	Blood path, indirect	A	X	X	X	X				X
		B	X	X	X	X	O			X
		C	X	X	O	X	X	X	O	X
	Tissue/bone/dentin*	A	X	X	X	O				
		B	X	X	X	X	X	X	X	
		C	X	X	X	X	X	X	X	
	Circulating blood	A	X	X	X	X		O^		X
		B	X	X	X	X	X	X	X	X
		C	X	X	X	X	X	X	X	X
Implant device	Tissue/bone	A	X	X	X	O				
		B	X	X	X	X	X	X	X	
		C	X	X	X	X	X	X	X	
	Blood	A	X	X	X	X	X		X	X
		B	X	X	X	X	X	X	X	X
		C	X	X	X	X	X	X	X	X

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X = ISO 5 Evaluation Tests for Consideration
O = These additional evaluation tests should be addressed in the submission, either by inclusion of the testing or a rationale for its omission.
Note 1 to T Tissue includes tissue fluids and subcutaneous spaces

The proposed changes are best summarized with the chart, with a new marking indicated as an O that were not in previous standards. For example, devices making contact with breached or compromised skin for 1-30 days will now likely have to conduct subchronic toxicity. Depending on the nature of the test and selected protocol, this can be in the neighborhood of $40k per iteration—just for one test, excluding prototype and internal communication costs, and assuming no failed attempts.

Product developers need to know how to budget regulatory testing early on in the development cycle. The introduction of testing that may (or may not) be conducted opens up an even larger window of uncertainty to budgeting. This may sway someone to not develop a product simply because they can’t know what testing requirements will be imposed on them, even after a submission is made.

One possible solution to stratify the applicability of these additional tests is to make it dependent on how the applications come in. If it is a PMA, do the additional tests. If it is a 510(k), and there is a history of similar predicates, don't do the additional tests. If you're somewhere in between, then the revamped DeNovo process comes to the rescue and a risk management file decides. And, as always, if specific guidance documentation is available, it overrides the above. This would leave less subjectivity in budgeting and scheduling to medical device developers, and avoid awkward discussions on how to interpret the standard.

How will the proposed changes to ISO 10993 impact your company? My evaluation is based on experiences working with colleagues in Regulatory Support [1] at StarFish Medical [2]. I would enjoy hearing from readers about their experiences and concerns.

Links:
[1] http://starfishmedical.com/services/regulatory-support/
[2] http://starfishmedical.com/