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Welcome to the ISPE podcast, Shaping the Future of Pharma,

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where ISPE supports you on your journey,

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fueling innovation, sharing insights, thought leadership,

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and empowering a global community to reimagine what's possible.

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Hello and welcome to the ISPE podcast, Shaping the Future of Pharma.

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I'm Bob Chew, your host, and today we have another episode

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where we'll be sharing the latest insights and thought leadership

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on manufacturing, technology, supply chains,

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and regulatory trends impacting the pharmaceutical industry.

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You'll hear directly from the innovators, experts,

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and professionals driving progress and shaping the future.

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Thank you again for joining us, and now let's dive into this episode.

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Our topic today is Unlocking Innovation,

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To share more about this topic, I would like to welcome Michelle Vuolo,

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head of quality at Tulip Interfaces and co-lead of the Validation 4.0 guide team.

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And fellow guide team member representing South America

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is Victor de Oliveira Silva Ferreira,

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Project Manager for PEQMS, Implementation of Electronic Systems

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for the Quality Management System at the Instituto de Tecnologia

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Em Imunobiológico Fundação Oswaldo Cruz.

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Michelle and Victor, welcome to the podcast.

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We're so glad to have you both with us.

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Thanks. Thanks for having us.

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I hope that's a thank you for invitation.

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Well, first, before we jump into some of the questions about the guide,

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I'm curious, how did you guys get involved in this guide?

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What's your background? What's your passion? Why this one?

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Michelle?

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Sure. Yeah, I'll go ahead and start.

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Yeah, I work at Tulip Interfaces,

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which is a technology company providing software for manufacturing environments.

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I've been here about five years, but before that,

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I spent about 25 years in life sciences and doing all things quality

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from lab to manufacturing operations quality to all the way to IT quality,

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probably my natural progression and decided to get engaged

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with the Pharma 4.0 community of practice.

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And so I wanted to help modernize the way we look at quality and validation topics

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and thought that it would best fit in the Pharma 4.0 community of practice.

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So fast forward five years and lots of PE,

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pharmaceutical engineering articles and conference speaking

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and lots of really great active members in the ISPE community.

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Later, we published the good practice.

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And Victor?

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I have to work with qualification and validation for entire of my career,

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mainly with the development new strategies to release new products in my company.

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For the last five years, I was dedicated to understand

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how technology can enhance quality and validation strategies.

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So I joined in validation 14 and have been working with Michelle for these years in GPD.

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Well, great.

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Well, let's start out with kind of the big picture.

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What exactly is validation 4.0?

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Yeah, I can start because I do recall when we first got our working group

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now called subcommittee together.

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That was the big question.

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Like, what is it?

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Because validation is such a broad topic covering so many aspects.

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And it was very clear that it wasn't computerized system validation specifically,

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because there's Gantt for that very well established group.

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But that we wanted to look at how we could modernize validation

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and look at how to become more efficient and effective with validation

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in this digital world, right?

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Like, it doesn't have to be digital, but what's happening

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or what's driving the change to look at validation was the digital transition.

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And I think bigger picture even on that is really trying to help enable

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real-time validation, again, with the usage of digital technologies,

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real-time validation, continuous validation, looking at upstream and downstream

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sort of impacts on validation of what you're trying to validate.

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So it's sort of the bigger picture.

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It's rooted in the guideposts of the IEH guidelines,

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in particular quality risk management and quality by design

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to fundamental and foundational principles to enable validation.

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Really, when you look at validation as just like going back and saying,

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what is validation?

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It's really the demonstration of control.

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And so those are two fundamental principles and foundational aspects

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that need to be understood to really do validation on any focused way.

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Yeah.

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I don't like I did that.

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I see validation for is looking to data on the quality by design lens.

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So you need to ensure that the probability data

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is available for users during the entire life cycle.

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So there is an operational approach that approach itself.

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How do you need to do validation for?

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But there is an aspect, the business aspect regarding

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how you deal with validation quality as a business strategy,

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because it was discussed in years.

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Validation quality need to be work as business strategy

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to enhance control around the product process.

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So what triggered the creation of Validation 4.0?

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Was it the Pharma 4.0 good practice guide,

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or was it other factors in industry?

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Yeah.

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So, you know, we started working together as a group.

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There's, you know, there's an ebb and flow of folks

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that come and join on these groups,

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which is understood because people are volunteering their time to do this

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and have day jobs, so to speak.

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But, you know, I think our group was doing a lot.

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Like I said, we did a lot of

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pharmaceutical engineering magazine articles.

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We are trying to develop and define case studies.

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Then we moved on.

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We did a couple of presentations at most of the ISTE annual meetings,

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both in the EU and in the US.

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Also in the Eastern communities, too,

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because the co-lead of the Validation 4.0 working group is out of Bangkok.

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So we're able to do a lot of seminars and webinars out there in India as well.

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I'm forgetting.

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It's been five years.

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But then we got involved in one of the chapters,

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the quality chapter of the Pharma 4.0 baseline guide, right?

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So there's baseline guides, which are sort of higher level overarching,

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which is what GAMP is, for example.

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I think a lot of people with ISPE are very familiar with GAMP.

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And then under that umbrella,

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there's lots of good practice guides that are on specific topics.

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Like, for example, GAMP has an MES specific good practice guide.

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So, yeah, the Pharma 4.0 baseline guide was published in December of 23, I think it was.

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That's when we started saying,

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what are good opportunities for documenting more information

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on how to execute this Pharma 4.0 approach on particular topics?

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And so Validation 4.0 is prime for that.

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We've had our approach, our guideposts, our methodology defined.

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We've had a few case studies.

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So we started writing the good practice guide.

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And, you know, with the intentions of really trying to demonstrate to the industry

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how to do this more specifically than, you know, sort of this conceptual idea.

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If I go back many decades, there was an FDA aseptic process validation guide,

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if I recall correctly, talking about media fills or aseptic process simulation.

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And it specified a minimum of three lots.

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Now, in that case, one lot was at least 5,000 units.

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So you really were looking at the aseptic contamination possibility

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spread across 15,000 instances.

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But those three lots then kind of morphed into validation, process validation.

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And we need to do three lots.

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Now, we all would agree that three lots is not statistically significant

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and does not capture potential variability in raw materials and all this stuff.

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Now, up front, you're supposed to have development work

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that covers that base.

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And then you do these three lots.

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And then you do continuous process verification.

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Tell me how this validation 4.0 changes that.

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I can go first.

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And, Victor, jump in for sure if you want to help support or add anything different.

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But, yeah, so what we're trying to get away from in this validation paradigm

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towards a new paradigm is, you know, I think traditionally the three,

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you know, the tradition, the golden three-batch run,

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like that's always sort of like people immediately think of that

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when they think of, oh, how am I going to validate?

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What we're trying to do is shift the thinking away from,

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I have to do three runs of process validation

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towards how have I demonstrated the controls in my process?

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The only way to do that really is to understand your process requirements,

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which in my opinion are around quality by design, right?

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Quality by design, basically the fundamental of quality by design

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is the more you know about your product and process,

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the more you can control it, right?

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So the idea through CPP, CQAs, these critical aspects to your process

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are defined and identified as critical, right?

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Using your quality risk management principles

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and identifying the controls around each of those individually

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and developing controls around them.

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The validation of that is not just running through it three times.

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The validation of that is really building an evidence story

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around each of those controls and how you demonstrate them, really.

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So the idea is like the culmination of all these controls,

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the evidence of these controls really starts to become your validation
package,

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not whether you ran it three times.

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You could have run it several times on, I don't know,

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different parameters and different things on a particular control area

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or a particular critical area of the process.

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But you're building this evidence file on an ongoing basis.

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If you can do this during product development, right?

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These iterations of like through risk management though, right?

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A controlled process of identify a risk and put a control in place,

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determining if it's effective or not,

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and iterating on that in this sort of continuous loop.

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That's where we also want to get into this continuous validation

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or the idea that we can, at any one point in time,

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understand our state of control.

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Yeah, we, using Go, said that we are going to move

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from the stage of validation to stage of validation.

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Because in the moment that we're starting,

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Go have control about the data since the development.

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You have confidence to scale up all validation activities

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through their all study, clinical studies,

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and to reach the commercial match understanding for the entire process.

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This is what you should know about holistic control strategy,

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is have all control for all strategies need to be implemented during the life cycle.

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Okay, you mentioned quality risk management.

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There's a lot of different views on that.

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There's a lot of different practices on that.

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I think those of us who have done it would agree that in most cases,

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certainly many cases, it's subjective.

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The probability, the effectiveness of the controls,

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and the probability given those controls, et cetera.

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How is validation 4.0 dealing with those,

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that subjective nature of quality risk management?

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And can technology turn subjectivity into objectivity?

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Yeah, I can go first or Victor,

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I want to give you the opportunity to go first if you want.

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Okay, I think that we are thinking validation 4

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in quality risk management.

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We are not speaking about using spreadsheets,

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but using digital tools to enhance the entire management.

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So, this allows to have capability to integrate systems with MERS,

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LIMS, and other kind of stuff to get data since the development,

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going through this system, provide the control.

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Obviously, there is some kind of complexity in doing this,

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but in the moment that you take quality validation group and IT group,

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look into the strategy of the whole process,

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you can provide control for all decision

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and activity that will occur in your manufacturing process.

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I believe this is the main point that quality risk management

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and validation can enhance.

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The possibility to, since the first time they start a process or product,

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you're working together to think,

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okay, what can affect my process, my product?

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How the sensor could be failed during my process

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and how this information put through quality risk management digital

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and send the trigger action that you can do in real time.

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So, these are, as I see, validation for enhancing quality risk management.

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Yeah, I think just to add to that too,

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is like one of the things that we have,

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like in all the presentations I've given on this,

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like one of the things we do say is like

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we are not prescribing a particular risk methodology at all.

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Like we're not saying FMEA is great or not or whatever.

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What we do, like what I do with myself

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and what I do like about ICHQNAN is risk identification,

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risk assessment, and risk control.

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Just logically that process works really well.

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And if you're doing a three-by-three matrix or a two-by-two matrix

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or you're using detectability or frequency or likelihood,

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we don't get into that level of detail.

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But what we're saying is we need to identify and understand

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the risk associated with certain data points, right,

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associated with your process.

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And so, and the idea is, again, as you are identifying the risk,

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you're like a sterility assurance,

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you identify the control, whichever it might be,

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and then you ultimately then verify the effectiveness of that control

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right away through several iterations or several runs.

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But the idea is that as soon as you get an effective or ineffective data point,

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that gets fed back into the risk,

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identified if the risk changes,

248
00:16:06,000 --> 00:16:09,000
which not often does the risk change itself,

249
00:16:09,000 --> 00:16:12,000
but the risk control is either effective or ineffective.

250
00:16:12,000 --> 00:16:16,000
And you determine if you need to adjust your risk control.

251
00:16:17,000 --> 00:16:20,000
So again, it's not a three-by-three matrix.

252
00:16:20,000 --> 00:16:22,000
It's not subjective or objective.

253
00:16:22,000 --> 00:16:27,000
It's, you know, the basis is product quality, patient safety always.

254
00:16:28,000 --> 00:16:32,000
So in those terms is where, again,

255
00:16:32,000 --> 00:16:34,000
that continuous loop allows you to feedback

256
00:16:34,000 --> 00:16:36,000
and adjust your controls as necessary.

257
00:16:37,000 --> 00:16:40,000
But again, I just think of many examples

258
00:16:40,000 --> 00:16:43,000
of having been in risk assessments in my previous life.

259
00:16:44,000 --> 00:16:46,000
And there is not that continuous loop.

260
00:16:46,000 --> 00:16:48,000
There's not that feedback loop.

261
00:16:48,000 --> 00:16:52,000
You know, we spend hours and hours and hours in a meeting room

262
00:16:52,000 --> 00:16:54,000
trying to determine the risk level of something

263
00:16:55,000 --> 00:16:59,000
and not really following up or understanding

264
00:16:59,000 --> 00:17:00,000

whatever control we put in place.

265
00:17:00,000 --> 00:17:01,000
Was it effective?

266
00:17:01,000 --> 00:17:02,000
Was it not?

267
00:17:02,000 --> 00:17:04,000
Did it impact other things?

268
00:17:04,000 --> 00:17:05,000
Like there's no assessment.

269
00:17:05,000 --> 00:17:07,000
And that is ultimately the most important piece.

270
00:17:08,000 --> 00:17:12,000
You know, coupling what Victor said is like in the digital world,

271
00:17:12,000 --> 00:17:16,000
digital is enabling us to do that more immediate feedback loop, right?

272
00:17:16,000 --> 00:17:19,000
And to look at things independently as well

273
00:17:19,000 --> 00:17:23,000
or look at individual controls as well,

274
00:17:23,000 --> 00:17:25,000
which I think is very important.

275
00:17:26,000 --> 00:17:28,000
This is, in my opinion, has not necessarily

276
00:17:29,000 --> 00:17:31,000
been done on a big scale until now.

277
00:17:32,000 --> 00:17:36,000
So risk assessments, as we just talked about,

278
00:17:37,000 --> 00:17:39,000
there's statistics behind them.

279
00:17:39,000 --> 00:17:43,000
They're probabilistically determined, right?

280
00:17:45,000 --> 00:17:46,000
It's a high probability.

281
00:17:46,000 --> 00:17:47,000
It's a low probability.

282
00:17:47,000 --> 00:17:49,000
There's a statistic to that.

283
00:17:51,000 --> 00:17:56,000
The concept of a design space assumes

284
00:17:56,000 --> 00:18:01,000
that you have some sort of statistical understanding

285
00:18:01,000 --> 00:18:04,000
of the interrelationships between different variables.

286
00:18:04,000 --> 00:18:06,000
Some of the relationships are strong,

287
00:18:06,000 --> 00:18:09,000
i.e. a high correlation coefficient.

288
00:18:10,000 --> 00:18:13,000
Some of them are weak, a low correlation coefficient,

289
00:18:13,000 --> 00:18:16,000
but it's statistics, right?

290
00:18:17,000 --> 00:18:20,000
Now, today we have AI,

291
00:18:20,000 --> 00:18:24,000

we have digital twins, process and equipment,

292
00:18:25,000 --> 00:18:29,000
and they're statistical tools, right?

293
00:18:30,000 --> 00:18:32,000
That's all they are.

294
00:18:32,000 --> 00:18:35,000
They're very sophisticated, but they're statistical tools.

295
00:18:36,000 --> 00:18:40,000
So we have a need over here from a design space

296
00:18:40,000 --> 00:18:44,000
and a risk assessment to have statistical analysis.

297
00:18:44,000 --> 00:18:46,000
And now we've got all these really cool tools

298
00:18:47,000 --> 00:18:49,000
that are statistical tools.

299
00:18:49,000 --> 00:18:51,000
How do we bring them together?

300
00:18:51,000 --> 00:18:52,000
Yeah, yeah.

301
00:18:53,000 --> 00:18:56,000
Well, so it was easy.

302
00:18:56,000 --> 00:18:57,000
Like one of my first things was like,

303
00:18:57,000 --> 00:19:00,000
oh, we just need digital risk assessment tools.

304
00:19:00,000 --> 00:19:01,000
And yes, that can help enable.

305
00:19:01,000 --> 00:19:04,000
Like I ultimately would like to see

306
00:19:04,000 --> 00:19:06,000
that some of these digital tools for risk management

307
00:19:06,000 --> 00:19:08,000
become validation tools, right?

308
00:19:10,000 --> 00:19:11,000
But even more importantly,

309
00:19:11,000 --> 00:19:13,000
and we have a few cases,

310
00:19:13,000 --> 00:19:15,000
I think we have two case studies in the guidance

311
00:19:15,000 --> 00:19:19,000
on utilizing a digital quality by design tool.

312
00:19:20,000 --> 00:19:23,000
What was really exciting about those case studies

313
00:19:23,000 --> 00:19:25,000
is that it was demonstrating the ability

314
00:19:25,000 --> 00:19:30,000
to use a digital quality by design tool to do that, right?

315
00:19:30,000 --> 00:19:33,000
And it was providing you the correlations

316
00:19:33,000 --> 00:19:35,000
between different control groups and different things.

317
00:19:35,000 --> 00:19:39,000
And it gave you the visibility or in a visual way

318
00:19:40,000 --> 00:19:42,000

about how like when you identify

319
00:19:42,000 --> 00:19:44,000
through quality by design,

320
00:19:44,000 --> 00:19:45,000
what's critical, what's not,

321
00:19:46,000 --> 00:19:48,000
what controls you put in place,

322
00:19:48,000 --> 00:19:51,000
and you can also link in what controls

323
00:19:51,000 --> 00:19:55,000
are impacting other critical aspects as well.

324
00:19:55,000 --> 00:19:57,000
But it provides you the ability

325
00:19:57,000 --> 00:19:59,000
to do statistical analysis

326
00:19:59,000 --> 00:20:02,000
on your control effectiveness as well,

327
00:20:02,000 --> 00:20:06,000
as you can plug in the evidence data

328
00:20:06,000 --> 00:20:07,000
after you execute this thing,

329
00:20:08,000 --> 00:20:10,000
you can determine whether those controls

330
00:20:10,000 --> 00:20:11,000
are effective or not,

331
00:20:11,000 --> 00:20:12,000
they might impact other things.

332
00:20:13,000 --> 00:20:16,000
So this is where we didn't wanna start

333
00:20:16,000 --> 00:20:18,000
with digital tools, right?

334
00:20:18,000 --> 00:20:20,000
Because we wanna get the fundamental aspects down,

335
00:20:21,000 --> 00:20:23,000
but we have a whole section on the main part

336
00:20:23,000 --> 00:20:26,000
of the document that's about enablers,

337
00:20:26,000 --> 00:20:27,000
digital tools and key enablers,

338
00:20:27,000 --> 00:20:29,000
which we feel like, yeah,

339
00:20:29,000 --> 00:20:31,000
if you wanna get to the state where we're,

340
00:20:32,000 --> 00:20:34,000
I don't wanna say promising,

341
00:20:34,000 --> 00:20:37,000
but the nirvana of this would be to get to the state

342
00:20:37,000 --> 00:20:39,000
of like just running continuously

343
00:20:39,000 --> 00:20:41,000
and being able to do a snapshot validation

344
00:20:41,000 --> 00:20:42,000
at any one point in time,

345
00:20:42,000 --> 00:20:44,000

you need to do that through digital tools, right?

346
00:20:44,000 --> 00:20:46,000
And I think the most effective ones

347
00:20:46,000 --> 00:20:47,000
that I have seen to date are,

348
00:20:48,000 --> 00:20:51,000
like I said, in the examples and the case studies

349
00:20:51,000 --> 00:20:54,000
on the quality by design tool that we used

350
00:20:54,000 --> 00:20:55,000
so that you could do that.

351
00:20:55,000 --> 00:20:57,000
So you could do the statistics

352
00:20:57,000 --> 00:20:59,000
so that you could see your effectiveness

353
00:20:59,000 --> 00:21:01,000
of controls in real time.

354
00:21:03,000 --> 00:21:06,000
So currently we've got three stages

355
00:21:06,000 --> 00:21:08,000
of validation, right?

356
00:21:08,000 --> 00:21:11,000
We've got what happens in development,

357
00:21:11,000 --> 00:21:14,000
then we've got the demonstration lots,

358
00:21:14,000 --> 00:21:16,000
and then we've got the ongoing.

359
00:21:17,000 --> 00:21:22,000
How does validation 4.0 change any of that?

360
00:21:22,000 --> 00:21:24,000
Or are they still those three phases?

361
00:21:25,000 --> 00:21:27,000
And will they ever change?

362
00:21:29,000 --> 00:21:30,000
My hope is yes.

363
00:21:30,000 --> 00:21:30,000
Do you wanna go, Victor?

364
00:21:32,000 --> 00:21:37,000
Yeah, I like to think that in validation 4,

365
00:21:37,000 --> 00:21:40,000
we are discussing about this stage of validation,

366
00:21:40,000 --> 00:21:42,000
thinking all in scalability.

367
00:21:43,000 --> 00:21:45,000
When you're looking for a new product,

368
00:21:45,000 --> 00:21:48,000
quality by phase appropriate is a tool

369
00:21:48,000 --> 00:21:51,000
to determine the level of effort

370
00:21:51,000 --> 00:21:52,000
that you need to put.

371
00:21:53,000 --> 00:21:55,000
But there is some difficulty to do

372
00:21:55,000 --> 00:21:57,000

in the paper-based way.

373
00:21:57,000 --> 00:21:59,000
So in the moment that you have control

374
00:21:59,000 --> 00:22:02,000
about all points of data,

375
00:22:03,000 --> 00:22:06,000
all aspects, all risk in your process,

376
00:22:06,000 --> 00:22:10,000
you can escalate this control organically

377
00:22:10,000 --> 00:22:12,000
because you have digital tools to do that.

378
00:22:13,000 --> 00:22:16,000
So I like to say that validation 4.0

379
00:22:16,000 --> 00:22:18,000
is about validation stage.

380
00:22:18,000 --> 00:22:22,000
I always consider that my process is validated,

381
00:22:22,000 --> 00:22:26,000
considering the level of the rigor of my phase.

382
00:22:26,000 --> 00:22:29,000
If my product goes to the phase one,

383
00:22:29,000 --> 00:22:32,000
to the phase two, I have control.

384
00:22:32,000 --> 00:22:35,000
And I know exactly what level of control

385
00:22:35,000 --> 00:22:38,000
I need to put because I have digital system,

386
00:22:38,000 --> 00:22:41,000
a digital ecosystem provide me visibility.

387
00:22:41,000 --> 00:22:43,000
How my strategy is going on

388
00:22:43,000 --> 00:22:45,000
and how this strategy can evolve

389
00:22:45,000 --> 00:22:47,000
uses the point to me.

390
00:22:47,000 --> 00:22:48,000
Yeah.

391
00:22:49,000 --> 00:22:52,000
Just on that, I heard an interesting quote

392
00:22:52,000 --> 00:22:54,000
and it's not direct word for word,

393
00:22:54,000 --> 00:22:57,000
but I'm reading the words a little bit.

394
00:22:57,000 --> 00:22:59,000
But the point was somebody asked

395
00:22:59,000 --> 00:23:00,000
at a conference I was at that said,

396
00:23:00,000 --> 00:23:05,000
can we get from R&D to manufacturing,

397
00:23:06,000 --> 00:23:10,000
shift to research and design and manufacturing?

398
00:23:11,000 --> 00:23:13,000
I don't know if you appreciate

399
00:23:13,000 --> 00:23:14,000

the subtlety difference there,

400
00:23:14,000 --> 00:23:18,000
but the idea is that can we get from this state

401
00:23:18,000 --> 00:23:20,000
that's like, again, R&D is this whole thing

402
00:23:20,000 --> 00:23:22,000
and then there's this tech transfer

403
00:23:22,000 --> 00:23:24,000
and then there's this manufacturing space.

404
00:23:24,000 --> 00:23:28,000
Can we get rid of this zone in the middle

405
00:23:28,000 --> 00:23:29,000
where we're getting from research,

406
00:23:29,000 --> 00:23:33,000
really just beginning stages of quality by design

407
00:23:34,000 --> 00:23:38,000
to development and manufacturing as a stage, right?

408
00:23:38,000 --> 00:23:39,000
And this is, in my opinion,

409
00:23:39,000 --> 00:23:41,000
this is like, again, now you're speaking to Nirvana,

410
00:23:41,000 --> 00:23:44,000
but hey, we need a North Star here.

411
00:23:44,000 --> 00:23:45,000
Get to the state of just getting

412
00:23:45,000 --> 00:23:47,000
to these iterative cycles really early

413
00:23:47,000 --> 00:23:50,000
in the QBD process, right?

414
00:23:50,000 --> 00:23:53,000
So if you are starting,

415
00:23:53,000 --> 00:23:55,000
you've got the infrastructure in place

416
00:23:55,000 --> 00:23:59,000
to identify risks, identify risk controls

417
00:24:00,000 --> 00:24:02,000
and have a repository for,

418
00:24:03,000 --> 00:24:08,000
or a place to capture evidence of control effectiveness

419
00:24:08,000 --> 00:24:09,000
and loop that back,

420
00:24:09,000 --> 00:24:11,000
very early in the process,

421
00:24:11,000 --> 00:24:14,000
it can be a design or a process development tool,

422
00:24:14,000 --> 00:24:14,000
in my opinion,

423
00:24:15,000 --> 00:24:17,000
which means that you're just building evidence

424
00:24:17,000 --> 00:24:19,000
of your control file from the very beginning.

425
00:24:19,000 --> 00:24:24,000
I mean, in reality, you've got two control strategies.

426
00:24:24,000 --> 00:24:26,000

You've got process control strategy

427
00:24:26,000 --> 00:24:29,000
and contamination control strategy, right?

428
00:24:31,000 --> 00:24:33,000
For contamination control,

429
00:24:34,000 --> 00:24:38,000
that's somewhat molecule agnostic.

430
00:24:38,000 --> 00:24:42,000
It's strictly, are you filling vials

431
00:24:42,000 --> 00:24:44,000
or are you pressing pills, right?

432
00:24:46,000 --> 00:24:48,000
On the process side,

433
00:24:48,000 --> 00:24:50,000
yeah, they're different molecules.

434
00:24:50,000 --> 00:24:54,000
And once in a while, it's really different,

435
00:24:54,000 --> 00:24:59,000
but still the basic key parameters

436
00:25:00,000 --> 00:25:03,000
around pills or filling vials,

437
00:25:05,000 --> 00:25:06,000
I'm not saying they're the same,

438
00:25:06,000 --> 00:25:09,000
but there's certainly a whole science

439
00:25:09,000 --> 00:25:10,000
behind it that we understand.

440
00:25:11,000 --> 00:25:13,000
How could we not start

441
00:25:13,000 --> 00:25:16,000
from a blank sheet of paper every time?

442
00:25:16,000 --> 00:25:17,000
Yeah.

443
00:25:17,000 --> 00:25:20,000
And how does validation 4.0

444
00:25:20,000 --> 00:25:23,000
bring in the lessons from other places?

445
00:25:25,000 --> 00:25:27,000
Yeah, I'm just giving you the term

446
00:25:27,000 --> 00:25:30,000
is maybe loosely adopted from pharma 4.0,

447
00:25:30,000 --> 00:25:31,000
but like plug and produce in a way,

448
00:25:32,000 --> 00:25:34,000
but in a very different sort of scope,

449
00:25:34,000 --> 00:25:37,000
but can you plug and play

450
00:25:37,000 --> 00:25:38,000
with different controls?

451
00:25:39,000 --> 00:25:42,000
Yes, it would seem like that, right?

452
00:25:42,000 --> 00:25:45,000
You're going to have to provide evidence

453
00:25:45,000 --> 00:25:48,000

for that on all of your products anyway.

454
00:25:48,000 --> 00:25:49,000
You're just going to have to, right?

455
00:25:49,000 --> 00:25:52,000
But can you plug in a control strategy

456
00:25:52,000 --> 00:25:58,000
for like pills or like vials

457
00:25:58,000 --> 00:26:00,000
or can you do that?

458
00:26:00,000 --> 00:26:02,000
It seems like, yes, with the digital world,

459
00:26:02,000 --> 00:26:03,000
you potentially could.

460
00:26:03,000 --> 00:26:06,000
Given the same parameters of X, Y, and Z,

461
00:26:06,000 --> 00:26:07,000
can you take your control

462
00:26:08,000 --> 00:26:10,000
and control evidence and plug it

463
00:26:10,000 --> 00:26:12,000
into a different product and process?

464
00:26:12,000 --> 00:26:12,000
It seems like you could.

465
00:26:13,000 --> 00:26:15,000
Obviously, there's nuances to that, of course,

466
00:26:15,000 --> 00:26:17,000
but like, again, just the infrastructure

467
00:26:17,000 --> 00:26:18,000
would be there.

468
00:26:20,000 --> 00:26:24,000
Yeah, I like I did that,

469
00:26:24,000 --> 00:26:25,000
but edition four, as I said,

470
00:26:25,000 --> 00:26:28,000
we said about data control of data,

471
00:26:28,000 --> 00:26:31,000
the next one is too much about data.

472
00:26:31,000 --> 00:26:33,000
There's several aspects

473
00:26:33,000 --> 00:26:35,000
in the requirements on X, Y, and Z

474
00:26:35,000 --> 00:26:38,000
saying that you need to evaluate

475
00:26:38,000 --> 00:26:41,000
all data for several control strategies

476
00:26:41,000 --> 00:26:42,000
in a holistic way

477
00:26:42,000 --> 00:26:43,000
because obviously,

478
00:26:43,000 --> 00:26:45,000
all pharmaceutical companies

479
00:26:45,000 --> 00:26:47,000
has on a certain level

480
00:26:47,000 --> 00:26:49,000

a contamination control strategy.

481
00:26:49,000 --> 00:26:51,000
But what an X, Y, and Z brings is

482
00:26:51,000 --> 00:26:54,000
we need to evaluate all these data.

483
00:26:54,000 --> 00:26:57,000
So validation for under this vision

484
00:26:57,000 --> 00:27:00,000
provide the tools and the approach

485
00:27:00,000 --> 00:27:03,000
to ensure that all controls,

486
00:27:03,000 --> 00:27:05,000
to ensure a serenity,

487
00:27:05,000 --> 00:27:07,000
ensure that there is no contamination

488
00:27:07,000 --> 00:27:10,000
in your facility is under control

489
00:27:10,000 --> 00:27:11,000
and evaluate together

490
00:27:11,000 --> 00:27:12,000
several source of data.

491
00:27:14,000 --> 00:27:20,000
OK, are there any other new philosophies,

492
00:27:20,000 --> 00:27:22,000
new approaches, differences

493
00:27:23,000 --> 00:27:24,000
that you would find

494
00:27:24,000 --> 00:27:26,000
in validation 4.0 guide

495
00:27:27,000 --> 00:27:29,000
versus the past practices?

496
00:27:30,000 --> 00:27:32,000
It's time for you to really show off

497
00:27:32,000 --> 00:27:33,000
the newness.

498
00:27:33,000 --> 00:27:34,000
What's cool?

499
00:27:37,000 --> 00:27:38,000
Do you want to go, Victor?

500
00:27:41,000 --> 00:27:42,000
OK, yeah.

501
00:27:42,000 --> 00:27:45,000
So I think what I started with is

502
00:27:45,000 --> 00:27:47,000
we didn't create quality by design

503
00:27:47,000 --> 00:27:49,000
nor did we create quality risk management,

504
00:27:49,000 --> 00:27:52,000
which are the fundamental key purposes.

505
00:27:53,000 --> 00:27:54,000
What we've tried to do is

506
00:27:54,000 --> 00:27:56,000
take an existing frameworks.

507
00:27:56,000 --> 00:27:57,000

Of course, we're not going to change

508
00:27:57,000 --> 00:27:58,000
the regulatory landscape.

509
00:27:58,000 --> 00:27:59,000
That's not our point.

510
00:27:59,000 --> 00:28:00,000
Or our objective.

511
00:28:00,000 --> 00:28:03,000
So we took the existing regulatory landscape

512
00:28:03,000 --> 00:28:05,000
and tried to articulate it

513
00:28:05,000 --> 00:28:08,000
in terms of where we are today,

514
00:28:08,000 --> 00:28:10,000
the capabilities that we have today.

515
00:28:11,000 --> 00:28:12,000
Also, I think the big piece

516
00:28:12,000 --> 00:28:13,000
is shifting the mindset away

517
00:28:13,000 --> 00:28:15,000
from methodology.

518
00:28:18,000 --> 00:28:20,000
I do, I say that because it's funny

519
00:28:20,000 --> 00:28:21,000
that one of the first questions

520
00:28:21,000 --> 00:28:22,000
that was asked was,

521
00:28:22,000 --> 00:28:23,000
what about the three runs

522
00:28:23,000 --> 00:28:25,000
of process validation, right?

523
00:28:25,000 --> 00:28:26,000
Always, because when you're talking

524
00:28:26,000 --> 00:28:27,000
to a validation person,

525
00:28:27,000 --> 00:28:29,000
that's immediately what comes to mind

526
00:28:29,000 --> 00:28:31,000
is three runs of process validation.

527
00:28:31,000 --> 00:28:32,000
And it's really starting to shift

528
00:28:32,000 --> 00:28:34,000
that mindset away from

529
00:28:34,000 --> 00:28:36,000
this sort of finite

530
00:28:39,000 --> 00:28:41,000
validation document package,

531
00:28:41,000 --> 00:28:43,000
which is, let's face it,

532
00:28:43,000 --> 00:28:44,000
it's a snapshot in time.

533
00:28:44,000 --> 00:28:46,000
It's a static thing, typically, right?

534
00:28:46,000 --> 00:28:47,000

That, oh, we might do it,

535
00:28:47,000 --> 00:28:48,000
redo it each year

536
00:28:48,000 --> 00:28:51,000
or some rendition of that.

537
00:28:51,000 --> 00:28:53,000
But what we need to start getting towards

538
00:28:53,000 --> 00:28:55,000
is a way, a methodology

539
00:28:55,000 --> 00:28:57,000
to start looking at these things

540
00:28:57,000 --> 00:29:01,000
sort of in uniquely

541
00:29:01,000 --> 00:29:02,000
and in real time.

542
00:29:02,000 --> 00:29:04,000
And the way to do that

543
00:29:04,000 --> 00:29:06,000
is through really rooting ourselves

544
00:29:06,000 --> 00:29:06,000
in the principles

545
00:29:06,000 --> 00:29:08,000
that are important to demonstrate.

546
00:29:08,000 --> 00:29:09,000
Again, I go back to

547
00:29:10,000 --> 00:29:13,000
demonstrating control, right?

548
00:29:13,000 --> 00:29:14,000
And if you ask any different

549
00:29:14,000 --> 00:29:16,000
validation experts,

550
00:29:17,000 --> 00:29:18,000
demonstrating control

551
00:29:18,000 --> 00:29:19,000
is probably not the first thing

552
00:29:19,000 --> 00:29:20,000
that they're going to say.

553
00:29:20,000 --> 00:29:22,000
Like, I've been around

554
00:29:22,000 --> 00:29:24,000
many validation people in my life

555
00:29:24,000 --> 00:29:27,000
and that word never really

556
00:29:27,000 --> 00:29:28,000
came up that often,

557
00:29:28,000 --> 00:29:29,000
which blew my mind

558
00:29:29,000 --> 00:29:30,000
when we started saying,

559
00:29:30,000 --> 00:29:31,000
what is validation?

560
00:29:31,000 --> 00:29:32,000
It really is about demonstrating control

561
00:29:33,000 --> 00:29:35,000

in the context of

562
00:29:35,000 --> 00:29:36,000
patient safety product quality

563
00:29:36,000 --> 00:29:37,000
at the end of the day.

564
00:29:38,000 --> 00:29:39,000
And so it's like really rooting ourselves

565
00:29:39,000 --> 00:29:40,000
in these principles,

566
00:29:40,000 --> 00:29:42,000
utilizing the requirements

567
00:29:42,000 --> 00:29:42,000
that are already out there.

568
00:29:42,000 --> 00:29:44,000
Again, I see HQ8, Q9,

569
00:29:45,000 --> 00:29:46,000
utilizing digital technologies

570
00:29:46,000 --> 00:29:48,000
because those are new capabilities

571
00:29:48,000 --> 00:29:48,000
we have now,

572
00:29:49,000 --> 00:29:52,000
new-ish, but new relative to,

573
00:29:52,000 --> 00:29:53,000
you know, previous approaches.

574
00:29:54,000 --> 00:29:55,000
And really getting ourselves

575
00:29:55,000 --> 00:29:58,000
into a state where we can determine

576
00:29:58,000 --> 00:30:00,000
and demonstrate validation in real time.

577
00:30:01,000 --> 00:30:02,000
This, in my opinion,

578
00:30:02,000 --> 00:30:03,000
will help us get to

579
00:30:03,000 --> 00:30:05,000
potentially quicker time to value

580
00:30:05,000 --> 00:30:06,000
on new products,

581
00:30:06,000 --> 00:30:07,000
but really also the evolutions

582
00:30:07,000 --> 00:30:08,000
of existing products,

583
00:30:09,000 --> 00:30:12,000
but also potentially taking account

584
00:30:12,000 --> 00:30:15,000
for upstream and downstream data, right?

585
00:30:15,000 --> 00:30:16,000
There's a lot of data out there

586
00:30:16,000 --> 00:30:16,000
we're not using,

587
00:30:16,000 --> 00:30:18,000
whether it's our raw material suppliers

588
00:30:18,000 --> 00:30:20,000

or it's real world evidence

589
00:30:20,000 --> 00:30:21,000
or whatever.

590
00:30:21,000 --> 00:30:22,000
Why does that not feed

591
00:30:22,000 --> 00:30:25,000
into our validation loop,

592
00:30:25,000 --> 00:30:26,000
our life cycle, right?

593
00:30:26,000 --> 00:30:28,000
Like now maybe in like

594
00:30:28,000 --> 00:30:29,000
annual product reviews,

595
00:30:29,000 --> 00:30:30,000
we might look at that stuff,

596
00:30:30,000 --> 00:30:31,000
but really as part of

597
00:30:31,000 --> 00:30:32,000
product and process

598
00:30:32,000 --> 00:30:34,000
and how that can help.

599
00:30:34,000 --> 00:30:36,000
Again, this is our North Stars

600
00:30:36,000 --> 00:30:37,000
trying to get to these places,

601
00:30:37,000 --> 00:30:38,000
but you got to get

602
00:30:38,000 --> 00:30:39,000
the infrastructure in place

603
00:30:39,000 --> 00:30:40,000
and the thinking

604
00:30:40,000 --> 00:30:41,000
and the cultural shifts.

605
00:30:43,000 --> 00:30:43,000
Victor?

606
00:30:44,000 --> 00:30:45,000
Michelle, it was perfect.

607
00:30:47,000 --> 00:30:50,000
Yeah, it was perfectly all sentence.

608
00:30:50,000 --> 00:30:52,000
So I believe this is the point

609
00:30:52,000 --> 00:30:54,000
that we shall stage,

610
00:30:55,000 --> 00:30:56,000
have control.

611
00:30:56,000 --> 00:30:58,000
There is a chapter in our guide

612
00:30:58,000 --> 00:31:00,000
that say that

613
00:31:00,000 --> 00:31:01,000
holistic control strategy,

614
00:31:01,000 --> 00:31:03,000
how you need to define

615
00:31:03,000 --> 00:31:04,000

this holistic control strategy,

616
00:31:04,000 --> 00:31:06,000
mapping the process,

617
00:31:06,000 --> 00:31:07,000
mapping the strategies,

618
00:31:07,000 --> 00:31:11,000
and how you can have this visibility.

619
00:31:11,000 --> 00:31:12,000
So this I think,

620
00:31:12,000 --> 00:31:13,000
this I believe is

621
00:31:14,000 --> 00:31:16,000
the core of the approach.

622
00:31:16,000 --> 00:31:18,000
Have control, have visibility.

623
00:31:18,000 --> 00:31:20,000
How this control is

624
00:31:20,000 --> 00:31:22,000
going through your process.

625
00:31:22,000 --> 00:31:23,000
Understanding in,

626
00:31:24,000 --> 00:31:25,000
how do you need to define

627
00:31:25,000 --> 00:31:28,000
a level of effort of activities

628
00:31:28,000 --> 00:31:31,000
to not to waste too much time.

629
00:31:31,000 --> 00:31:34,000
Because sometimes I have seen that

630
00:31:34,000 --> 00:31:37,000
there are a lot of work to do again,

631
00:31:37,000 --> 00:31:39,000
but if you have control of the data,

632
00:31:39,000 --> 00:31:41,000
mainly you can use to leverage

633
00:31:41,000 --> 00:31:42,000
previous knowledge,

634
00:31:42,000 --> 00:31:44,000
previous activities.

635
00:31:44,000 --> 00:31:46,000
So control is the fundamental

636
00:31:46,000 --> 00:31:47,000
of this approach.

637
00:31:47,000 --> 00:31:49,000
Have control of the data.

638
00:31:49,000 --> 00:31:52,000
Well, there's so many more dimensions

639
00:31:52,000 --> 00:31:53,000
that we could talk about

640
00:31:53,000 --> 00:31:55,000
for the next four hours.

641
00:31:56,000 --> 00:31:58,000
But to bring this

642
00:31:58,000 --> 00:31:59,000

to kind of a wrap up,

643
00:32:00,000 --> 00:32:03,000
I'm really excited about

644
00:32:03,000 --> 00:32:03,000
what's in this

645
00:32:04,000 --> 00:32:07,000
validation 4.0 good practice guide.

646
00:32:08,000 --> 00:32:11,000
What I see when you talk about

647
00:32:11,000 --> 00:32:12,000
quality by design

648
00:32:12,000 --> 00:32:14,000
and quality risk management

649
00:32:14,000 --> 00:32:16,000
as being the fundamentals,

650
00:32:16,000 --> 00:32:18,000
and then demonstrating

651
00:32:19,000 --> 00:32:23,000
that your controls are effective,

652
00:32:23,000 --> 00:32:23,000
that they work.

653
00:32:26,000 --> 00:32:28,000
To me, that's what

654
00:32:28,000 --> 00:32:30,000
the regulators have been

655
00:32:30,000 --> 00:32:32,000
wanting us to do all along.

656
00:32:33,000 --> 00:32:35,000
But we've kind of been

657
00:32:35,000 --> 00:32:37,000
shackled by past practices.

658
00:32:39,000 --> 00:32:42,000
And I'm hopeful that this document

659
00:32:42,000 --> 00:32:44,000
helps us move towards

660
00:32:44,000 --> 00:32:46,000
where the regulators

661
00:32:46,000 --> 00:32:47,000
really want us to be.

662
00:32:49,000 --> 00:32:50,000
And hopefully shed

663
00:32:51,000 --> 00:32:54,000
some non-value-added practices

664
00:32:54,000 --> 00:32:57,000
that we thought we had to do

665
00:32:58,000 --> 00:32:59,000
along the way.

666
00:33:00,000 --> 00:33:01,000
And really get us to where

667
00:33:01,000 --> 00:33:04,000
we're always evaluating the data

668
00:33:04,000 --> 00:33:06,000
as it comes in, in real time.

669
00:33:08,000 --> 00:33:09,000

Maybe even making adjustments

670
00:33:09,000 --> 00:33:11,000
without regulatory approval

671
00:33:12,000 --> 00:33:13,000
based on data.

672
00:33:13,000 --> 00:33:15,000
Yeah, I agree.

673
00:33:15,000 --> 00:33:16,000
I can't agree with you more.

674
00:33:16,000 --> 00:33:18,000
And you've summarized it really well.

675
00:33:19,000 --> 00:33:21,000
And just one little anecdote is,

676
00:33:21,000 --> 00:33:22,000
we did work with

677
00:33:22,000 --> 00:33:24,000
a quality innovation group

678
00:33:24,000 --> 00:33:24,000
out of the EMA.

679
00:33:24,000 --> 00:33:26,000
And that was really an exciting process

680
00:33:26,000 --> 00:33:28,000
that they were so willing

681
00:33:28,000 --> 00:33:29,000
to spend the time with us

682
00:33:29,000 --> 00:33:31,000
to review our concepts.

683
00:33:31,000 --> 00:33:33,000
And they had some great input

684
00:33:33,000 --> 00:33:34,000
and that did ultimately

685
00:33:34,000 --> 00:33:35,000
get into the guide.

686
00:33:36,000 --> 00:33:38,000
But I think they were excited.

687
00:33:38,000 --> 00:33:40,000
They were excited because

688
00:33:40,000 --> 00:33:40,000
they're like, this is what

689
00:33:40,000 --> 00:33:41,000
they've been trying to push

690
00:33:41,000 --> 00:33:43,000
for Annex 15 for so long.

691
00:33:44,000 --> 00:33:47,000
And there's wording in there,

692
00:33:47,000 --> 00:33:48,000
in the Annex 15 already,

693
00:33:48,000 --> 00:33:50,000
it states continuous validation

694
00:33:50,000 --> 00:33:51,000
and all these kinds of things.

695
00:33:51,000 --> 00:33:53,000
And it pushes the principles.

696
00:33:53,000 --> 00:33:54,000

And I think they thought

697
00:33:54,000 --> 00:33:56,000
that maybe this will help

698
00:33:56,000 --> 00:33:58,000
also push the industry

699
00:33:58,000 --> 00:34:00,000
to adopt something that, again,

700
00:34:00,000 --> 00:34:02,000
has been out there for a while now.

701
00:34:02,000 --> 00:34:04,000
Well, that brings us to the end

702
00:34:04,000 --> 00:34:07,000
of another episode of the ISPE podcast,

703
00:34:07,000 --> 00:34:09,000
Shaping the Future of Pharma.

704
00:34:09,000 --> 00:34:12,000
A very big thank you to our guests,

705
00:34:12,000 --> 00:34:13,000
Michelle and Victor,

706
00:34:13,000 --> 00:34:16,000
for sharing how Validation 4.0

707
00:34:16,000 --> 00:34:19,000
will help industry apply technology

708
00:34:19,000 --> 00:34:20,000
to improve quality,

709
00:34:21,000 --> 00:34:22,000
reduce cost of goods,

710
00:34:22,000 --> 00:34:25,000
and perhaps even speed time to licensure.

711
00:34:26,000 --> 00:34:27,000
Please be sure to subscribe

712
00:34:27,000 --> 00:34:30,000
so you don't miss future conversations

713
00:34:30,000 --> 00:34:32,000
with the innovators, experts,

714
00:34:32,000 --> 00:34:34,000
and change makers

715
00:34:34,000 --> 00:34:35,000
driving our industry forward.

716
00:34:36,000 --> 00:34:38,000
On behalf of all of us at ISPE,

717
00:34:38,000 --> 00:34:40,000
thank you for listening.

718
00:34:40,000 --> 00:34:41,000
And we'll see you next time

719
00:34:41,000 --> 00:34:44,000
as we continue to explore the ideas,

720
00:34:44,000 --> 00:34:46,000
trends, and people

721
00:34:46,000 --> 00:34:51,000
shaping the future of pharma.