Johner Institute

Production validation

With Dr. Michael Schoppol, Prof. Dr. Christian Johner

Transcript

00:00:05 Speaker 1

Medical Device Insights, a podcast by the Ione Institute for medical device manufacturers, authorities and notified bodies.

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In this episode of the Medical Device Insights podcast, we also take care of medical devices, of course, because that is our topic here at the institute.

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Many of you know that we also have a focus on active

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product and that's why we often have topics related to development.

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But of course, the life cycle of a medical device is somewhat more extensive than just the development.

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There are many other processes that we are also looking at, that we support.

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And one of these processes concerns production, or there may be several processes.

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And today

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In the interview, I got an expert on the topic of processes and also process validation.

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And that is Doctor Schopol, who may introduce you very briefly so that our listeners can assess and classify you, Mr. Schopol.

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Thank you very much for the introduction, Professor Jonah.

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Thanks also for the expert.

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I try hard.

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As already described, I am the one who

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closing ranks with what is going on in the direction of development and then accompanying the transition to design transfer into production.

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But my focus is actually on the entire area of production, i.e. both value-adding and non-value-adding processes, in this case everything that is knitted around production, including testing, including equipment, all the topics that we will address again today in the podcast.

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Doctor Michael Schuppo, the doctor, is a mechanical engineer with a doctorate,

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with a focus on production technology, has been working very intensively for 12 years now on the approval of medical devices in the sense of the approval of production processes and in advising on production processes of medical device manufacturers.

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However, this is then done across all risk types of medical devices and risk classes worldwide, which is a lot of fun.

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And now I'm giving the ball right back to Professor Juna.

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Yes, this brings us to the middle of the topic of production and I think it would be a good time to open this black box, to see which processes, which process steps are we talking about here at all.

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So that we have an overview, but we want to concentrate on these processes and process steps that have an impact on functionality, safety, i.e. on the quality of the medical devices.

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Which processes and process steps should be kept in mind, Mr. Schopold?

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I could make it very simple, I could say on all processes.

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This means that they have to deal intensively with every single production step, with every single transport step that their medical device undergoes, from the point of view of risk management.

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They have to determine what influence, as they have just described, what influence this process step has on the

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Quality, i.e. the safety and functionality of my medical device in the end.

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And it doesn't matter whether it's a manufacturing process, logistics or a warehouse process.

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K., that is, now we have already got to know 3 classes.

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Yes, so production, storage, logistics and have also learned that you can't say a priore what the processes are that have an influence, but it's the result of an analysis and not the a priori assumption.

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With that, we have to go straight into the next step.

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Yes, how do I proceed in these steps to identify these risks with sufficient reliability?

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And perhaps you can also give us a few examples of such risks.

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Of course, you would hook in very well with your development, because in the context of the development of the medical device, and we have already talked about these processes relatively often in advance.

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At the same time, the manufacturing process should also be developed so that the entire process, manufacturing process and medical device can be transferred to the corresponding pilot series as part of the design transfer.

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When we think of such processes, of production steps, we think, for example, of production steps, such

as typically steps that we actually take in the context of a verification of the results, the process results.

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, then you are obliged.

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This is what stands above production, 100% verification of process results specified for your medical device in production.

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That is, all the results that you can't check 100%, where you can't confirm the result 100%, typically processes that you just have, whose results you can't prove non-destructively,

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For such processes, you have to strive for appropriate validation, and in the case of processes that require validation, for example, we start from all joining processes, whether it is welding, whether it is laser welding, whether it is soldering, whether it is any other bonding technology, joining technology.

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Here you have the problem that you identify the production step at this point via risk management.

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It is usually mandatory for the safety and functionality of your medical device, i.e.

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You need to validate this process accordingly.

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That would be a typical case for a corresponding process, which you have to look at very carefully.

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Other processes are, for example, cleaning processes.

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You need to determine the extent to which contamination for your medical device can happen in production and to what extent you are able to clean this contamination off this medical device.

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This all-in-one woolly lactic acid at the end of the process chain

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in the production of a medical device, which then purifies everything down in a blanket sense, there is none.

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In production, we often have the case that we have a very large purification stage in quotation marks at the very end of the concept and an attempt is made to clean down everything that arises in the process

chain for the medical device during production.

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This only works to a limited extent.

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This means that it may make much more sense to insert decentralised intermediate cleaning at certain points in production at certain points in production, if you are aware of the process chain, in order to actually ensure that a cleaned product already goes into the next production step.

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O.K., that was a lot.

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Let me briefly summarize.

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Well, on the one hand, you have distinguished between production steps.

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The final result of which can be fully checked and also fully checked on those where this is not the case.

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Because for those who don't, they said we need validation.

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You have now also mentioned a whole series of such process steps or processes.

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The first class was everything that has to do with fuming, as they called it.

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So gluing, welding and so on, soldering.

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And the second class of processes requiring validation was everything in the area of cleaning, probably also sterilization.

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You had given the valuable hint that cleaning, a major cleaning, may not be the right approach at the end, but that you can better minimize the risks and also validate the sub-steps better if you do this in several steps, i.e. after certain production steps already an intermediate cleaning, if I may call it too amateurish, .

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Is that so correctly reproduced?

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This is one hundred percent correct.

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You can already see that it bubbles out as well as it does.

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When I'm in production, it's always a little bit more.

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Yes, so with that you have already mentioned the first measure to minimise such risks.

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If we now perhaps go back into these joint processes, what do you see as possible risk-minimizing measures?

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Outside of validation, ultimately

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If we come across such processes or processes that actually require validation, then this means that we have to ensure from the outset that the equipment, i.e. the machine-machine-plant device that we use for the series production of medical devices, is appropriately qualified.

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That's a basic requirement, a basic requirement of the regulatory requirement.

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K., of course, you already have a perfect transition, because I think you'll dive a little closer.

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So into the question,

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What regulatory requirements are now for manufacturers in this context in particular production, machines, machine systems, tools, measuring equipment, what must be complied with?

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What would you call then, what should you pay attention to as a manufacturer or, more precisely, what do you have to pay attention to as a manufacturer?

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So, what regulatory requirements do we have, perhaps also which standards?

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Ultimately, if you are in the European sector, the 13485 is of course the clear leader.

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Derived from it, it is quality management, the quality management system standard, which I want it, I don't want to say, is required by the MDR.

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But the MDR in particular places a very large emphasis on production and in derivation of the quality of the quality management system, 13485 then lays the foundation in the area of production.

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very own chapters and very own sub-points, which only deal purely with production.

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You should investigate this very intensively.

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If you want help, guidance documents from the FDA, for example, which also deal very, very strongly with production in the area of 21 CFR 820, usually help.

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This is a bit due to the fact that the FDA

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In the course of the inspections, of course, it also takes a very close look at the production, because the other faction of the F.D.E., which deals with the approval of the medical device, has issued the approval according to the paper situation and is now being checked accordingly in the course of the inspections to what extent the specifications from the development file are then also complied with accordingly.

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That is, it is precisely from this point and these are the points that will then be used for the

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consulting companies or companies to be advised.

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It is precisely these points F.D.A., what is the top ten of findings, that come up again and again in the areas of production that deal with the validation of processes, that deal with the qualification of equipment.

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In other words, these are all things that are absolutely necessary and also run through all regulatory requirements worldwide, be it European-based

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regulatory requirements, be it American-based regulatory requirements, and that applies to them in Russia and China as well.

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Mhm, so that means I'll try to sort it out again briefly, so we have a large, so a limited number of regulatory requirements for the time being, you have now mentioned above all, the M.

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i.e. the prescriptions, i.e. M.

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of course completely analogous to U.

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21 CFR 820 and then on the European side the

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The pardon, the meanwhile harmonized 13 for 85, so to speak, that's the beginning.

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You have already said that we are currently in the 13 for 85 Nemmingen.

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So you are probably referring to Chapter 75 in particular, where it is about the means of production, the tools that we also find elsewhere, measuring equipment, perhaps also the qualification of employees.

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I think it's always a popular point of attack and you're already there.

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and said, what are the most common findings we have?

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You might want to summarize this very briefly or perhaps expand it if necessary?

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So, what are the points that are found again and again during inspections, audits or other analyses?

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Typically, the F.D.A. says, and this has been in the top five for years, for example design transfer, for example the validation of processes

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And as I described it earlier, the qualification of equipment.

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This means that machines, machines, plants, devices, tools used for the series production of medical devices must be qualified.

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If the tenor is always on I.Q.O.Q.P.Q., i.e. Installation Qualification, Operations Qualification and Performance Qualification and, based on this, the

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Validation of processes.

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If you cannot qualify an equipment, i.e. machines, machines, plant or device, you have no chance with validation.

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This is one of the core issues that we currently have in the field of the medical device industry, that we have a very large number of very heterogeneous companies that are very mixed in terms of the age of the machines, machine systems and devices, some of which are

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do not have a CE marking for their machines and machine systems, which I would like to build on and must also rely on.

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This means that the documentation situation of the machine and machine systems in production sometimes does not provide the basis for validation at all, and that is what the FDA and what the notified bodies notice again and again in the course of audits and which also leads to strong deviations again and again and where we also repeatedly

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to carry out a new production structuring.

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Mhm, I suspect that this topic will continue to boil up, because now in the context of the M.

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Above all, we have the topic of approval again and I can imagine that at the moment there is still a lot of focus on the products, on which the development part is directed, but at the latest then with the follow-up audits the focus will also be on production again.

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Yes, what can you do now as a manufacturer to

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to prevent such deviations?

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So, is there, what would you like to give as a best practice or what would you like to give as a very concrete tip for next steps?

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In principle, I can reassure you a bit, not every machine, machine, system and device in production is actually significantly responsible for the safety and functionality of the medical device in terms of the result.

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What I recommend at this point is to carry out a production structure analysis.

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That means that from the cradle to the bar, I almost said, from the first step into the hall, you actually look at the state of the machines.

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Where are the machines located?

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What do these machines do?

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For which product portfolio?

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What are the processes that are run on this machine?

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And once you have done this analysis, you can find out about the risk on the basis of this analysis, about risk management approaches.

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In 14971, we had previously mentioned very briefly which processes are actually significant for the safety and functionality of the medical device, in order to then explain them in more detail, to determine them in more detail and, if necessary, to

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non-existent process validation for processes requiring validation.

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That is, really with my eyes open, I always describe it as an intelligent inventory, i.e. really going through and recording in production, which machines, machines, systems, devices are there for the series production of medical devices, what exactly they do and what effects does this have on my corresponding product.

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In doing so, they take into account not only machines, machines, systems, devices and tools, but also everything where they have storage space, for example.

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For example, it is forbidden to place surgical instruments on wooden boxes or the like in humid environments, because they are then immediately confronted with biosafety at the site.

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But that would be the first step to actually get a clear picture of the process flow of the individual products through production.

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So that means, as you said so beautifully, to take stock.

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The way you described it, I think it is also very easy to handle, because they are really visible things.

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All this equipment that you have described may no longer be quite as visible, so how is the inventory of the associated processes and procedures?

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But I think that once you've catagonized and inventoried all the machines, the tools and so on, then you already have a

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Necessary, if perhaps not sufficient, certainty to have thought of everything.

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And of course, your advice to look at this from the perspective of risk management is also valuable, because we have one goal, namely to guarantee the safety and performance of the products and not to do a validation for the sake of validation.

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Yes, Mr. Schoppold, thank you for this insight.

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As always, I will also show your

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Deposit contact details so that those who need support can then really find this P.Q.I.Q.O.Q.

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or to decide whether it is necessary at all for them to get help.

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In the show notes you will also get further information, once in the sense of specialist articles that give you a bit of background information or audit, where you can of course also include exactly these topics.

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So, you should have all the support with you so that you can also work in the area of production.

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remain compliant with the regulatory requirement.

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Yes, Dr.

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Sobol, thank you again very much for your time.

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Thank you for the invitation.