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Q&A: New Standard For Device Irritation Nudges Industry Away From Animal Testing – And Toward Tests On Lab-Made Human Skin

by Shawn M. Schmitt

An ISO-recognized expert tells *Medtech Insight* why international standard ISO 10993-23:2021 urges irritation testing on laboratory-grown skin – also known as *in vitro* reconstructed human epidermis (RhE) – and why device makers will like it.

A new standard on medical device irritation from the International Organization for Standardization (ISO) is nudging manufacturers away from testing on animals.

Published by ISO in January, *ISO 10993-23:2021* urges irritation testing on laboratory-grown skin – or *in vitro* reconstructed human epidermis (RhE) – instead. The standard includes an RhE test model that can replace old-school animal tests that have been used for decades, such as the *Draize Test*.

Device makers "are ready for new science. Some of these tests have been around since the 1950s and 1960s. It's pretty ridiculous that we still rely on them," said Thor Rollins, director of toxicology at Nelson Laboratories.

Rollins also is a member of ISO Technical Committee 194, the group that oversees the ISO 10993 set of standards, "Biological Evaluation of Medical Devices." That series gives manufacturers tools to assess device biocompatibility and manage any associated risks.

ISO 10993-23 marks the first time irritation has been separated from sensitization in the series. Before it had its own standard, irritation was included in *Part 10 of the set*, "Tests for Irritation

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and Skin Sensitization." ISO 10993-10 was first published in 1995, and updated in 2002 and 2010. (Part 10 is currently undergoing a revision to strip out irritation.)

> *"A lot of standards are currently being worked on, revised and reevaluated, so buckle up." – Thor Rollins*

"Lumping irritation and sensitization together into one standard made sense way back when, even though they're two different test methods and two different biological reactions," Rollins said.

"But five years ago, there was some new science that came out that took the emphasis away from animal testing and moved into *in vitro* alternatives, using RhE tissue," he said. RhE tissue is "stem cells that are differentiated into skin. So they're little human skins that we buy on a plate – they're kind of cool."

Companies like *MatTek* and *Episkin* make lab-grown skin for product testing.

"So ISO 10993-23 isn't just separating out sensitization and irritation, it's also putting in this *in vitro* alternative," Rollins said. "It's not completely removing the animal test, but for Europe and Japan, once this standard is accepted, they're going to rely on the *in vitro* test above the animal test. And that's great – the idea is to get away from the animal tests."

In an interview with *Medtech Insight*, Rollins added more context.

Q **Medtech Insight: What type of medical device is covered by ISO 10993-23 on irritation?**

A Thor Rollins: Any device that directly or indirectly contacts the patient. Absolutely anything, really. Direct would be anything that directly contacts the patient's skin or tissue or blood; indirect would be things like fluid or gasses coming through the device and onto the patient. Any of those devices, this impacts.

Q **What's the big takeaway for manufacturers when it comes to this new standard?**

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A Rollins: Besides the fact that we're changing to two separate standards – but I don't really see that as too big of an impact. It's news because now you have to reference a different standard for irritation when you do your submissions, but the main impact is that this is the first time that we successfully in this ISO committee for medical devices moved away from an animal test to an *in vitro* test – a purpose-built *in vitro* test for the medical device field.

The standard is impactful because, one, we're not testing on animals, and two, these tests are cheaper and quicker than the animal tests. So yeah, medical device manufacturers love the idea of going toward it, as long as the regulatory bodies accept it.

Q **So industry is behind this standard?**

A Rollins: Yeah. I think long term it's great because these tests are cheaper and quicker. To do tests for sensitization and irritation right now is going to cost about $15,000 and take about eight to nine weeks to run. I know those don't look like huge numbers, but when you're doing device after device, that starts to add up. And the eight- to nine-week wait to get the test done, the turnaround time of that test, is a huge impact for some of these devices. So if we can get that down to three to four weeks, then that's a huge revenue savings for the company.

Q **How is it that tests are run faster using RhE?**

A Rollins: These *in vitro* alternatives are quicker because we can see those reactions happen much faster than when we have to inject an animal. Plus, you have to wait for the animal to come in and acclimate to the testing lab, things like that.

Q **And it's more animal friendly.**

A Rollins: Much more, and that matters to a lot of people. It matters to me. That's one reason we've worked so hard on this. But honestly the thing that matters the most to companies is getting their device on the market quicker.

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Q **So run those numbers past me again. You say these tests can run roughly $15,000…**

A Rollins: The irritation test, the animal test, costs around $1,500 and the RhE skin test costs around $1,000. So it's about $500 in savings or so. And the turnaround time is not that different. They're both three- to four-weeks long.

Rather, it's the sensitization [under ISO 10993-10], which we're working on now, that would save them a lot. So for an *in vitro* sensitization test, they'd go from $12,000 to $13,000, down to $1,500 or $2,000, and eight to nine weeks down to three to four weeks.

Q **So the news is also that ISO 10993-10 is under revision. When will that go out?**

A Rollins: It depends. There's a lot of work to do there. It could maybe be another four or five years before we get that one updated.

Q **So ISO 10993-10 is a long term project…**

A Rollins: We'll update -10 right away because we have to separate irritation out of there. But to change that standard to an *in vitro*, it's probably five years down the road.

Right now if you look up -10, it's still for sensitization and irritation. So we have a little contradiction going on where we have a standard just for irritation, and another standard with both sensitization and irritation. We're working on that right now. We're expected to have that out by the end of the year to update -10 to be just for sensitization so we can have two distinct standards.

Q **Any parting words?**

A Rollins: There's more coming. A lot of standards are currently being worked on, revised and reevaluated, so buckle up.

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