Interview: Frans Vlaar – Business Unit Director Europe/America, DSM Sinochem Pharmaceuticals, The Netherlands

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Antimicrobial resistance is classified by the WHO as one of the top threats to humanity. The Business Unit Director for Europe and America of DSM Sinochem Pharmaceuticals, a global leader in environmentally friendly anti-infective molecules, explains the risks related to antimicrobial resistance, the role of the pharmaceutical industry and how the company is at the forefront of technological and process developments in this sphere.

Could you please briefly walk us through the history of DSM Sinochem?

The company was founded as the Nederlandsche Gist-en Spiritusfabriek (NG&SF) in 1869. Originally the group produced yeast and spirits and has always been ahead of its time in regard to technology, human resource management and corporate citizenship. In 1879 it was the first Dutch company to found a works council, a workers magazine and built employee housing (today the Agneta park in Delft). In the 1980s it developed unique biological waste water treatment process and was the first in the world to operate industrial scale enzymatic beta-lactam antibiotics production.

In the 1940s, then NG&SF started producing penicillin under the codename BACINOL. Soon it had covered most of the penicillin needs of the country and started exporting across Europe. By the

1970s, the group had become the leading producer of penicillin in the world.

In the following years, the company consolidated and grew its business by global expansion and by applying radically new technologies. In 1997 we introduced the first industrial scale enzymatic process to make beta-lactam antibiotics. This increased purity and dramatically reduced waste from production, significantly improving the eco-footprint of the company. The technology was later rolled out globally, and, in the early 2000s, we implemented an enzymatic direct route production for 7-ADCA, a building block to make cephalosporins in Delft: it's an innovative technology using microorganisms, which in one step transforms sugar into the key intermediate elements to make the antibiotic. Today the Delft facility stands as the only plant of this sort in the world, and is the leading provider of cephalosporin intermediates worldwide.

In 2011 DSM, which acquired Gist-brocades in 1998, established a joint venture with the Chinese chemical company Sinochem. What was the rationale behind this move?

China is one of the largest markets in the world, so we decided it was important to have a strong foothold in that country. This was established via a partnership with one of the most important local players. It was a significant milestone for the company. Sinochem decided to partner up with us because of our innovation-driven footprint, which contributes to a more sustainable manufacturing process of anti-infective molecules. The Chinese industry faces huge challenges in terms of waste disposal and environmental pollution, and our type of technology, which has already been implemented in our Chinese production facilities, ensures eco-friendly production.

What is your current business strategy for the company?

We defined our strategy in 2008 on three strategic pillars: first, strengthen our beta-lactam antibiotics business in the Netherlands and worldwide; second, ensure the finished products are made available globally in the most efficient way; and third, implement innovative biotech processes in new generic molecules in a sustainable way. Since I took over in 2012, my main priority has been to further build sustainable growth for the European and North American markets based on our sustainability proposition.

Antimicrobial resistance (AMR) is classified as one of the top threats to humanity by the WHO. How have you worked to pair DSM Sinochem's mission in this field with the ongoing political debate?

We are strongly interested in the debate, which is crucial for survival and long-term sustainable business development. The AMR Review, headed by Jim O'Neill, estimates that by 2050 10 million

people will die annually due to Antimicrobial resistance, if we do not act fast. This would make AMR the biggest cause of death in the world. The same commission indicates that already today 700,000 people fall victim to antibiotic resistant bacteria. It’s a threat to humanity, but also to our business.

While AMR is part of the political debate, currently, the major focus of public efforts aims at the right prescription and use of antibiotics by doctors, pharmacists and patients, both in the human and veterinary field. This is very important, but there is another key dimension that is largely missing from the debate but must be addressed in the context of AMR: the manufacturing of antibiotics itself, as well as the management of waste and waste water, which is an inevitable part throughout the entire supply chain. Producing antibiotics creates waste in the form of water, air and solids. If these waste streams are not managed responsibly, the pollutants they contain end up in our environment, creating a breeding ground for resistant bacteria.

We are trying to remain very close and interact with the public debate and support the efforts by joining industry initiatives. Waste management is a first crucial step, which needs to be supported by effective legislation. The hidden costs of irresponsible antibiotic manufacturing to the global problem of AMR should be taken into account. I also believe it is the shared responsibility of both the industry and legislators to improve transparency of the supply chain of the pharma industry. In the beta-lactam industry 80% of intermediates come from China and India. In order to sustainably provide such molecules to the global population, the supply chain needs to be under control. At DSM Sinochem Pharmaceuticals, we are fully backward integrated, which enables us to adequately control our supply chain and apply our business and environmental standards from start to finish.

That being said, we take a strong position on the topic and actively engage stakeholders and legislators around the globe. We are also working with both our shareholders to bring this important topic to the debate and both shareholders are fully supporting our initiatives.

What policies have you implemented in-house to ensure AMR does not become a bigger problem?

First and foremost, we implemented enzymatic technology as of 1997 and have been rolling it out globally. The purity of our components has increased so drastically that we produce less waste and by-products, which often contains antibiotic activity. Secondly, we have implemented dedicated wastewater treatment facilities at all our plants. And thirdly, we introduced antibiotic residue testing in our effluent management. After treatment we test our waste water before we release it to the municipality waste water network. We are proud that our tests confirm there is no

detectable antimicrobial activity found in our waste water effluents.

DSM Sinochem's Delft site is the most advanced 7-ADCA site in the world, using a sustainable enzymatic direct-route to manufacture. What is the Netherlands' continued attractiveness as a manufacturing center for pharmaceutical products given lower-cost alternatives?

We use top-notch innovation, which requires highly skilled people and collaboration with universities. In Delft, where our roots lie, we look back a decades of successful cooperation with the Technical University Delft. We are close to several biotech institutes and academic institutions that has played a key role in product developments.

We also continuously work on improvement of our strains, enzymes, processes and technologies to keep our Delft site competitive. The implementation of these requires a downstream process with a high level of automation and innovation. I am proud that in Delft we have self-steering teams in our plant, which leads to a high productivity and also creates an inspiring and innovative workplace, something we clearly see in our annual employee engagement survey. To put it short: the Netherlands simply provides a combination of elements, that feels fit for the future and which suites our needs best.

What is the importance of R&D developed locally?

Much of our R&D is done locally. In the case of our Semi-Synthetic Cephalosporins (SSCs), the R&D work was done in the Netherlands. Production of our active pharmaceutical ingredients (API) takes place in Spain. We also have API factories in China, India and Mexico. Within DSM Sinochem Pharmaceuticals we always evaluate what is the best manufacturing site to produce which intermediates or API and leverage on the strong global network we have. Overall, The Netherlands offer a very stimulating environment for life sciences and biotechnology to us.

The Dutch tradition of collaboration in the chemical and life sciences domains is quite strong. How is it implemented at DSM Sinochem?

Collaboration is a must-have for us. Universities are a source of knowledge to develop new ideas and a rich pool of talents, who join the company as trainees or PhDs and come back later to start their professional career. Our wastewater management system, for instance, was developed in collaboration with a university.

How are you promoting a company culture that fosters innovation?

In the past, our employees were not much aware about the importance of the products we manufacture. So we now explain the impact of antibiotics on the world and how they really help save lives in a clear way. Our employees have thus become much prouder members of the team and are contributing to building a sustainable business with their hard work.

You have spent your entire career in the DSM organization and have been in your present leadership position since 2012. What explains your exemplary loyalty to the company?

I'm a graduate of the Technical University of Delft, and my roots are in chemical engineering. I started working at DSM in 1990, and one of the reasons to embark on the journey was the interest the company takes in the development of people. I wanted to start in chemical engineering but was interested in broadening myself, and the company has allowed me to do it in different disciplines. I would have not thought to be here after so many years, but being part of this company motivates me every day. Becoming a father I realized how much we and our children need antibiotics, and it's stimulating to work in an environment, which makes that happen.

What has been the moment you are most proud of?

When I took over the position in 2012 and started advocating on the importance of AMR in a broader perspective, it made me even prouder to be part of this company. It is about doing something essential in the world.

What are your expectations for the evolution of DSM Sinochem in the coming five years?

We have to continue building what we have done so far so successfully. It's key to remain very open to new challenges that may arrive and to solidify the availability of antibiotics, as AMR is a real threat to humanity.

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