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Welcome to the ISPE podcast, shaping the future of pharma, where ISPE

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supports you on your journey, 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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00:00:21,000 --> 00:00:22,000  
I'm Bob Chew, your host.

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And today, we have another episode where we'll be sharing the latest  
insights

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00:00:27,000 --> 00:00:32,000  
and thought leadership on manufacturing, technology, supply chains

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and regulatory trends impacting the pharmaceutical industry.

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You will hear directly from the innovators, experts and professionals  
driving progress

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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 accelerating technology adoption.

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I am recording this podcast from a National Geographic ship in the Antarctic.

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If you hear occasional crashes or sounds like thunder, that is likely the

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ship moving through the ice pack.

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I have no special guest for this episode and will instead offer my thinking on this

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topic of accelerating technology adoption.

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As part of doing this podcast series, I attend many ISPE

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and other industry conferences, hearing case studies, listening to executives,

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regulators, and technical experts talk about the future and the present.

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I hope you will find this thought provoking and perhaps create your own innovative

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approaches to shape the future of pharmaceutical manufacturing.

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In this session, I'm going to discuss three broad topics: documents, data,

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and statistics.

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Now what do these have to do with the subject of this podcast,  
Accelerating Technology

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Adoption?

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Well, innovative technologies such as AI and digital

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twins are based on sophisticated statistical algorithms.

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When we train these models, we feed them data, lots of data, data

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that is relevant to what we want the model to do.

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The more data, the more statistically relevant outputs we will get.

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Of course, large language models are trained based on language, I e,

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documents.

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Now GMP regulations contain many references to

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and expectations of documents.

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Our quality systems are largely document based.

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We have policies, procedures, protocols, work instructions

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by the thousands.

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Let me ask this question.

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Should our quality systems continue to be document based or should we

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move towards a more data driven quality system?

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Now, our production and process control systems provide data

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by the boatload continuously.

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Separately, we have data generated by our QC laboratories.

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Separately, we have information about human performance, including training records.

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Today, technology exists to monitor operators and assess human performance,

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which could focus on how the operators contribute to process and contamination control

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and record proper or improper aseptic techniques, for example.

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Thus, we can even include information about human performance

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into the category of data.

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Now, new technologies and computing power exist to synthesize

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all the above and create a production model which could

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analyze the effectiveness of the process and contamination control strategies

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and even identify opportunities for improvement through statistical evaluation.

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In other words, data, a data driven quality system.

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Let's examine how data could supplant documents as the foundation of

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our quality system.

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Today, when we have a deviation, we create a document.

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That document describes what happened and offers root cause analysis,

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corrective actions, and preventive actions for the future.

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We agonize over the wording of these documents since they will be

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used to explain to future inspectors what really happened and

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provide a convincing case that the corrective and preventive actions were

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both justified and sufficient.

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What if in the future we had a combination of Process Digital Twin constantly

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monitoring the process and an AI platform that integrated

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past deviation data, past what happened, what

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were the corrective actions, and what were the results of those actions.

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When we have the next deviation, these technologies can provide a statistically

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ranked set of possible root causes with associated

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probabilities and recommended corrective actions that are based on observed

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effectiveness of similar actions in the past.

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The human can still provide the machine generated still approve the

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machine generated recommendation but using statistics based on data.

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And from time to time, the human may identify new

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root causes and new opportunities for innovative improvements.

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But we no longer agonize over the wording of documents.

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Further, today, our conclusions can often be operator error

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or laboratory error.

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If AI is assessing these situations based on data, it

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might point to other root causes based on the real data and the statistical

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probability that it really isn't operator error or

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laboratory error.

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Let's broaden the conversation and consider quality risk management.

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First, I'd like to remind ourselves that each and every GMP

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regulation is designed to control a risk to

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manufacturing quality.

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In other words, the original quality risk management system is our

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GMP regulations.

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For example, GMP regulations tell us that we must have procedures

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for cleaning and that those cleaning procedures

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be validated.

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Why is that?

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Well, it is to control the risk that cleaning is

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not sufficient and that it doesn't clean properly.

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And so we have these regulations.

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How might we use a statistically based technology to automatically

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generate risk assessments?

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Well, if we had an AI model of aseptic

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processing And that AI model

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was trained on a combination of regulations

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for aseptic process control like Annex one.

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If it was trained on how equipment is designed

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for aseptic, control, contamination control, if it was

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trained on the actual observed effectiveness of those controls

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during ongoing aseptic production operations, we

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could then have a tool that is automatically updated around

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the concept of contamination control.

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And it would be assessing risks, new risks,

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old risks, how effective are those controls, and constantly

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reporting out that these controls are effective and these controls

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might need, improvements.

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I think it would be super powerful if we could apply, statistical

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techniques through process digital twins, through aseptic

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process digital twins to generate automatically

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quality risk management metrics.

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Now how might equipment digital twins be used to accelerate startup

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and qualification of equipment?

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After all, digital twins of jet engines have been used for a long time to

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analyze performance and to model failure modes and effects.

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Well, imagine an aseptic filling line.

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Imagine a digital twin of such a filling line, which, by the way, has

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already been created and used in at least one aseptic manufacturing

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plant in Ireland.

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There was a case study presented at an ISPE conference about a year ago.

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Imagine training this digital twin during factory acceptance testing.

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And so now this digital twin has a representation,

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a model of how that aseptic line should work, how each and every

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manipulation on that line should work, its performance.

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Now we disassemble the line, we ship it, we set it up at the,  
manufacturing

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site, and as we go through the startup process, we plug

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in the digital twin.

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It monitors how the machine is operating, and it's able to point

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that you need to adjust, make this adjustment on this part.

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You need to look at this connection.

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It's not working right.

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But at the end of the day, it's able to automatically say

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that the equipment is qualified.

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Wouldn't that be sweet?

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Today, AI writes computer code and

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it self tests that computer code.

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Not necessarily in the pharmaceutical industry, but that technology  
exists.

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Imagine being able to apply that technology to automatically generate

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the process control automation software and

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to automatically test it.

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That would certainly be an acceleration of the delivery of manufacturing capability.

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Now I'm going to suggest a break from past approaches to process validation.

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First, unless you're doing a site to site transfer, it's

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unreasonable to expect that development batches supplemented

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with a few engineering batches will yield a statistically valid

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design space.

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Let me say that again.

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Design space is that three-dimensional or multi dimensional

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model of where you can manufacture and get a

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successful batch.

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That takes quite a few statistical, batches to build.

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Nor can we really say that a process is truly validated based on three successful

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batches, which are not always without a failed batch or two interspersed.

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I will offer that a robust process digital twin

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is nothing more than the design space from an underlying statistics

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perspective.

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It takes quite a few batches to train a digital twin.

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But once you have it trained, you also have a robust

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design space defined.

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As we then continue to manufacture and problems arise, the digital

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twin can either point to the root cause or

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it can say unknown new source of variation identified,

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which might be that you change bioreactor bag supplier or the supplier altered

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its methods or raw materials without understanding the impact on your process.

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In short, getting a process to a validated

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state is a continuous process and it will take

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quite a few batches to really develop that robust design space.

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Okay, you might agree with me theoretically, but from a practical perspective,

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when would regulators give the green light to market the product?

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How many batches must be produced first?

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Well, I can imagine a regulator having an AI tool

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that statistically assesses the degree of control exhibited by the

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process as reflected in consistent process performance data.

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The licensed applicant would have the same data and would notify regulators

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when it feels that it has its process in a full state of control, regardless

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of how many batches that is.

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The regulator would access the process data and,

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using its AI tool, analyze the data and render an approval decision.

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This would automate and accelerate the licensing process.

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Couple this with machine digital twins reporting out to regulators that a qualified

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state has been attained, and we take the guesswork and time delays

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out of, preapproval inspections.

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If we agree that new technologies based on statistics will drive us

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towards a data centric quality system, then data integrity

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takes on even more importance than it has up to now.

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Data integrity has focused on ensuring that data meets the ALCOA

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plus characteristics of attributable, legible, contemporaneous,

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original, accurate, complete, consistent, enduring,

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and available.

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But in addition, when it comes to training an AI or digital twin model, the

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data must also be relevant to the situation or application being

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trained.

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Now I will leave it to our Pharma four point o colleagues to expound upon this dimension

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of data and data integrity.

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So back to the title of this podcast episode, Accelerating Technology

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Adoption.

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How can we achieve this acceleration?

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My answer is, by recognizing how these new technologies really

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work, we accept the use of statistics to assess clinical outcomes,

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the basis for all drug approvals.

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We understand that quality risk management is founded on probabilistic estimates

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of hazards and controls.

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Therefore, we should embrace the power of new statistical tools of

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which AI and digital twins are prime examples and implement

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such tools across the manufacturing operation.

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In conjunction, we need to deemphasize documents and base

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our quality systems on data.

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Both industry and regulators should come together to discuss how

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to transform our industry to a nimble, data driven approach to process control,

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contamination control, and quality assurance.

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Old expectations of documents should be replaced by new expectations

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of data analysis.

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The quality function should evolve from one of compliance to procedures

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to one of a true quality engineer, driving innovation and changes for

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improvement.

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We must get comfortable with the use of AI and digital twins for

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automated process control and continued refinement of the design space.

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In summary, if we view AI and digital twins from the lens

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of statistics and if we can appreciate that the more data we feed these

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tools, the more useful and robust they become, we conclude

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that we should move away from a document centric quality system and towards a data

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centric quality system.

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Quality management throughout the life cycle of a product and facility becomes

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a continuous improvement journey.

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Each improvement, each change, should be made based on the statistics of

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real data and in most cases can be implemented either automatically

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or without a change control package.

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That brings us to the end of another episode of the ISPE podcast, Shaping

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the Future of Pharma.

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Please be sure to subscribe so you don't miss future conversations with the innovators,

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experts, and change makers driving our industry forward.

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On behalf of all of us at ISPE, thank you for listening, and we'll see

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you next time as we continue to explore the ideas, trends, and

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people shaping the future of pharma.