DIMITRI GRASSWILL Nemera

Following a first R&D experience in automotive industry, Dimitri Grasswill joined the pharmaceutical device area in 2004. He has practiced in various settings, starting from device manufacturing and quality environment to development and industrialisation project management. In 2010, he moved to a innovation lead position, where he started to structure and develop the Innovation Center of Nemera (formerly Rexam Healthcare) with the target to establish a "state of the art" innovation and development organisation for pharmaceutical devices and drug delivery solutions. He has always been convinced that strengthening device R&D activity in healthcare industry would contribute to addressing patient needs better.

Mr Grasswill speaks with ONdrugDelivery Magazine, in the context of the changing market and technology around inhalation devices, about Nemera's strategic decision a few years ago to build design and development capability and integrate that with the company's considerable manufacturing expertise and infrastructure.

Q Nemera's capabilities span a range of drug delivery device classes. Please could you tell us about Nemera's pulmonary drug delivery device offering in the context of the company's overall offering?

A Nemera is a design, development and manufacturing company focusing 100% on drug delivery devices and we operate mainly within five segments, five delivery routes: nasal, ophthalmic, parenteral, inhalation and dermal. We have a large customer-owned-device manufacturing business but over the past few years we have introduced a strong innovation path, where we develop our own products. We operate both models across the five delivery routes, including pulmonary (see Figure 1). Another aspect of our business model is co-development, where we contract develop a product for a customer and then take it on to manufacturing.

So on one side you have the Nemera IP business, on the other you have the pure industrialisation and manufacturing, and in the middle of these you have what we call the co-development business, where we develop products from scratch or continue the development of products whose development has already started.

We have four plants where we industrialise and manufacture devices: two in France, La Verpillière close to Lyon and Le Tréport in Normandy; one in Germany at Neuenburg am Rhein; and one in Buffalo Grove in Illinois, USA. At La Verpillière we have a campus that includes our headquarters and also our development centre, which we call the Innovation Center (see Figure 2). All of our activities on the development side are located in this one area.

We have a team of around 75 engineers and experts who work on designing, developing and qualifying products. We then transfer this to any of these four plants for industrialisation / scale-up and manufacturing.

In terms of plants, we do have plants where we have a stronger history of manufacturing, for example, parenteral devices, and others where nasal devices or ophthalmics have historically been the focus, but there is no barrier between the different segments. It's more a question of the industrial layout, or geography of the different plants than a question of specific know-how at specific plants. We have strong knowledge across the different device types which is centralised and can be co-ordinated amongst our different plants.

Q Focusing on Nemera's pulmonary offering, I wondered if you could take us through each of the three areas: design, development and manufacturing?

A We believe we have a unique approach and we are genuinely able to be a one-stop-shop for our customers because we integrate the whole process of a drug delivery solution – we're able to design it, develop it and manufacture it.

Our approach is a very simple one. We started focusing on our own IP several years ago and by doing that our only objective was to put these devices on the market, which we knew meant

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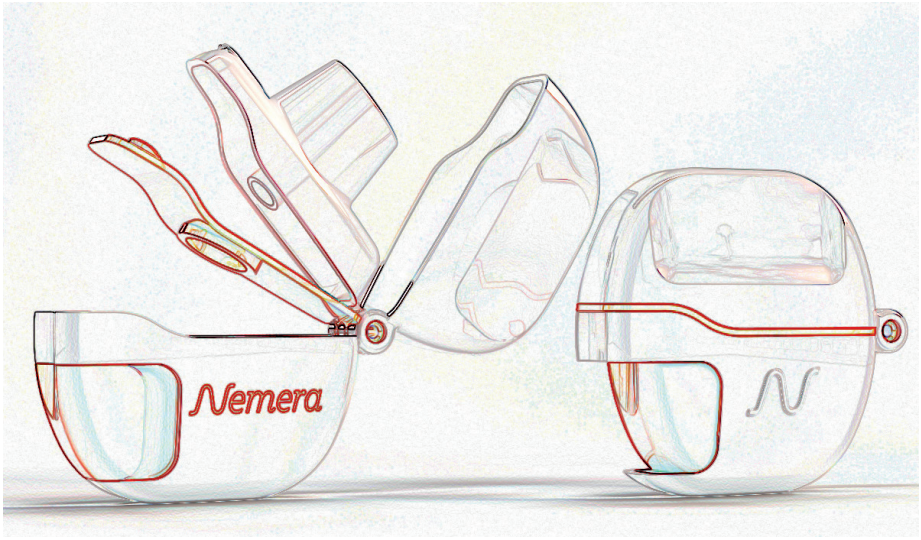

Figure 1: Design sketch of new inhalation device concepts.

> "What we offer clearly is this ability to do this concurrent engineering for industrialisation during design and development in order to be able to move very rapidly to the market. We are able to fine tune the product and the process at the same time, not one step after the other. It is not only fast, it is efficient."

we needed to make a very strong link with our manufacturing. Nemera, previously Rexam, is a very well-known manufacturing partner in this industry. This is in our DNA.

So when we started to develop our own products, we established a new centre of knowledge, additional to the manufacturing. Drug delivery devices are extremely complex, in terms of their mechanical function and in terms of their interaction with the drug, the patient and so on. And with inhalers in particular there is of course complexity arising from the fact that device performance is ultimately really a combination of the device itself and the way the device works with the formulation in terms of preparing the dose and it being inhaled by the patient. Increasingly, we are also talking about connectivity which adds another level of complexity. We think in the context of increasingly complex systems involving the device itself and the formulation, and their interaction patient, all the tiny tolerances that are required on all the materials and moulded parts, that this link we have between development and manufacturing is absolutely crucial.

We do not believe it is an efficient strategy today to develop a device with one partner and then ship the project out to another partner who then begins thinking about the industrialisation. What we offer clearly is this ability to do this concurrent engineering for industrialisation during design and development in order to be able to move very rapidly to the market. We are able to fine tune the product and the process at the same time, not one step after the other. It is not only fast, it is efficient. And by considering the process very early, sitting all the experts around the table from the start, we are also already talking with and preparing our industrialisation colleagues so the design transfer, as it is known in the pharma world, then becomes much easier and avoids all the risks of designing a device to begin with and then when it comes to the industrialisation process having to go back and revise the design because some of the specs were not robust enough in terms of full-scale manufacturability.

Q Are Nemera's clients able to access each category individually (ie design only, or manufacturing only) if they wish?

A We are not dogmatic. Whilst we understand the advantages of considering the manufacturing process from the outset, throughout the design and development stage, and we have built up this capability very successfully, our objective ultimately is to manufacture the device. We are not a design house, we are there to manufacture and so whatever the stage of development we are constantly asking the question, "How is it made?" We see our device design and development capabilities as essential for the rapid and efficient development of the manufacturing process. So if a customer comes to us with a given product, for us to industrialise it, then absolutely we are very happy to do it. Whatever stage it is at, perhaps a partially designed product, for example, we are fully able to interact. We can put around the table all the expertise required to get that product from whatever stage it has reached, to the market.

Figure 2: The Innovation Center at La Verpillière, near Lyon, France.

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Q What do you think are the most significant trends in field of inhalable drug delivery, and how is Nemera positioned in the context of these trends?

A We all feel that connectivity will have a huge impact not only in our field but across all industry. There is a global consensus in the pharmaceutical industry that connectivity will have a significant impact but what is interesting is that nobody really knows exactly how fast or how deep the impact will be.

There is a continual increase in the degree of patient interaction with delivery devices. For example, for inhalation, today you have increasingly intuitive devices, and better instructions and training of how to use them, and you also now have the availability of a means to see how many doses remain in your device – dose counters. Additionally, things like the portability and the general attractiveness of the appearance is improving. But in the end the main driver has to be the quality of the treatment, or therapeutic outcome.

The other major trend, which is not a new one, but one which will continue and likely intensify, is the role of generics. As new chemical entities are becoming rarer every year, for a company such as Nemera the ability to be able to provide delivery solutions for generics will become more important still.

Q Looking to the future, what lies ahead for Nemera – with reference to pulmonary delivery devices in particular, and also more broadly for the organisation as a whole.

A In a way, the future for us started some years ago when we looked forward and began to build capabilities in the design and development area in order to become the global solutions provider we are today, having gone beyond just contract manufacturing. This prescient decision was taken partially to enable us to work more with generics companies, but also to be able to be a real partner of choice for pharma companies as the market evolved.

Another focus is electronics, including connectivity, and for us to be the provider of a mechatronic device. But importantly we are ensuring that we will have the right value proposition in the end. We believe in finding the way that technology brings added value to our devices, and to the patients.

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Everyone is very focused on the fact that connectivity will increase compliance but only a few truly understand the mechanism of how, and connectivity increasing compliance is only one part of it. We are looking at how electronic technology, including but not only connectivity, can bring added value and help improve all aspects of the treatment, not just compliance. Integrating electronic sensors with dose counters, and employing electronic technology to control particle size are examples where this may come into play.

Also, Nemera is proud to contribute to the EU-funded project CUPIDO (Cardio Ultra-efficient nanoParticles for Inhalation of Drug prOducts), that started in February 2017. This project will foster the translation of nanomedical inhalation applications toward the cardiac field. The role of Nemera in this consortium will be the development of the devices for the administration of the nanoparticles by inhalation, to the heart.

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