Johner Institute

Why Animal Testing Is Almost Always Unnecessary

With Sarah Gruber, Prof. Dr. Christian Johner

Transcript

00:00:05 Speaker 1

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

00:00:19 Speaker 2

In the case of medical devices that come into contact with the human body, we always have the issue of biocompatibility and in this context the question arises again and again,

00:00:28 Speaker 2

Do we have to conduct animal experiments to prove this biocompatibility?

00:00:34 Speaker 2

And there are rumors that this is actually always required by notified bodies and also by the F.D.A.

00:00:40 Speaker 2

And in today's podcast, I would like to explore exactly this question with Sarah Gruber: Are animal experiments mandatory?

00:00:48 Speaker 2

If so, when and, above all, when can we do without them?

00:00:51 Speaker 2

Yes, Sarah, welcome, because maybe not everyone knows you yet.

00:00:54 Speaker 2

If you say 23 more sentences to yourself

00:00:56 Speaker 2

to be able to classify you, then that was great.

00:00:59 Speaker 3

Yes, very much.

00:01:00 Speaker 3

Hello, my name is Sarah Gruber.

00:01:02 Speaker 3

I am responsible for the biocompatibility of medical devices at the Jona Institute.

00:01:08 Speaker 3

I used to work in the test laboratory for biocompatibility tests in the field of toxicology for a few years and have now been working in this field for over 10 years.

00:01:18 Speaker 2

Yes, you are exactly our woman for this topic.

00:01:22 Speaker 2

Let's start with these basics.

00:01:25 Speaker 2

What is biocompatibility all about?

00:01:28 Speaker 2

So, I somehow suspect whether the physical tissue is somehow negatively influenced by the materials you come into contact with.

00:01:35 Speaker 2

But could you elaborate on that for us?

00:01:38 Speaker 2

In other words, what you have to prove or what you might have to make sure that doesn't happen.

00:01:43 Speaker 3

Yes, gladly, as you rightly say, so the name already says, organic means life, compatible.

00:01:49 Speaker 3

is compatible.

00:01:50 Speaker 3

In other words, the aim is to evaluate the compatibility of materials that come into contact with the human body directly or indirectly via liquids or gas, for example.

00:01:59 Speaker 3

Compatible means that no damage to health is caused, for example skin irritation, allergies or even cancer, thrombosis or rejection reactions.

00:02:10 Speaker 3

So, in the end, you have to prove that no substances are dissolved or dissolved down in quantities that are toxicologically relevant.

00:02:18 Speaker 3

In other words, they can trigger harmful effects on health during the use of medical devices.

00:02:23 Speaker 3

Different endpoints have to be considered depending on the application.

00:02:27 Speaker 3

So, for example, if there is now application to the skin, then in addition to the physical chemical properties of the materials used, the endpoints cytotoxicity, irritation and sensitization must also be evaluated.

00:02:39 Speaker 2

Well, there is a catalog of them, so to speak, you just called it endpoints, which you have to check depending on the situation.

00:02:48 Speaker 2

And the situation probably depends on how much, how long the product comes into contact with the human body.

00:02:55 Speaker 2

My layman's guess would be that if it is very long and perhaps an open wound comes, it is better to be careful somewhere if it is only short and gets to the intact skin.

00:03:03 Speaker 2

But maybe help me to sort it out very briefly, so how that would work out

00:03:08 Speaker 2

differs from the, and ultimately also the intended purpose.

00:03:10 Speaker 3

Yes, exactly, absolutely right.

00:03:12 Speaker 3

So it depends on the type of contact, as you have already said, whether it is on the skin or whether it is invasive, whether it comes into contact with circulating blood, of course other endpoints have to be considered and of course the duration of contact, which also plays a role.

00:03:25 Speaker 2

O.

00:03:26 Speaker 2

K., we know what we have to pay attention to or what we have to prove, that there is no irritation, that it is not toxic, that it does not trigger allergic reactions, in other words, everything you just said.

00:03:37 Speaker 2

Now the question arises, which of these proofs do animal experiments help with at all?

00:03:43 Speaker 2

So, there we have the large crowd, so to speak.

00:03:45 Speaker 2

Afterwards you have to see whether it makes sense to do animal experiments.

00:03:49 Speaker 2

But are there areas where animal experiments make sense and areas where it doesn‘t make sense at all, you can say that.

00:03:55 Speaker 3

Yes, so in the end, for every endpoint of physical chemical information and in vitro cytotoxicity according to Part 5, there are animal experiments for each endpoint that can serve as evidence.

00:04:07 Speaker 3

For example, irritation, sensitization, then systemic toxicity, which is acute, subacute, subchronic, chronic toxicity, then material-induced pyrogenicity, genotoxicity, carcinogenicity, reproductive toxicity, but also implantation effects or blood compatibility.

00:04:28 Speaker 2

So you could say whether that‘s good news or not, that‘s an open question, but we can ultimately prove animal experiments for all

00:04:37 Speaker 2

for all proofs, that‘s how I just understood you.

00:04:40 Speaker 3

Exactly, with the exception of in vitro cytotoxicity and, of course, the physicochemical information on the material itself, you don‘t do animal experiments, but you can do animal experiments on all other endpoints.

00:04:50 Speaker 2

Yes, afterwards we have to see through it if we get it restricted a bit in order to protect the animals.

00:04:55 Speaker 2

But that we might first think about what animal testing means, i.e. what, how is it and I don‘t know if the term is correct, as a physicist you will call it the experimental setup.

00:05:05 Speaker 2

in other words, what do you do to the animals, in other words, in order to be able to determine exactly these endpoints.

00:05:11 Speaker 3

So first of all, it is important that one animal experiment is necessary for each endpoint and exposure, i.e. there are a lot of them and per animal experiment, of course, a certain number of animals is necessary, i.e. at least 5 animals per group and this may also include preliminary tests to determine concentration, then control groups must be carried along,

00:05:31 Speaker 3

if necessary, additional tests are then necessary to confirm positive reactions.

00:05:37 Speaker 3

And after the tests, the animals are usually killed painlessly to assess the influence.

00:05:43 Speaker 3

So, of course, rules for compliance with animal welfare must be followed, that's quite clear.

00:05:48 Speaker 3

But the question generally arises, does it make sense, for example, to test a polyethylene housing of a control element for the umpteenth time with an animal test, whether

00:05:58 Speaker 3

whether allergic reactions can be triggered, although it's just a standard plastic and it's actually clear that it won't happen, just to somehow tick off a checklist.

00:06:06 Speaker 3

So as a rule, with standard materials, it doesn't really make sense to carry out the thousandth animal experiment.

00:06:11 Speaker 2

You are already one step further, namely with the question of where it can be saved, perhaps back to the experimental setup.

00:06:17 Speaker 2

So you have already described, so there are several animals that are necessary for each end point, maybe what kind of animals do you typically sip?

00:06:26 Speaker 3

Yes, exactly, mice, rabbits, guinea pigs, those are the typical ones.

00:06:31 Speaker 2

And now the structure.

00:06:32 Speaker 2

So, will then, how do you have to imagine it, will the guinea pig's hair be shaved somehow and then somehow the fabric will be glued to it or how, so what does such an experimental setup look like?

00:06:41 Speaker 3

Yes, exactly.

00:06:43 Speaker 3

As already indicated, animal welfare is of course taken into account.

00:06:47 Speaker 3

So, the exposure is done in such a way that the animal gets through it as well as possible, just painlessly.

00:06:54 Speaker 3

So, that in any case exactly, but.

00:06:56 Speaker 3

This is a typical attempt now, for example, for sensitization, that the hair is then removed.

00:07:01 Speaker 3

Then the product is extracted beforehand and then put on top and then it is looked at whether there is a reaction and then through further investigations whether an allergy can be triggered.

00:07:12 Speaker 2

Is it dripped on it or how is the material attached there?

00:07:16 Speaker 3

There are patch tests, for example, that it is then put on the patch and then stuck on it.

00:07:21 Speaker 2

You had hinted earlier that things are tested with implants.

00:07:25 Speaker 2

I suspect that something will be implanted in the animal.

00:07:29 Speaker 3

Exactly, exactly.

00:07:29 Speaker 3

O.

00:07:30 Speaker 2

K., so these are the more invasive measures that are used and

00:07:34 Speaker 2

when it comes to contact with flowing blood, you also mentioned that briefly, is the animal opened or how do you get the blood?

00:07:40 Speaker 3

Exactly, so that's mainly the case, if you have to check now, for example, implants against the circulating blood, so stents or something like that, as a rule, the blood compatibility is more in vitro actual, but I included it because there are already medical devices, animal experiments are common.

00:07:57 Speaker 2

O.K., the message you gave us, so you can use it everywhere.

00:08:02 Speaker 2

Now, of course, let's narrow it down a bit.

00:08:04 Speaker 2

For the sake of animals, we have a legal obligation to always do these animal experiments.

00:08:10 Speaker 3

So, the standard does not require that animal experiments be carried out.

00:08:13 Speaker 3

This requires an adequate assessment of the biocompatibility of the final end product, which is yes, but this should be done in the first step via material characterization and in vitro tests.

00:08:23 Speaker 3

So, this is clearly required before animal experiments are carried out.

00:08:27 Speaker 3

biocompatibility must first be assessed via material characterization and Vito tests, and if that is not enough, then animal experiments can be used.

00:08:37 Speaker 2

So you've already started to say what you can do alternatively, but maybe half a step back, for which of these many proofs, I think you mentioned endpoints, you can do without animal experiments particularly well.

00:08:51 Speaker 3

So actually with all systemic endpoints, i.e. systemic toxicity such as acute, subacute, subchronic, chronic toxicity, genotoxicity, carcinogenicity, reprotoxicity, so here is clearly the way via chemical analyses using T.T.C.

00:09:08 Speaker 3

concept possible and even required.

00:09:10 Speaker 2

Then there is the opposite question, where do you think it will hardly be possible to do without animal experiments?

00:09:17 Speaker 2

at which endpoints?

00:09:18 Speaker 3

There is an opinion that or what means, there is an opinion, but it is the case that the C.T.C.

00:09:22 Speaker 3

Concept excludes irritations, sensitization.

00:09:25 Speaker 3

But if standard materials are used, animal experiments are still not absolutely necessary for the endpoints.

00:09:32 Speaker 3

This can still be evaluated via material characterization and, in the case of standard materials, on the history of the material, literature, experiences and in vitro tests of the basis.

00:09:44 Speaker 3

Of course, the situation is different if we now use new materials

00:09:47 Speaker 3

materials, i.e. no standard materials, animal testing is usually necessary.

00:09:52 Speaker 3

Or if, for example, I find out in material characterization that a substance is released that affects an endpoint and we cannot sufficiently classify this as safe on the basis of the toxicological assessment, then animal experiments may also be necessary to show that the product is still safe and that this may be removed because of the exaggerated conditions.

00:10:14 Speaker 2

So then we could summarize you, so with the

00:10:17 Speaker 2

In most endpoints, animal experiments can be avoided anyway and with this subset with the irritations, as you just said, or allergic reactions, it can be avoided if it is known materials for which this data is already available.

00:10:31 Speaker 2

And only for new materials do you have to go this way via animal experiments, so to speak.

00:10:37 Speaker 2

O.

00:10:38 Speaker 2

K., maybe somehow at the end.

00:10:40 Speaker 2

As for motivation: Well, I think everyone should actually be motivated to see animal welfare very high there and to refrain from animal testing.

00:10:47 Speaker 2

So apart from these ethical aspects, what other advantages would manufacturers have if they did not test on animals?

00:10:54 Speaker 3

So, animal experiments are usually quite expensive and time-consuming.

00:10:57 Speaker 3

In contrast, in vitro tests are usually more cost-effective, less time-consuming, are much more sensitively reproducible and the result can often be transferred directly to the material.

00:11:08 Speaker 3

So, especially if you are somehow on the cause research for something, then you can find out about it.

00:11:13 Speaker 3

if necessary, where that comes from.

00:11:15 Speaker 3

After all, several endpoints can be advertised with one test.

00:11:18 Speaker 3

So with animal experiments, as I said, you have to do an animal experiment at every endpoint.

00:11:22 Speaker 3

I can then do this via chemical analysis, I can cover all the systemic endpoints at the same time and the comparability of products is also possible.

00:11:29 Speaker 2

O.

00:11:30 Speaker 2

K., that should be very motivating.

00:11:32 Speaker 2

You just mentioned time and cost as the second of these factors.

00:11:36 Speaker 2

So I think it depends extremely much on the respective situation or on the end point.

00:11:41 Speaker 2

but can you give us a rough estimate of how long such an animal experiment takes, so if you probably won't do it at home with your own guinea pigs, but go to a corresponding laboratory and what, what does it take from the first request to the results?

00:11:57 Speaker 3

Phew, it's difficult to name anything now, especially because the laboratories with chemical analyses are taking a very long time at the moment.

00:12:05 Speaker 3

But you have to say that there is also an animal experiment at every end point

00:12:09 Speaker 3

are necessary and if I need several weeks for an endpoint for an animal experiment, then of course it drags on, if I actually have a product that has longer contact, is invasive, then it drags on, it can drag on for up to a year if I were to check all endpoints one after the other.

00:12:23 Speaker 3

Of course, this can also be done in parallel, but you have to spend a lot of time, I would say.

00:12:28 Speaker 2

O.

00:12:28 Speaker 2

K., yes, O.

00:12:29 Speaker 2

K., but that's a huge argument, if you can shorten it clearly.

00:12:33 Speaker 2

How can you and your team help,

00:12:36 Speaker 2

In the specific case, finding out whether an animal experiment is necessary or not, in the specific case it helps to prove biocompatibility.

00:12:44 Speaker 3

So, we offer that we write a tailored biological evaluation plan for the medical device in the BEP and in this we then justify the strategy for assessing biocompatibility without animal experiments on the basis of data, i.e. on the basis of the application of the medical device and the materials used.

00:13:02 Speaker 3

And we then work together with cooperation laboratories that are specialized in their field.

00:13:08 Speaker 3

That means a laboratory with a focus on chemical analysis, a laboratory with a focus on cell culture.

00:13:13 Speaker 3

And in the final Biological Evaluation Report, the BAER, we then evaluate the available data toxicologically on the basis of limit values for humans and type of exposure and can then justify that the strategy without animal experiments is sufficient and that no further experiments are necessary.

00:13:30 Speaker 2

Yes, and you have a lot of success there.

00:13:32 Speaker 2

So, you have most or almost all of the requirements of Notified Bodies or F.D.A.

00:13:37 Speaker 2

for animal experiments that can invalidate and argue why they are not necessary and thus save the manufacturers a lot of time and some animals survive.

00:13:46 Speaker 2

Yes, Sarah, thank you so much.

00:13:47 Speaker 2

That was exciting, especially for a non-biologist, not a chemist.

00:13:51 Speaker 2

It's a whole new world.

00:13:52 Speaker 2

So, if you are interested in it or are faced with the task of having to prove the biocompatibility of your product,

00:13:59 Speaker 2

Just get in touch.

00:13:59 Speaker 2

Sarah Gruber and her team are happy to help.

00:14:02 Speaker 2

Sarah, thank you very much.

00:14:03 Speaker 3

Gladly, thank you.