INTERVIEW

In this exclusive interview with *ONdrugDelivery*, Mathias Romacker discusses a broad range of topics, from his professional expertise and history seeing the parenteral sector evolve first-hand, to his personal experience as a Crohn's disease patient making use of the very devices he's seen grow and develop, ahead of his presentation, "My Lifelong Patient Journey as an IBD Patient: Insights from an Industry Insider", at the Parenteral Drug Association (PDA) Universe of Prefilled Syringes & Injection Devices 2021 virtual conference (October 5-6, 2021).

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Mathias Romacker is an independant Injection Devices Strategy Consultant. He was most recently employed as Senior Director, Device Strategy at Pfizer, having joined Pfizer in March 2015. In this commercial role, he focused on the front end of device technology. He worked with multiple functions and sites across the organisation with the goal of developing device strategies for Pfizer's pipeline and inline products.

Previously, he worked in the device area for nine years at Amgen. Before joining Amgen, he held multiple sales and marketing positions with Becton Dickinson and Gerresheimer, in Germany, South Africa, and the US. Mr Romacker holds a Master's equivalent degree in economics from the University of Freiburg in Germany, and is a member of the Board of Directors of PDA.

Q Many of our readers will know you already, but for those who do not, would you begin by giving as overview of your career path and how it led you to become a world leading technical and market expert in drug delivery systems, in particular parenteral drug delivery systems?

A That's a very kind way to frame the question, I appreciate it. In terms of my career path, I was lucky enough to be in exactly the right place at the right time – from the very beginning, even in my entry level job, I was stepping into an exciting story that was just about to evolve. As my career progressed alongside the rise of the parenteral delivery sector, I've spent about half my time on the supplier side and the other half actually on the pharma and biotech side, so at this stage I've got a broad range of perspectives!

Fresh out of college, my first job was with BD. I was in the pharmaceutical systems division and, at the time, the division's lead product was a prefillable glass syringe. For context, this was in the early 1990s – there was only a handful of customers in Europe interested in such a thing, mainly focused on anticoagulation drugs and vaccines. Today, in contrast, prefilled syringes are manufactured in the billions and are used across a huge range of therapeutic areas. That's the ride I've been on, accompanying prefilled syringes from a niche product to being broadly accepted and used by pharma companies to present their products in a user-friendly format, not to mention becoming the container of choice for disposable and reusable autoinjectors.

I was then approached by Amgen, and later by Pfizer, to bring the expertise and skill set I'd built on the supplier side and apply it to the pharma side. They saw that bringing on someone with my set of skills and experience would help them understand how device suppliers think and operate. I didn't miss the opportunity and moved to California to start at Amgen in 2006.

It was incredibly interesting. After being on the supplier side for all those years, you think you've got a good understanding of pharma, but when I crossed over I found I had much to learn about what the pharma side is actually like in reality. It was a great experience to be able to switch perspectives and look out from within pharma and see the supplier side from the outside.

And again, during the last 15 years, we've really seen the market evolve. In 2006 there were two prefilled syringe-based disposable autoinjectors commercialised; now in 2021 there are over 50. I count myself as very lucky to have been a part of this evolution. And then alongside that, during the same time span, other technologies, like wearable injectors and pen injectors, have also continued evolving.

All of this is, of course, in the context of an industry-wide push to move more injectable therapies from a clinical to a home setting. That's the main driver for all the innovation we see in parenteral devices and the rapid growth in the sector. It's been a privilege to have my career progress alongside it.

Q What fewer people will know is that, throughout much of your career, you have lived with Crohn's disease – a chronic condition treated using therapies delivered by the very parenteral delivery systems that you have specialised in over the course of your professional life. Can you give us a brief overview of Crohn's, with a particular focus on the treatments offered and their delivery systems?

A I've not been public historically about the fact that I'm also a patient, but I think it's given me a really interesting perspective that is worthwhile sharing. Think about it – when you're having conversations within pharma about ongoing projects, you're always talking about the patients and their perspective, so, if you are patient yourself, doesn't that put you in a really interesting position? For one thing, what's said in those conversations really hits home.

In brief, I was first diagnosed with a form of colitis in my late teens. Back then, it was believed to have psychosomatic

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causes; we didn't really understand what an autoimmune disease was at the time. I was prescribed an oral medication, which probably wasn't very effective. I had a few relapses – it wasn't nice – but, over the years, it got better. I went into remission. I can't explain why, but it really did get better. After that, I had quite a few decades where I wasn't being medicated. Compared with other patients that I've talked to over the years, I was very lucky.

Then I had a bad relapse. I've no idea what happened, but it was a major inflammation. This time, however, compared with when I was a teenager, more was known about what Crohn's is, that your own immune system is in overdrive and causing a painful inflammation. The idea with autoimmune disease medication is to "level down" your immune response, ideally to the point that you no longer have any inflammation, or at least only a little.

It's at this point that I had my first encounter with biologics as patient. I went on a TNF inhibitor, which was delivered as a bi-weekly injection with a disposable autoinjector. For me, the experience was – I'm not sure if funny or ironic is the right word – but, all of a sudden, the very class of delivery systems that I'd been a part of talking about, testing and advocating for was something I had to use myself. I became a self-injector.

The loading dose was actually four injections at once, which I found a little bit unpleasant, as you can imagine. After that it was two injections after two weeks, and then one injection every other week. What I found out as a patient self-injecting with an autoinjector is that, while, from a professional perspective, they're all different products from different manufacturers, when I was looking at them as a group from a patient's point of view, they're actually really nice products in a way I hadn't appreciated before. Obviously, given my part in the industry, I thought it would be a bit embarrassing if I messed up an injection. I wouldn't call it anxiety, but I was very skittish and cautious about getting it right when I first started. But, in practice, I didn't mess up once.

As for actually self-injecting, I chose Saturday morning as the time to do it. So, every other Saturday, I had to take my drug out of the fridge and let it warm up to room temperature. I've found you can go after 30 minutes, but sometimes I waited a bit longer, which might be an expression of some kind of discomfort. Similarly, when you inject, you're supposed to hold the device against the injection site for 10 seconds, but I typically left it there for longer to just make sure I'd got the whole dose delivered. It was a very interesting, not to mention instructive, experience to do it myself.

Two and a half years ago, I was switched to an infusion therapy. For that, I have to go into a clinic once every eight weeks and the procedure is performed by healthcare professionals. I believe that the drug is actually available in Europe as an autoinjector and, if you were to ask me to choose, I would easily pick the autoinjector at home.

Q So, from a patient's point of view, is it your opinion that it's better to be able to self-inject with an autoinjector at home yourself rather than go into a clinic for an infusion?

A Let's start with the baseline that, obviously, the clinical result is the most important thing. No matter how nice a self-injection device is, I'd rather go into a clinic once a month for an infusion if it's going to give me clinically superior results. It really is the most important parameter for me. On the other hand, having convenience and the freedom to travel and go about life as normal, that's clearly a major upside to self-injection.

In my case, going in for infusion treatments hasn't been easy for a number of reasons. I have to be able to schedule clinic visits once every eight weeks, which presents extra difficulties if you're not settled down in one place for the long term. Then there's been the covid-19 pandemic, which has added a whole other set of problems. If I'd been given autoinjectors to self-inject my treatment, that would have been a lot easier.

As it happens, I understand that some pharma companies reported in their quarterly reviews that some of their drugs took a hit because patients, especially before vaccinations became available, were very concerned about going to a hospital or clinic to be injected during the pandemic. So, clearly, if more self-injected drugs had been available during the pandemic, it probably would have been better for patients and for pharma alike.

Q Could you tell us a little more about how, as a patient, the coronavirus pandemic impacted your experience of receiving your treatment?

A As I mentioned, it became much more difficult. I was fortunate in that I found a home nurse service, where a nurse would come to my house and administer my infusion. To be honest, with no vaccine available in 2020, I felt uncomfortable with the idea of going to a clinic, but I think that was a pretty universal experience. I managed, but it wasn't easy. There were a lot of hoops to jump through, and I think it's pretty obvious that if I could have had a delivery of autoinjectors, like I did when I was self-injecting, it would've been a lot easier and more convenient. Plus, when you want to isolate, self-injection is safer, because you're still seeing a nurse no matter what when you get your infusion and you don't need to see anyone when you self-inject.

Q Let's broaden the discussion a bit. Combining your perspectives from both the industry and patient points of view, can you talk a little bit more on how the parenteral sector is currently evolving and where it's going looking forward?

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A Reusable devices are one thing that I'm keeping an eye on. My self-injection experience was with a disposable autoinjector, which, in practice, meant that I built up a collection of used autoinjectors that I needed to dispose of fairly fast. Even now, I know that some companies aren't offering a reusable electromechanical autoinjector as an alternative for their autoimmune disease products, which are weekly injections. The reusable devices – where the drug is basically in a prefilled syringe, which is held in a cassette that gets loaded into the main device, used for the injection, and then ejected and discarded afterwards – are one way that delivery systems are evolving at the moment. Personally, I think that the trade-off of the device having some additional use steps but creating much less waste is a good one.

As someone involved in the industry, I know there's a buzz around connectivity, and that's something I'd like to see as a patient – I already spend hours a day on my smartphone, after all. With the newer class of reusable electromechanical autoinjectors, some connectivity would be quite handy. They're in use for one of the multiple sclerosis drugs, but I think it would be good if this were to expand across other therapeutic areas over the years. I like the idea that you could log your injections, maybe keeping a diary with symptoms, letting you keep track of everything in one place. I personally think that could really enhance the patient experience moving forward.

Most people now are quite comfortable with smartphones and that area of technology, and that is increasingly true even of older demographics, who are the most likely to be using these treatments. The number of patients that could really get some use out of connectivity is getting bigger by the day, so why not leverage this for convenience, comfort and, of course, improved outcomes?

I should also talk about the fact that a new class of large volume injectors has evolved – that being on-body or wearable injectors. These devices could be a great opportunity for the loading dose to be administered more comfortably; remember how I said the loading dose when I started self-injecting was four injections at once? A wearable injector could have made that a lot less unpleasant. Thinking about them that way, while it might seem like a waste to train a patient on a device for one injection, wearables have the potential to be used by healthcare professionals in clinics as an alternative to infusion, which could improve safety and patient turnover.

A running theme with where innovations in the parenteral space are taking us is adherence. It's one of the major things pushing what are traditionally IV therapies towards subcutaneous delivery. I would expect that, moving forward, my peers in the industry will only become more interested in all things self-administration, especially as connectivity becomes normalised and more advanced electronic devices are able to provide proof that drugs have been administered correctly. Obviously, if a patient is not adherent you don't get the desired treatment outcomes, which leads to increased healthcare costs all around. This is an area to continue to pay close attention to.

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There are definitely a few more things we need to figure out when it comes to connectivity. Patients are concerned about privacy, data protection and security, and we need to allow them to be comfortable sharing data with a variety of stakeholders. It's no wonder that the better approach at this stage for connectivity is an "opt-in" one.

A lot of new companies are entering the connectivity space, offering ideas, as well as services and ecosystems. However, having been an industry watcher for many years, I think we're still waiting for something to catalyse mass adoption. I'm excited for the future here – we're going to see some interesting developments this decade.

Q Where industry talks about "unmet needs", a patient simply sees room for improvement in their treatment. As a patient, what do you wish was possible in terms of treatment, and how close is the industry to making those things happen?

A Obviously, an injection will always be an invasive process, so making it as quick and comfortable as possible comes near the top of the list. This is something I think about where it comes to wearable injectors – what trade-offs would I be willing to make for these slower, larger-volume injections? The number one priority is to make it a single administration event. That means only one needle prick regardless of the dose, whether it's a small or large dose, and balancing delivering it as fast as possible with minimising perceived pain, or any kind of discomfort.

Also, I place a lot of value on the "out of the box" experience. What is the size and shape of the device? What's the onboarding experience like? What sort of training is there? These are factors that really have an impact on how easy it is for patients to get to grips and become comfortable with their therapies, which is so important if you're going to self-inject.

It's something that comes up regularly in market research. On the whole, patients are currently quite happy, but there's still a feeling that some things can still be done better. One way of thinking about it is to imagine an example from a totally different area; as an example, let's say you asked somebody 20 years ago if they were happy with their cellphone. Most people probably

would've said yes, but then think about phones nowadays – everyone has a smartphone, right? I don't think there are many people who would like to go back to the kinds of phones we had 20 years ago. It's the same principle with autoinjectors, just because patients say they're mostly happy doesn't mean there isn't still plenty of opportunity for the industry to innovate and make an even better user experience.

Q On the subject of onboarding, from your experience as a patient, have you found that the reality lines up with the way we within the industry imagine onboarding is done?

A When I was onboarded, I got a needle-free demo device and had a travelling nurse available to train with me if I had felt that I needed it. I assume the nurse could have also been present during my first self-injection. However, given my background and the fact that I'm far more knowledgeable about these devices than the average person, I felt bad asking that nurse to come to my home, so gave that opportunity a pass. Overall I was quite impressed with how it was done.

Don't forget that this whole idea of onboarding patients by providing needle-free reusable training devices is only around eight years old. The first patients who self-injected didn't have anything like the tools we're discussing today. A training device to mimic the actual injection is a huge plus for making onboarding smoother and more comfortable for patients. Also, some of the newer therapies, anti-migraine for example, are monthly injections. I can't say for sure if a month is long enough to forget how to self-inject, but I can say that if you have one of those reusable onboarding devices available, you can always do a mock injection before you give yourself your real one if you're not entirely comfortable with the procedure.

Q To what extent do you feel that the industry is "in tune" with patient needs, or is there room for a better flow of information from patients back to the industry?

A There's probably always room for more communication, right? I mean, with all the conversations we have with patients, delivery devices are very important, but the drug is still the star – you still want to have the best possible drug in terms of efficacy and safety. You could have the most incredible, patient-centric device ever designed, but if the drug inside it doesn't help patients they're not going to be interested.

I do feel that, while we've gotten a lot better at devices during my time in the industry, the pharma industry does have a tendency to be very risk averse – companies are very prone to defaulting to the highly de-risked technologies they've relied on for years, or even decades! Even existing platform technology is higher risk than pharma is sometimes comfortable with, which may potentially inhibit looking at further advancements to make things more patient-centric and patient friendly. There's definitely an inherent idea that the drug is the absolute

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priority, which unfortunately means that the device, while important, may not necessarily be a key focus for many pharma companies.

If you dig a bit deeper, you can see that the pharma companies that have multiple disposable autoinjectors on the market tend to use the same device platform across all of their products. A product portfolio could include, for instance, a rheumatoid arthritis drug, an anti-migraine drug and, say, something like a GLP-1, but they'll all be commercialised using devices based on the same autoinjector platform. I find this really interesting, that the same platform is leveraged across all of these therapeutic areas, even though the patient populations for each are very different. Think about it, the demographic for anti-migraine patients includes a large population of middle-aged women, while with rheumatoid arthritis patients you're looking at a lot more geriatrics and patients with limited dexterity. These are very different patient populations, but you still find pharma companies taking a one-size-fits-all approach with their platform choice.

Q Moving on to our last topic, tying all your experiences together into a broad perspective, what do you see as the major primary trends in the injectable drug delivery sector at present, and what are the top significant advances we'll see emerge over the coming years?

A The one that springs to mind most readily is drugs moving from IV to subcutaneous delivery. There are a few examples that have already been commercialised, such as for lupus and rheumatoid arthritis, but what is really interesting is that oncology, a huge therapeutic area, is really embracing this shift. It is pretty clear, if you just search online, that there are a lot of clinical trials for new IV-to-subcutaneous reformulations going on right now, and that I find very, very interesting. It doesn't guarantee that those therapies will be made available for at-home self-injection, but it absolutely opens the door to the possibility. I would tend to assume that they will try to mimic the same injection frequency as the IV version, so maybe once every four or six weeks. You can imagine the increase in comfort, especially if it could be administered in the patient's home.

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Then, of course, there's the question of the delivery devices supporting this shift. I would speculate that a handheld autoinjector would be the preference from the patient's perspective. But if you need a larger dose and you still want to mimic the injection frequency of the IV, then this newer class of wearable injectors that can deliver doses of 10 to 20 mL, or in some cases even more, become a very interesting option for pharma companies.

Another topic that I hear a lot about is sustainability. Consider chronic diseases that require lifelong management, if you can move those patients onto reusable devices where the disposable piece you throw away is a lot smaller than a full-blown disposable autoinjector, you're significantly reducing the environmental impact of their self-injection regimens. If you could potentially recycle these disposable components, all the better.

We're discussing sustainability in so many aspects of our lives these days, why would it be excluded in pharma and drug delivery? Remember how I mentioned before that I was throwing away a lot while I was self-injecting? I think that's indicative of a shift in our general awareness. 20 or 30 years ago we wouldn't have thought twice, we'd just throw everything away in the same bin and it just went away and that was that. Whereas now, I find that having lots of waste piling up makes me feel uncomfortable, and I think it's the same for a very large – and growing – number of people. My feeling is that this discomfort will make itself felt in the industry, both from consumer preferences for greener products and from pressures to reduce carbon emissions coming down from governments and multinational organisations, all fuelling this trend towards more sustainable products and industry practices.

Finally, one other topic we as an industry talk about a lot, and have touched on already here, is optimising the patient experience. For example, it seems to me that needles keep getting thinner, certainly for pen injectors – they're now going down to 34 gauge! Also, what we learned over time is that if you're injecting into the subcutaneous tissue, you don't have to go very deep. It may not be a major topic, but I can absolutely imagine us really enhancing injection quality with shorter and even thinner needles. I can say from experience that, as a patient, every step forward in comfort and ease-of-use helps.

Mathias Romacker will give his presentation, "My Lifelong Patient Journey as an IBD Patient: Insights from an Industry Insider", at the PDA Universe of Prefilled Syringes & Injection Devices virtual conference, October 5-6, 2021.