Johner Institute

No need to worry about FDA inspections

With Luca Salvatore, Prof. Dr. Christian Johner

Transcript

00:00:05 Speaker 1

Medical Device Insights is a podcast from the IONE Institute for medical device manufacturers, authorities and notified bodies.

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The Corona pandemic is now largely over for the FDA.

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We can see this in the fact that it is becoming more and more apparent, even with European manufacturers,

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During this pandemic phase, it was not allowed to, or did not send its inspectors out into the world.

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But this is starting again now and the companies are therefore asking us: Yes, how do we prepare for this?

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What do you have to do there?

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How does such an inspection work?

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Or if it has already taken place, how do we deal with these results?

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And to convey exactly that now, so that after this podcast they know: How do I prepare?

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How does it work?

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How do I make sure it's a successful inspection?

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This is exactly the topic today that I would like to discuss with Luca Salvatore and

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Luca, you've been involved in this topic for a long time.

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Please introduce yourself again very briefly anyway.

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Gladly, hello Christian.

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Yes, I have been with the Jona Institute since 2015 and yes, I am mainly concerned with the topic of international approvals and there has always been the F.D.A.

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at the forefront.

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So, that's what you do every day, you could say.

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You also accompanied many, yes, made preparations, led submission meetings.

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So, this is yours,

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Curve and that's why I would say you get in directly.

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So perhaps with the banal question, what is an F.D.A.

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Inspection, perhaps also compared to an audit, for example by a notified body.

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Yes, good question.

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So in general, an inspection is a legal authority of an authority, in this case now the F.D.A.

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to monitor certain entities such as medical device manufacturers.

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The aim is always to check conformity with legal requirements, with a focus on

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identifying any non-conformities and that is exactly what makes them a big difference to audits.

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The aim of the audit is often to identify potential for improvement.

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The inspection is really only about identifying legal violations, which can then also have serious consequences.

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K., we definitely have to talk about it, yes, what can happen about this topic, which is already happening with Schwang, i.e. with the

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successful audit, you can shine somehow.

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You can also get a certificate then, yes, at the F.D.

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Maybe a bit too flat now, but you can still lose there.

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Well, there is the wish that nothing happens, if I understand you correctly.

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Yes, exactly.

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So in the best case you can get through it without deviation.

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O.K., so now you know about what it is.

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Now the question is, how does an inspection come about?

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Inspections often take place in this way.

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Is that rather something related to something different?

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Is that more of a thing?

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which takes place after a regular cycle.

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Yes, it really depends on the type of inspection.

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So there are different types.

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There is the pre-approval inspection, which means that the F.D.A.

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as part of an approval process, in this case pre-market approval for high-risk products.

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That is, they lead, they are carried out within the framework of the P.M.A.

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approval process before the actual approval.

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then there is the routine inspection, which is carried out on a risk-based basis.

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This means that risk factors include the risk class of the products, the inspection history of the specific manufacturer, how the previous inspections were conducted, i.e. whether the result was good or bad, whether the manufacturer initiated recalls or generally released reportable adverse events.

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Yes, so there are many factors,

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it is not possible to say exactly how often you are audited or inspected, in this case especially with foreign manufacturers.

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I have now looked at the figures from last year, we had or the F.D.A.

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had carried out 350 inspections abroad in the medical device sector, in Germany it was 55 OK.

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That means that there was probably still a small number of manufacturers who were tested.

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These are probably also a bit of the Corona late effects.

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So you have to expect that and we can already see that.

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That the activities are increasing again.

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K., so we know it's partly following a pattern, but there are also occasion-related ones.

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You said that once, when something was somehow negative, it was noticed, or when you also have a P.M.A.

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then they are occasion-related inspections.

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How do they work in general?

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So maybe, if you sketch that very briefly from

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I don't know, from the first letter, there comes the, I don't know if it's also mail now, until the thing is completed, so to speak, those would still be typical phases.

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So now it's more e-mails that arrive, that is, the F.D.A.

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usually announces itself before the inspection.

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If you now look at the U.S.A.

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sits as a manufacturer, then you usually only have a few days, so typically 5 days.

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Abroad, that's, say, 4 weeks

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are typical, but even there rather longer, i.e. about 3 months.

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The F.D.A.

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now some information, so the Q.M.

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Have you ever seen which products are currently available in the U.S.A.

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whether there is also a person present who speaks English and he typically also sends a selection of appointments for the inspection.

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Exactly, then during the inspection

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the inspector will then identify himself directly after his arrival.

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There is an opening meeting, so we also know that from the audits with notified bodies, where the agenda is discussed.

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Here it is typically a good idea to introduce the company, present the products and then suggest a tour of the company, so that the inspector can first get an impression of the company or the premises.

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the actual inspection is carried out by the F.D.A.

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then carried out in the so-called Q.SIT process.

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This stands for Quality System Inspection Technique.

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That's a top-down approach, so it's actually similar to an audit.

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That is, the F.D.A.

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starts with the higher-level process and then drills deeper and deeper down to individual recordings.

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And the inspector also has to take a certain number of random samples, how much that is, this Q.SIT also specifies.

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Yes, during the inspection

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If there are deviations or not, they are called inspectional observations there.

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The inspector notes them on a so-called 483 form.

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So this is the number of the deviation form.

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In addition to these inspectional observations, the inspector notes down so-called discussion items.

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So these are points worth discussing, which perhaps do not yet constitute a legal violation.

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all this is documented on this four hundred and eighty-three.

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Exactly, and at the end, but this is only after the inspection, a final report, which is the so-called Establishment Inspection Report, is then prepared.

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Maybe about the duration, such an inspection usually takes 4 days and until you get this final report, it takes another 30 to 50 days roughly.

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K., so that's

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A period of, I have now heard, 3 to 3 months of preparation and up to 50 days of follow-up.

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So, you have high blood pressure for half a year during this time.

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That's why it's important now of course to behave correctly.

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Maybe let's take a look at the right behavior, especially now in these different phases.

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So, for example, what should you do right?

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if the F.D.A.

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, i.e. before the person then or the person then really

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is actually on site, what would be your recommendations?

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So, high blood pressure was already a real keyword, namely you should first keep calm and not panic right away.

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The best thing to do now is to receive the e-mail from the F.D.A.

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you immediately inform the management, those responsible for the various areas and first discuss the questions of the F.D.A.

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information requested and how to respond to it.

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It is best to answer promptly and Yes, one of these suggested appointment options

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or prioritize 2.

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It can also be that the company is closed exactly during this period.

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Then you should also call the F.D.A.

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inform about it.

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Then in the next step, of course, you should check the conformity with the F.D.A.

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Review requirements.

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Specifically, this is the Quality System Regulation.

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Ideally, of course, this has already been done annually through internal audits and any gaps are known.

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If not, you should take care of it as soon as possible.

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If necessary, for example, if there are not enough resources or

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if you do not have the expertise, then you have to resort to external support, if you know the extent of the deviation, you should also start planning necessary corrections or even corrective measures immediately.

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In the case of larger problems, this is also referred to as remediation.

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So, the elimination about that we will make our own podcast again.

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the remark has still started, so we help exactly with such preparatory audits inspections

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find out these gaps and now we have 2 areas, if I understand correctly, where there can now be gaps, namely once in the internal specifications, so they cover, for example, the requirement, the Q.S.A.

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requirement and then you have also adhered to these specifications yourself.

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I just understood you that the F.D.A.

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very quickly the Q.M.

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Manual wants to see that if I understand you correctly, it means.

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that you don't have as much time at the level of the specification documents as you do later, for example, at the level of recording, i.e. the evidence that you have actually adhered to it.

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Is this assumption correct?

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Yes, the assumption is correct, so the F.D.A.

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or inspectors really invest a lot of time to really look at the

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drawing.

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So, they have the whole day for the topic of Kappa, to look at Kappa, to look at complaints.

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So, there are typically a lot of random samples.

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But now back to my question, that is, the Q.

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M.

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System, i.e. the manual, the specification documents, the process descriptions, you have less time to react, to repair, because I understood correctly, you have to submit it in advance.

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So, am I right, right?

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Yes, at least that's exactly what the Q.

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M.

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Manual, you don't have to submit every single procedural instruction now, so you can still work on it, but I'll put it this way, the entire overview of the Q.

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M.

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system with the processes that you submit.

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K., that's good news.

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Yes, that means you still have reaction time for the relevant things, i.e. S.

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you just said now and of course afterwards especially with the recordings.

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K., so now we have

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just learned from you how to behave correctly in advance.

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What would be your tips?

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during the inspection, how to behave there, the dos and don'ts, perhaps.

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Yes, so it is very important that you have simulated this process beforehand, rehearsed it, i.e. really from the receipt of the inspector to the end of the inspection.

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This means that everyone should know their role.

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And have also rehearsed accordingly.

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In any case, you should always be friendly.

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also remain, yes, in the course of the inspection.

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On the other hand, maybe you shouldn‘t tell too much.

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So, it is also important to always answer only what the inspector has asked and not to show documents that were not requested at all or that do not discuss or even argue before the inspector.

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Yes, that doesn‘t make a good impression.

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OK, that‘s what I think takes place in this back office.

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Can you perhaps say a word about that?

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Exactly, so typically you have a front room, where the inspector sits.

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Most of the time the quality management officer is there and the area that is currently on the agenda and then you have yes, some call it warroom, backroom.

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There is then another team, which is then informed, for example via chat, which questions have been asked, which documents have been requested and they take care that

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the inspector receives the information as quickly as possible.

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So more tips on how to behave, you‘ve already hinted at it a bit.

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Nevertheless, I would like to ask the question again.

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So, now this inspection is taking place and you said there can be no conformities now.

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Maybe give us this range.

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Of what can happen there, from the one is yes, pats on the back to yes, what is the worst case and what is in between, yes.

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There are 3 types of results.

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In the best case, it is the so-called No Action Indicated.

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That is, the F.D.A.

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could not detect any violations.

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There is nothing more to do for the time being.

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Then there‘s something in between, which happens quite often.

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This is a Voluntary Action Indicated.

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Here, real legal violations have been identified.

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But they are not so serious that the F.D.A.

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plans any regulatory measures, such as a warning letter or an import ban.

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Then in the worst case

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there is an Official Action Indicated.

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So here, too, there are major legal violations and here you have to act in any case, because otherwise the F.D.A.

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within the scope of their powers, be it through a public warning letter to the seizure of injunctions or even for criminal prosecution.

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K., that is, then we actually have almost 4 levels, namely nothing at all,

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then the voluntary action and then the action and the then again paired with other F.D.A.

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Measures, for example warning letters or then really enforcement of these official measures, that can then be added to the Major Non Conformities, but it doesn't have to be, if I understand you correctly.

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Exactly, you can still avert that if you react appropriately, it always depends a bit on the individual case.

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K., but now we have this whole range and I, we should take that seriously.

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Yes, otherwise you don't want to end up where you just described.

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You've also started to say a bit about what companies, how they should behave properly, i.e. they or how they shouldn't behave.

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Yes, you just said, there is somehow too much now for babbling out, which may not have been asked at all.

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What other things do you have that companies should perhaps not do and what are such typical mista-

kes that they have made, i.e. in the sense of non-conformities?

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Yes, so maybe a problem or what you shouldn't do is also try to buy time.

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So then really take a lot of time before you show a required document.

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That doesn't go down well either and can really lead to a finding if it just takes too long.

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So that will, I wouldn't even try.

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Yes, no good idea, the inspector realizes that quite quickly.

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Typical problems or or non-conformities concern, so the top 3 I would say, is the Kappa system, i.e. correction and preventive measures.

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Complaint processing is often a problem, vigilance, reporting.

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This is because, for example, manufacturers often understand the actual purpose of this core element of a Q.M.

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System, i.e. the Kappa process.

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Didn't really understand and then didn't really live properly and that's a big problem then.

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Yes, because then the F.D.A., the Q.M.

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System doesn't work at all.

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and that can really lead to more serious consequences.

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If you have now mentioned something about a few non-conformities, but maybe it has happened, what are the measures that manufacturers should take now, or how do you proceed from now on?

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So.

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The best thing to do is to have a final conversation.

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Then the inspector presents his observations again.

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and it's best to react directly there, it's best to have even worked out an action plan in that time.

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This is always welcome, is evaluated positively and can then directly avert worse.

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Otherwise, if such a four hundred and eighty-three has now been issued, you should always start immediately with root cause analysis, planning, implementation of measures.

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So, as I said, that's the remediation.

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which I had already mentioned

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And you should also react promptly.

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So, on such a four hundred and eighty-three is the recommendation of the F.D.A.

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and that should be taken seriously, a maximum of 15 working days.

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So, this is not mandatory, but highly recommended.

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And the answer is also very important.

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On such a four hundred and eighty-three should be clear.

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So, there should be a clear answer to every observation.

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Just saying, yes, we have now recognized the problem, we are taking care of it, that is not enough.

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Also, da will die F.D.A.

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already see more.

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Really a root cause analysis, appropriate correction or preventive measures and also very important, really a schedule.

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If measures have already been implemented in these 15 days, then it is best to send appropriate evidence or records directly.

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I can also give you more tips in our Remediation Podcast.

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That's exactly what I wanted to point out now.

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So let's go even deeper into this topic.

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So that's the starting point, so to speak, where you have noticed.

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that there is a non-conformity.

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What are such typical triggers of remediation?

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So, once this is the inspection, have we learned, what else could trigger a remediation?

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So, it can also be an audit by a notified body in general, where several perhaps major deviations are now detected, but it can also be an internal audit, perhaps by an independent third party,

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Where a lot of problems are found that you haven't recognized yourself.

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Let's get back to the inspections for a moment, then we're already on the home stretch.

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How can you, how can your team, how can we help with inspections?

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In other words, in which steps, through which activities can we accompany and support medical devices, manufacturers or suppliers?

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Yes, so we can actually support you with the whole range.

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For example, we can facilitate communication with the F.D.A.

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take over in the run-up to and also in the aftermath.

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We can do a first gap analysis, so that you first get a picture of the state of the Q.M.

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system.

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and maybe here too prioritized according to the severity of the problems and then really also in this re-mediation phase we can support.

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So, we can guide, but we can also really take over the work, the processing of the measures completely.

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We also do

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or also lead F.D.A.

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Mock inspection.

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It's all about coaching, so that you really put yourself in such an inspection situation and play through the process.

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And of course, we also accompany you during the actual F.D.A.

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Inspection usually then in this warroom.

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In this way, one can perhaps still prevent one or the other deviation.

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O.K., so the answer is actually about the whole process, through doing and not just through clever

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Tips, but really roll up your sleeves by taking over from work, really get things done and you've done that countless times.

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What is the success rate?

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So I'll say in all cases: Were we able to avert a walling letter?

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Yes, there have been cases with deviations, but fortunately we have never had that in this case that it really came to a warning letter.

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Great, Luca, thank you from the bottom of my heart.

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For the insights you have given us, very gladly.