SUSTAINABILITY

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Report

SINOCHEM | DSM

DSM Sinochem Pharmaceuticals

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For us sustainability means being profitable while taking care of our planet, our people and the communities in which we operate

Contents

Letter from the CEO

Dear Reader,

At DSM Sinochem Pharmaceuticals we provide high-quality, reliable and sustainable active pharmaceutical ingredients and drug products.

Every day, our products help people around the world to fight illness and live healthier lives. Countless people rely on our antibiotics to battle life-threatening infections. With this comes a lot of responsibility. Our company values – Quality.Reliability.Sustainability – are deeply embedded in our people and organization, and guide us in meeting this responsibility.

Quality comes first

We ensure the quality, safety and efficacy of our products through regulatory compliance, established at every DSP site. In addition, our good manufacturing practices meet the most stringent global standards and are defined in our corporate policies on quality. All our sites adhere to these policies for all their products, ranging from intermediates to drug products.

In 2016, we successfully completed health authorities' inspections at our sites in Mexico, Europe, India and China. By year's end all our plants were FDA approved. Through various audits, our sites were shown to meet the quality standards of our customers.

We are a reliable partner, and our customers and marketing partners can count on us to deliver the solutions and high-quality products they need. Our supply chain for key intermediates is largely backward integrated or with trusted suppliers with whom we have longstanding relationships. Our customers can rest assured regarding the origin and traceability of our products, as well as the quality and sustainability with which they have been processed and manufactured.

Besides delivering the highest quality and reliability, ensuring the highest safety standards across our global operations has always been a top priority. We have therefore had a safety program in place since 2001 and have been monitoring associated recordable injuries at all our operations. Through various projects grouped under the program "Together, we're making DSP injury-free!" we continuously work to further strengthen our safety culture. It is good to see that in 2016 we improved compared to the previous year and are truly progressing towards our goal of zero injuries.

Quality, reliability and sustainability guide us in everything we do

An important part of our strategy is to provide high-quality, reliable and sustainable drug products and making these available to more end-users in more countries. In 2016, we continued our forward integration into drug products, receiving 112 new marketing authorizations and bringing our total number close to 200. Our Drug Products business gained sales traction with more and more customers launching products and applying dossiers coming from DSP. I expect our Drug Products business unit to continue developing DSP's forward integration in the value chain and changing the face of our company.

Innovative leader in sustainable production

Our continued success is being driven by our ability to develop new products and, increasingly, to develop more sustainable ways of making our products. Our patents safeguard our intellectual property against counterfeiting and dilution of quality. To ensure we can continue to invest in innovation programs now and in the future, we will defend our intellectual property position more rigorously.

Our PureActives® are yet to be matched in our industry and with good cause. They are produced using our proprietary, sustainable, and environmentally friendly enzymatic technology, and bring our customers differentiated solutions through superior quality, outstanding reliability and leading sustainability performance.

For us, sustainability means simultaneously pursuing social responsibility, environmental accountability and economic performance. Sustainability is an integral part of our business operations, strategic actions and decisions, and something close to my heart. We provide sustainable solutions for our customers and end users, while taking care of our own people, the communities in which we operate and our planet.

However, in this day and age, we believe it is not enough to just look at ourselves. Only if we look at the entire value chain can we create truly sustainable solutions. For example, we require our suppliers to participate in supplier sustainability assessments via the Together for Sustainability initiative and perform Life Cycle Assessments (LCAs) for all our PureActives® API products. We plan to launch our own Sustainability Assessment Question-

naire for suppliers in 2017. By following this route, we safeguard not only the quality and reliability of our products and business in a sustainable way, but also the well-being of the planet and those who live on it.

Year of truth

2016 proved to be a year of truth for the recognition of the environmental angle of antimicrobial resistance (AMR), and more specifically antibiotics pollution associated with ingredient manufacturing as a cause of AMR. We have been raising awareness on this topic since 2014 through our Sustainable Antibiotics Program.

The final report of the UK Review on AMR, presented in May 2016, made it clear that the environmental angle on AMR can no longer be ignored and proved to be a spin-off point. AMR has since become a matter of public debate. Over the course of the year, commitments were made by the industry, and international agencies and media publicly recognized the problem. Moreover, activists, environmentalists, NGOs and universities increasingly started putting pressure on the industry.

In early 2016, over 100 companies worldwide, including DSP, signed the Davos declaration to call for collective action on creating a sustainable market for antibiotics. But the biggest highlight for me was our presence at the United Nations General Assembly (UNGA) in September 2016 and the co-signing of the Industry Roadmap, together with 12 other industry leaders. In this Roadmap, we defined concrete commitments on environmental stewardship, misuse of antibiotics, access to high-quality antibiotics, science and development, and public/private engagement.

Receiving the 2016 CEFIC Responsible Care Award for Product Stewardship is not only an acknowledgement of DSP's efforts, but also encourages us to proceed with our work to implement higher sustainability standards in our value chain.

We became member of the Pharmaceutical Supply Chain Initiative (PSCI), a group of 24 pharmaceutical and healthcare companies who jointly promote responsible supply chain management and better business conditions across the industry. Through this membership, we can play a leading role in establishing industry-wide guidelines that reach into the entire value chain to ensure antibiotics are produced responsibly and sustainably.

I am proud of our achievements in 2016. It proves we are more than capable of continuously moving forward and raising the bar in delivering our promise to our customers and other stakeholders. At the same time, I am excited about the journey ahead. 2016 was a pivotal year in many respects. It has clearly pointed out the direction in which we will proceed in our commitment to providing high-quality, reliable and sustainable pharmaceutical ingredients and drug products to those who need and rely on them.

Sincerely,

Karl Rotthier
CEO, DSM Sinochem Pharmaceuticals


Linde
Uitgezonderd bestemmings-verkeer

Our Business

DSM Sinochem Pharmaceuticals is the global leader in sustainable antibiotics, next-generation statins and anti-fungals.

We develop, produce and sell intermediates, active pharmaceutical ingredients and drug products.

Our employees worldwide work together to deliver cutting-edge generic solutions that help our customers to stay ahead of the competition.

Founded in the Netherlands in 1869, DSP today is headquartered in Singapore, with manufacturing sites and sales offices in China, India, Egypt, the Netherlands, Spain, the USA and Mexico.

DSP is a 50/50 Joint Venture of Royal DSM, a global science-based company active in health, nutrition and materials, and Sinochem Group, a Fortune 500 enterprise.

DSP at a glance

We are the global leader in sustainable antibiotics, next-generation statins and anti-fungals. Our aim is to further grow our position in generic pharmaceuticals by building on our key strengths and continuing our forward integration into drug products.

Our mission

Our mission is to provide people in need of healthcare with high-quality, reliable products. To do this, we continuously explore innovative technologies that positively impact patient care and environmental sustainability.

Our vision

We aspire to become the global leader in generic pharmaceuticals. To achieve this ambition, we build on our strong foundation of leading technology and our heritage of sustainable, world-class operations. We produce cutting-edge science and use the most economical, reliable, high-quality and sustainable manufacturing methods.

Our strategy

We aim to create value for our customers and shareholders by combining our key capabilities in technology and operations with our global sales footprint. As a leading global pharma-house, we focus on highly regulated markets in Europe, the USA, Canada, Asia (e.g. South Korea, Japan and Australia), South Africa, and on growth markets in Asia, Mexico, Latin America and the Middle East.

We aspire to become the global leader in generic pharmaceuticals

Our customers

Our customers include the world's major pharmaceutical companies as well as leading regional pharmaceutical companies on all continents.

Our markets

Thanks to our global manufacturing footprint and regulatory coverage, we can serve markets in all parts of the world. In regulated markets in both Western and emerging economies, we have an excellent track record, while seamless collaboration between all our regional business units means we are able to serve customers wherever they are.

Quality. Reliability. Sustainability. Our promise

Quality. Reliability. Sustainability. These three elements together make up our brand promise and serve as a guiding compass for our business. Closely linked, they inevitably impact and enhance each other. Using them to guide us in everything we do helps us to continuously deliver more value using fewer resources.

In this way, with our partners and customers, we create increasingly sustainable, high-performing solutions. Living and breathing our brand promise also makes sure we remain an outstanding innovator, partner and corporate citizen of the world, while at the same time giving our employees clear purpose and fulfillment in their work.

Quality

We provide pharmaceutical ingredients and drug products based on our fully integrated global manufacturing capabilities. Building on our unique skills in fermentation, synthesis and biotechnology, our products meet the highest quality standards.

For us, quality means more than just compliance with current Good Manufacturing Practices (cGMP). We have a comprehensive set of Quality and Safety, Health and Environment (SHE) policies that go beyond cGMP and which we apply globally – not only to ourselves but also to our manufacturing partners. These policies are supported by our membership of the PSCI and the Together for Sustainability (TfS) initiative (see p. 47).

Combining these standards with our unique technology platform allows us to provide the world with high-quality, life-saving medicines, which are safe and effective, in a sustainable and responsible way.

Reliability

We are known as a reliable, long-term partner in our industry. Our customers and marketing partners can count on us to deliver the solutions and high-quality products they need – at the right time and place, and in the right quality and quantity.

Our supply chain for key intermediates is largely backward integrated. In addition, we work with trusted suppliers, with whom we have longstanding relationships. Customers can rest assured that the origin and traceability of our products are impeccable, as are the quality and sustainability with which they have been manufactured and processed.

Our production is supported by multiple plants across the globe and by operations in each of our regions.

Our sites meet (and often exceed) the highest local and international standards.

Sustainability

To measure our progress in creating sustainable value, we map our efforts along three dimensions: People, Planet and Profit. We are pioneers of the most eco-friendly technologies and production processes for APIs, such as our unique enzymatic technology, proven by 500 individual patents.

Our Sustainable Antibiotics Program (see p. 28) provides a comprehensive platform through which we address serious global issues related to the manufacturing and use of antibiotics, and aim to increase the sustainability of our industry as a whole.

Our portfolio

Our active pharmaceutical ingredients portfolio
We are market leader in enzymatic beta-lactam APIs, with 500 individual national patented innovations in this field. We are pioneers in combining the most eco-friendly technologies and production processes for our sustainable antibiotic, anti-fungal and statin APIs.

Penicillin G
Penicillin G potassium
Penicillin G procaine
Penicillin G procaine sterile
Penicillin G benzathine sterile*

Beta-lactam Intermediates
6-aminopenicillanic acid (6-APA)
7-amino-deacetoxycephalosporanic acid (7-ADCA)

Semi-Synthetic Penicillins
Purimox® Powder (Amoxicillin Trihydrate, powder)
Purimox® Powder extra dry (Amoxicillin trihydrate, powder extra dry)
Purimox® Powder grade C (Amoxicillin trihydrate, powder)
Purimox® Powder grade E (Amoxicillin trihydrate, powder)
Purimox® Compacted DC (Amoxicillin trihydrate, compacted for direct compression)
Purimox® Compacted grade A (Amoxicillin trihydrate, compacted)
Purimox® Compacted grade A extra dry (Amoxicillin trihydrate, compacted extra dry)
Purimox® Compacted grade P (Amoxicillin trihydrate, compacted)
Purimox® Fine (Amoxicillin trihydrate, fine powder)
Purimox® HBD (Amoxicillin trihydrate, high bulk density)
Puricillin® Powder (Ampicillin trihydrate, powder)
Puricillin® Powder grade X (Ampicillin trihydrate, powder)
Puricillin® Compacted grade A (Ampicillin trihydrate, compacted)

Isoxazoles
Cloxacillin Sodium Compacted
Cloxacillin Sodium Powder
Dicloxacillin Sodium Compacted
Flucloxacillin Sodium Compacted
Flucloxacillin Sodium Powder
Oxacillin Sodium Monohydrate Compacted

Semi-Synthetic Cephalosporins
Purilex® Compacted (Cephalexin monohydrate, compacted)
Purilex® Powder (Cephalexin monohydrate, powder)
Puridrox® Compacted (Cefadroxil monohydrate, compacted)
Puridrox® Powder (Cefadroxil monohydrate, powder)
Puridin® Compacted (Cefradine, compacted)
Puridin® Powder (Cefradine, powder)
Puriclor® Compacted (Cefaclor, compacted)
Puriclor® Powder (Cefaclor, powder)
Cefprozil**

Statins
Atorvastatin (Atorvastatin calcium trihydrate, micronized)
Rosuvastatin (Rosuvastatin calcium)
Pitavastatin*

Anti-Fungals
Nystatin Powder
Nystatin Micronized
Nystatin Mycellium

* under development
** available for sampling

Our drug products portfolio

We are also a business-to-business (B2B) provider of generic drug products. What sets us apart, however, is our backward integration and control of our supply chain.

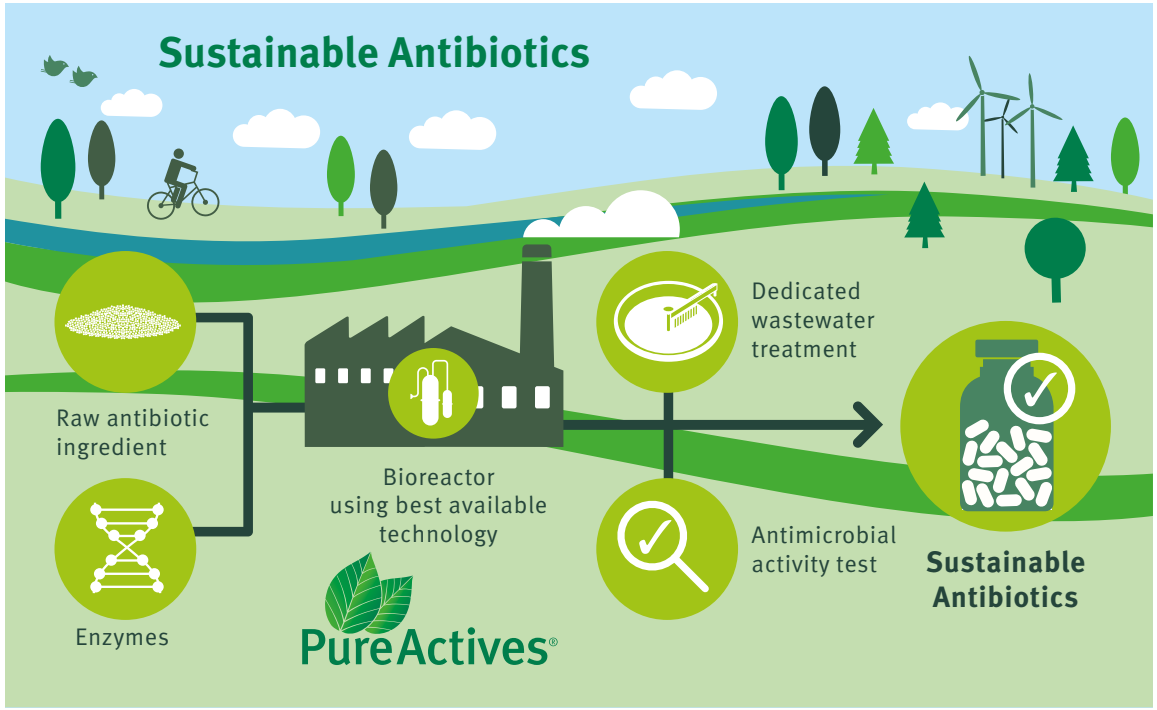
Our antibiotic and statin products are manufactured using our own high-quality PureActives® APIs. We also use high-quality APIs developed in-house for our anti-fungals. Our backward integration and control of our supply chain guarantee unique quality and performance in the finished dosage formulation. Naturally, we do not compete with our marketing partners in their end markets.

Molecule	Dosage form	Strength	Availability
Beta-lactams			
Amoxicillin	Capsules, hard (CAP)	250 mg 500 mg	EU
	Dispersible tablets (DTA) Tablets (TAB)	500 mg 750 mg 1,000 mg	Worldwide
	Powder for oral suspension (POS)	125 mg / 5 ml 250 mg / 5 ml 500 mg / 5 ml	Worldwide
	Powder for oral suspension in sachet (SAC)	250 mg 500 mg 1,000 mg 3,000 mg	Worldwide
Amoxicillin + Clavulanic acid	Film-coated tablets (FCT)	250 mg + 125 mg (2:1) 500 mg + 125 mg (4:1) 500 mg + 62.5 mg (8:1) 875 mg + 125 mg (7:1)	Worldwide
	Powder for oral suspension (POS)	125 mg + 31.25 mg (4:1) / 5ml 400 mg + 57 mg (7:1) / 5ml 250 mg + 62.5 mg (4:1) / 5ml 500 mg + 62.5 mg (8:1) / 5ml 200 mg + 28.5 mg (7:1) / 5ml 600 mg + 42.9 mg (14:1) / 5ml	Worldwide
	Powder for oral suspension in sachet (SAC)	500 mg + 125 mg (4:1) 1,000 mg + 125 mg (8:1) 875 mg + 125 mg (7:1)	Worldwide
Statins			
Atorvastatin	Film-coated tablets (FCT)	10 mg 20 mg 30 mg 40 mg 60 mg 80 mg	Worldwide
Rosuvastatin	Film-coated tablets (FCT)	5 mg 10 mg 20 mg 40 mg	Worldwide
Pitavastatin*	Film-coated tablets (FCT)	1 mg 2 mg 4 mg	Under development
Anti-Fungals			
Caspofungin	Powder for concentrate for solution for infusion (PFI)	50 mg 70 mg	Worldwide
Micafungin*	Powder for concentrate for solution for infusion (PFI)	50 mg 100 mg	Under development
Nystatin*	Oral suspensions (ORS)	100.000 I.U.	Under development

PureActives® – the enzymatic difference

DSP's enzymatic platform completely replaces the traditional 13-step antibiotic production process with natural processes that eliminate the use of solvents or other chemicals. Most of the chemical steps in producing our statins have been replaced with enzymatic processes as well. The APIs and drug products we manufacture using this green technology are collectively marketed under the name PureActives®.

All PureActives® contribute to our promise of Quality. Reliability. Sustainability. They have undergone a Life Cycle Assessment (LCA), confirming their superior green credentials compared to chemical products. Not only do they consume fewer natural resources and use less energy, they also deliver increased yield and efficiencies in raw materials (see ECO+ on p. 48). Because they are so extremely effective in use, our PureActives® have enabled us to reduce our carbon footprint by 64% compared to the traditional chemical process. Strict quality control and a transparent backward-integrated value chain guarantee their quality, effectiveness and traceability.



64% | **carbon footprint reduction**

Where we are

Global mindset

Our global corporate staff provides our strong regional units with solid support. This setup allows us to act in a coordinated way on a global level, while keeping a bird's eye perspective that helps us to constantly improve our products and services.

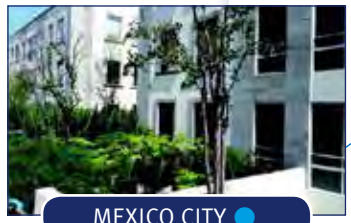
Local presence

Four regional units and one global unit for Drug Products are the cornerstones of our customer and supplier relationships. Together, they span the entire globe. Individually, they are close to you – our valued partners.

PARSIPPANY

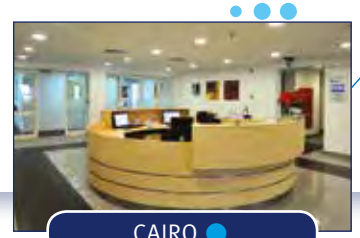
DELFT

RAMOZ ARIZPE



MEXICO CITY

BARCELONA



CAIRO

- Head office
- Sales office
- Manufacturing site
- R&D site

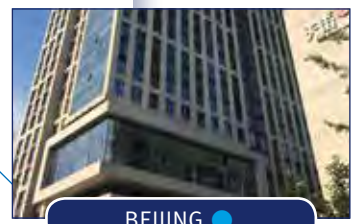
* DSP office not shown in the picture

TOANSA

GURGAON

YUSHU

ZIBO



BEIJING

MUMBAI

BANGALORE*

SINGAPORE

A history of innovation

DSP has had numerous milestones that substantiate our brand promise of Quality. Reliability. Sustainability.

19th CENTURY

1869 – Company is founded as the "Nederlandsche Gist- en Spiritusfabriek" (NG&SF) in Delft, the Netherlands.

1884 – NG&SF builds Agnetapark, the first workers' housing in the Netherlands (now a national heritage site).

1879 – First Dutch company to set up a works council and employee magazine.

20th CENTURY

1970s – Under the name "Gist Brocades", the company rises to become the world's No. 1 Penicillin G producer.

1940s – Production of Penicillin G (initially under the code name BACINOL) starts. Chemical-based SSPs and SSCs soon follow.

1990s – Global production and sales network achieved through acquisitions and joint ventures.

1983 – Construction starts of dedicated anaerobic digestion wastewater treatment facilities at Delft site.

1997 – In a joint venture, DSM and Gist Brocades develop the first industrial-scale enzymatic process for beta-lactam antibiotics production. Commercial production of cephalexin, a semi-synthetic cephalosporin, starts.

1998 – DSM acquires Gist Brocades. The newly formed leader in beta-lactam antibiotics is called DSM Anti-Infectives (DAI).

1869 | 1879 | 1884 | 1940 s | 1970 s | 1983 | 1990 s | 1997 | 1998

21st CENTURY

2003 – The first enzymatically produced Amoxicllin, Purimox®, is commercially introduced to the world. It is the first member of the PureActives® family of "green" antibiotic APIs.

2005-2011 – Global rollout of enzymatic technology for beta-lactam APIs to all sites.

2014 – Statins produced at the new world-class statins plant in Toansa, India, using our proprietary enzymatic (bio)technology route and second-generation biofuels.

2014 –Launch of the DSP Sustainable Antibiotics Program to address the threat of antibiotic resistance and to ensure sustainable, reliable and clean production of our high-quality antibiotics.

2016 – DSP signs the Davos Declaration and is a driving force and signatory of the UN Industry Roadmap on AMR.

2016 – At all our sites routine AMA testing is implemented and no antimicrobial activity is detected in our effluents.

2016 – One of the first three companies in the world to offer generic Rosuvastatin in Europe, using our unique fully backward integrated process.

2003 | 2005 - 2011 | 2011 | 2012 | 2014 | 2015 | 2016

2011 – In a joint venture, Sinochem of China acquires 50% of DAI from DSM to form DSM Sinochem Pharmaceuticals.

2012 – Introduction of the first enzymatically produced statin, Atorvastatin, to the world.

2012 – DSP introduces its first drug product (finished dosage formulation), made exclusively using its own high-quality enzymatic PureActives® API.

2015 – DSP joins DSM in becoming member of Together for Sustainability, an industry initiative to standardize and share supplier sustainability assessments.

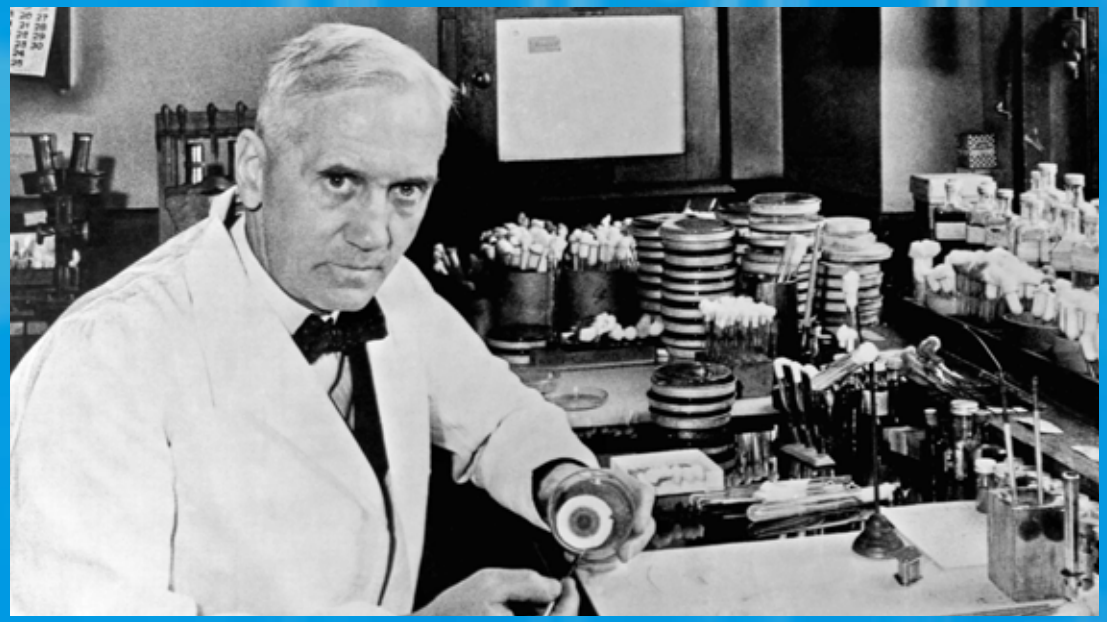
2015 – Start of waste stream analysis and development of the antimicrobial activity (AMA) test.

2016 – Winner of the 2016 Cefic European Responsible Care Award in the Product Stewardship Category.

A chance discovery that changed the world

Our DSP core product range is the penicillin family of antibiotics. Although basic penicillin can only protect against a limited range of bacteria, its discovery has been the starting point for more than a hundred other antibiotics that are highly effective against many different bacteria. Essentially, penicillin has laid the foundation for modern healthcare, making surgery, cancer treatments, organ transplants, and other major interventions possible. And yet it was discovered purely by accident.

There will be few people in the developed world who have not taken penicillin at some time in their lives. Before it was discovered in 1928, if you had an infection, you could wait to see whether it cleared up, or you could cut it out. One in three people who had an operation or caught pneumonia did not survive. Things changed dramatically when penicillin became widely available just after World War II. Since then, life expectancy has increased by an average of 30 years, due in part to the discovery and use of antibiotics such as penicillin.



When being untidy is good

As the story goes, Alexander Fleming, a bacteriologist at St. Mary's Hospital in London, came back from vacation in September 1928 to find someone had left some Petri dishes with staphylococcus bacteria out on his bench. When he looked at them under a microscope, he saw they had been contaminated by a mold called Penicillium notatum. But what really surprised him was that the penicillium mold was inhibiting the growth of the staphylococci, even reducing their number.

But unfortunately, Fleming had neither the laboratory resources nor the chemical background to do what needed to be done next. It was not until 1938, when Howard Florey, professor of pathology at Oxford University, came across Fleming's paper on the Penicillium mold in *The British Journal of Experimental Pathology*, that work on penicillin started up again. In the summer of 1940, Florey and his colleague Ernst Chain, a biochemist who had fled Nazi Germany, set up experiments centered on a group of 50 mice that they had infected with deadly streptococcus. Half the mice died. The other half, which received penicillin injections, survived.

After several attempts, and studying different kinds of penicillin, they worked out how to mass-produce the antibiotic in the vast quantities that would be needed to save human lives. They did so just in time to save the lives of troops injured during the Normandy landings in 1944. Throughout history, the major killer in wars had been infection rather than battle injuries. In World War I,

the death rate from bacterial pneumonia was 18 percent; in World War II, it fell to less than 1 percent.

Code name "Bacinol"

Meanwhile, in the Netherlands, which was under German occupation, a group of Dutch scientists, specialized in yeast fermentation, were working secretly and independently on a similar project, based on a small piece of key evidence provided by Dutch physician Andries Querido. Querido, who was interned at a concentration camp in the Czech Republic at the time, had a large network of biochemists in the USA, from which he would receive useful information. The Dutch team worked for the Nederlandsche Gist- en Spiritusfabriek (NG&SF: Netherlands Yeast and Spirit Factory), which would eventually become DSM Sinochem Pharmaceuticals (DSP).

One of the first to scale up industrial production of penicillin

Under the code name "Bacinol", they successfully developed an industrial fermentative process for making penicillin in large quantities. They benefited from the expertise that had been built up since the company's founding in the nineteenth century, as well as from the data in the Netherlands' extensive national collection of fungi.

World leader

When the war ended in 1945, the Delft group was quickly ready to scale up production of industrial penicillin, which was much needed in post-war Europe. With its acute shortages, rampant malnutrition, and widespread disease, penicillin was a valuable black market commodity, with demand far outstripping supply. As early as 1946, NG&SF was producing enough to meet the needs of all Dutch hospitals, and by 1948 the needs of the entire country. Exports began in 1949, and NG&SF quickly became one of the largest producers of penicillin in the world.

Review of business in 2016

Strong performance in difficult market circumstances

Results

In 2016, business performance was strong despite challenging market circumstances in several parts of the world. In low-regulated markets, price pressure increased and competitors, mainly in India and China, drove an overall price decline. This price decline was mitigated by DSP through continuous efforts in maximizing new

Close to 200 authorizations for drug products in Europe

product sales and higher – margin sales in regulated markets. The quality offering of DSP's products continued to command a premium in all market segments. Besides the price pressure, we faced overcapacity in the active pharmaceutical ingredients (API) markets for our 6-APA intermediate, semi-synthetic penicillins and semi-synthetic cephalosporins. In spite of the market challenges, we successfully maintained our global leadership position with volume growth rates higher than the market.

In Asia, and in China in particular, we see stricter enforcement of environmental regulations by governments, and stricter environmental standards have led to more stringent manufacturing practices. An example of this is the policy change made by the Shijiazhuang municipal government in November 2016, which forced local manufacturers (including pharmaceutical companies) to halt production temporarily in order to reduce air pollution.

This trend will lead to incremental costs for manufacturers of active pharmaceutical ingredients (APIs), and we expect this will drive further consolidation in the industry. In regulated markets, pressure is increasing on reducing the use of antibiotics for non-human purposes, coupled with greater attention to the global health threat of antimicrobial resistance (see p. 27). At the same time, worldwide pressure on rising healthcare costs due to price setting for pharmaceutical products is not likely to diminish.

Antimicrobial resistance

The rise of deadly superbugs, which render even the strongest of antibiotics ineffective, is causing widespread concern around the world. In September 2016, along with 12 other leading pharmaceutical companies, we presented a Roadmap for Progress on Combating AMR at the United Nations General Assembly (see p. 33). It was only the fourth time in the United Nation's history that a health topic was discussed at the assembly. The publication of scientific studies and NGO reports have attracted major media attention to the topic of the environmental impact of irresponsible antibiotics production. This underscores the importance of leading brands acting responsibly in their supply chain by sourcing from companies, like ourselves, that produce to the strictest environmental standards.

Operations

Our production base at Yushu, China, which applies enzymatic fermentation technology to produce the intermediate 6-APA, ran at full capacity in 2016. The multi-purpose production plant in Toansa, India, produced Atorvastatin and Rusovastatin throughout 2016, using our proprietary biotechnology, enabling us to meet the increasing demand for high-quality products in the cardiovascular market (see p. 50). Most notably, in 2016, we received approval for Caspofungin, our new antifungal. We also received a CEP for Rosuvastatin, produced in Toansa, India, and another for Cefaclor, produced at our facility in Zibo, China.

Our global business unit Drug Products made excellent progress, empowering DSP to achieve further integration in the value chain. DSP obtained 112 marketing authorizations (MAs) in Europe during the year, bringing the total close to 200, with an additional 237 MAs still in filing. The Drug Products business unit started to gain sales traction with more and more customers launching products and applying dossiers coming from DSP.

Sustainability in action

Sustainability is an integral part of our everyday business operations, strategic actions and decisions. Being driven by our ability to create sustainable innovations, we aim to continuously provide better solutions for our society, the planet, communities and people.

Our responsibilities

People

The company from which DSP originated was, from the start, an innovative employer. It was the first company in the Netherlands to set up a works council, for instance, and it built social housing for its workers. Today, we continue that innovative tradition. At our intermediates plant in Delft, for example, employees work in self-steering teams of operators, the world's only direct-route 7-ADCA plant to be run by employees in this way. In addition, we always strive to treat our own people and others we come into contact with in such a way that we have a positive influence on their lives. This begins by providing a safe and inspiring work environment that nurtures employees' talents, and it extends to providing people with clean, safe and compliant medicines to keep them healthy, and making sure those same medicines will continue to be available.

Planet

Our efforts to protect the planet are brought together in our ECO+ program. Launched in 2007, ECO+ focuses on developing innovative products and manufacturing processes that have demonstrable ecological benefits when compared to their mainstream alternatives. Our ultimate goal is to make our whole value chain more energy efficient and less wasteful. Between our base year 2008 and 2016, we reduced our energy consumption by a full 42%, which puts us well on target to achieving our 2020 energy efficiency goal of 43%.

Profit

DSP can only make a difference to people and the planet if our activities are economically sustainable. Our ECO+ products contribute to this with their superior and innovative characteristics, environmental benefits, and business advantages. Today, no less than 84% of our net sales come from ECO+ products and we continue to increase this percentage.

Our ECO+ program is our ongoing drive to provide the market with greener products. ECO+ solutions have undergone a Life Cycle Assessment and score significantly better in at least two of the three main categories of environmental impact: human health, ecosystem quality and resource depletion.

Antimicrobial resistance and sustainable antibiotics

One of the biggest health threats

Like every life form, bacteria and pathogens are able to adapt and evolve in response to the pressure of natural selection. Those that survive exposure to a medicine that would normally kill them or stop their growth, develop resistant genes. Bacteria can multiply fast and exchange genes. This can lead to the emergence of "superbugs", bacteria that are difficult or even impossible to treat with existing antibiotics. And because we lack new drugs to fight these superbugs today, the damaging effects of antimicrobial resistance (AMR) are already manifesting themselves across the world.

Conservative estimates contained in the Review on AMR[1] put the global number of deaths due to AMR already at 700,000 per year. Without urgent action, a staggering 10 million people will be killed annually by resistant bacteria by 2050, the Review on AMR predicts. This makes AMR the biggest threat facing humanity today.

Industry pollution under-estimated

AMR is a natural phenomenon, but it is accelerated and spread by human behavior, such as poor sanitation, insufficient measures to prevent and control infection, the misuse of antibiotics, pharmaceutical pollution of the environment, and international travel and the food trade. A drug-resistant bacterium that was found in 2014 in India has since been identified in more than 70 countries worldwide. Reports indicate that increasing numbers of travelers return home with superbugs in their digestive systems.

Any use of antimicrobials, no matter how appropriate or conservative, contributes to the development of resistance. But widespread unnecessary and excessive use makes it worse. For example, overuse and misuse of antibiotics, sometimes of inferior quality, is facilitated in many countries by the fact that they are available over the counter and without prescription. At the same time, prescribing practices vary hugely between countries, and even from doctor to doctor, and unavailability of certain antibiotic classes, diagnostics or vaccines also contributes to AMR.

Antibiotics have saved billions of lives. Now it is time to save them

A second major cause of AMR is the excessive use of antibiotics as a general prophylactic in animal feed, including in fish farming. There are circumstances where antibiotics are required in agriculture and aquaculture – to maintain animal welfare and food security. However, much of their global use is not for treating sick animals, but for prevention and as a growth stimulator. This has led to retention of antibiotics in food, the release of antibiotics into the environment, and the spread of drug-resistant bacteria.

The third key reason for the rapid spread of AMR is antibiotics pollution associated with ingredient manufacturing. Some concentrations of antibiotics found in public waters close to factories (mainly in China and India, which are responsible for 80 to 90% of all antimicrobial production) are thousands or even 10,000 times higher than normal, creating hotspots for resistant bacteria. Until recently, this cause of AMR was severely underestimated.

Time to take action

In 2016, the Review on AMR called for the rapid development of minimum standards to prevent antibiotic waste from being released into the environment. It also called for improved surveillance, pointing out that the way antibiotics are manufactured and inadequate waste treatment are of particular concern.

According to the Review on AMR, the supply chain generates an estimated annual amount of 30,000 to 70,000 tonnes of waste containing antimicrobial activity. Several scientific studies report high concentrations of antibiotics, and the presence of resistant bacteria or genes in the close vicinity of ingredient manufacturing plants. A recent study even measured levels of fluconazole (an anti-fungal) approximately 950,000 times higher than suggested environmental limits, and it found extensive presence of multiple-drug-resistant bacteria, such as ESBL (extended-spectrum betalactamase) and CRE (carbapenem-resistant enterobacteriaceae) in many of the water samples taken.[2]

[1] "Tackling drug-resistant infections globally: final report and recommendations," published by the Review on AMR, May 2016.
[2] Christoph Lubbert et al., 2017, Leipzig University Hospital, "Environmental pollution with antimicrobial agents from bulk drug manufacturing industries in Hyderabad, South India, is associated with dissemination of extended spectrum beta lactamase (ESBL) and carbapenemase producing pathogens (CRE)." Source: https://link.springer.com/content/pdf/10.1007%2Fs15010-017-1007-2.pdf

Our Sustainable Antibiotics Program

The aim of our Sustainable Antibiotics Program is to promote the responsible manufacturing and use of antibiotics. Launched in 2014, it was established to help us define our position in what was then observed as one of our business continuity risks: drug resistance could lead to a situation in which our products would become ineffective.

During this process, we came to the conclusion that – as a leading manufacturer of responsibly made antibiotics – we needed to play a leading role in the important global fight against AMR, and particularly in reducing the negative effects of production, namely the antibiotic active waste we generate while producing the miracle drug. At that time, we had already implemented enzymatic technology, which has the smallest carbon footprint, and we were already operating dedicated wastewater treatment plants at production sites as an integral part of our manufacturing operations. But we then found that we also had to assess their effectiveness. Consequently, we developed and implemented our own antimicrobial activity test (see p. 38).

If we fail to act now, we will bring the post-antibiotic era nearer

In addition, DSP has taken on a high-profile campaigning role in the fight against AMR by calling on both the industry and the entire value chain to act responsibly and stop buying, using or selling irresponsibly made antibiotics. By actively going public with our message, while at the same time reaching out to a wide range of stakeholders, we aim to create awareness that industrial antibiotics pollution significantly contributes to antimicrobial resistance and that the sustainable and responsible production of antibiotics is not only imperative, but also economically feasible.

We are proud that this initiative was recognized by Cefic – the European Chemical Industry Council – who awarded the Sustainable Antibiotics Program its Responsible Care Award for Product Stewardship (see p. 35).

Increasing stakeholder pressure on the industry to act

The final publication of the Review on AMR report in May 2016 prompted a whole range of declarations, action plans and international acknowledgements. Academia, NGOs, international bodies, governments and investors increasingly called for responsible manufacturing of antibiotics. This has led to increased media attention, and the launch of a number of initiatives in the battle against AMR, triggering in turn commitments from some of the world's largest pharmaceutical companies.

Review on AMR

The Review on AMR was commissioned in July 2014 by the UK Prime Minister, who asked the economist Jim O'Neill to analyze the global problem of rising drug resistance and to propose concrete actions to tackle it internationally. The Review on AMR engaged widely with international stakeholders to understand the situation and to propose solutions to the problem of drug-resistant infections from an economic and social perspective. The Review on AMR acknowledges pharmaceutical pollution as a significant driver of AMR and urges regulators and industry players to act on this.

In its concluding report, the Review on AMR estimated that drug-resistant infections are already responsible for killing 700,000 people annually and will kill more people than cancer by 2050, resulting in a staggering 10 million deaths and a cost to the world economy of $100 trillion every year.

The way that antimicrobials are produced, the by-products which result, and particularly the impact of effluent from factories on AMR are issues that have too often been neglected in discussions about this topic. There is growing evidence that there are still API manufacturers which do not treat waste products adequately, with the result that high concentrations of antibiotic active ingredients are disposed of into the local environment, creating "reservoirs" of antibiotic-resistant bacteria.

Proposed interventions

Global bodies/national governments and regulators should establish evidence-based, enforceable targets for maximum levels of antimicrobial active pharmaceutical ingredient (API) discharge associated with the manufacture of pharmaceutical products.

Pharmaceutical companies should improve monitoring of API emissions from directly operated manufacturing facilities as well as those of third-party suppliers, and support the installation of proper waste processing facilities to reduce or eliminate API discharge. Such efforts should be based in voluntary, transparent and auditable commitments, with a globally consistent "quality mark" applied to end products produced on an "environmentally responsible" basis. (Review on AMR, May 2016)

Academia

One of the first scientists to draw attention to the problem of pharmaceutical pollution as a cause of AMR was Professor Joakim Larsson, of the University of Gothenburg, Sweden. As early as in 2007, he published evidence of contamination of surface, ground and drinking water from antibiotics production. He and others have pointed out that poor wastewater treatment is a major factor in the spread of AMR, as unusually high concentrations of active antibiotics are disposed of in one place. For instance, Larsson found that inadequate treatment of pharmaceutical wastewater led to rivers in Patancheru, India, having higher concentrations of active antibiotics than the blood of patients undergoing treatment![3]

In 2016, the Chinese Academy of Sciences and the Academy of Environmental Science and Technology mapped concentrations and discharges of antibiotics in Chinese waterways and found high concentrations of antibiotics.[4] Earlier studies reported high concentrations of drug-resistant bacteria.[5]

[3] D.J. Larsson, C. de Pedro, and N. Paxeus, 2007. "Effluent from drug manufacturers contains extremely high levels of pharmaceuticals." Journal of hazardous materials, 148(3), pp. 751-755.
[4] Q.Q. Zhang, G.G. Ying, C.G. Pan, Y.S. Liu, and J.L. Zhao, 2015. "Comprehensive evaluation of antibiotics emission and fate in the river basins of China: source analysis, multimedia modeling, and linkage to bacterial resistance." Environmental Science & Technology, 49(11), pp. 6772-6782.
[5] http://www.the-scientist.com/?articles.view/articleNo/38730/title/Resistant-Wastewater/

NGOs

Several NGOs have put increased pressure on various value chain players to increase transparency, clean up their supply chain, and introduce legislation. In addition, various NGOs have published reports and articles in which they highlighted the role of pharmaceutical pollution in the spread of AMR. For example:

- In August 2016, the European Public Health Alliance (EPHA) published a report entitled *Drug resistance through the back door*[6], calling on national purchasers to blacklist polluters and add environmental criteria in purchasing decisions. It urged large purchasers of medicines to blacklist pharmaceutical companies which are contributing to the spread of AMR through irresponsible manufacturing practices and to demand greater transparency. Additionally, it insisted that they reviewed their procurement policies and supplier codes of conduct, including environmental criteria in GMP.
- In October 2016, Changing Markets published *Superbugs in the supply chain – How pollution from antibiotics factories in India and China is fueling the global rise of drug-resistant infections*[7]. This report focussed on the illegal dumping of antibiotics near factories, especially in India and China.

[6] 'Drug resistance through the back door – how the pharmaceutical industry is fuelling the rise of superbugs through pollution in its supply chains', published by EPHA and Changing Markets, August 2016. Source: https://epha.org/wp-content/uploads/2016/10/Superbugsinthesupplychain_CMreport.pdf

[7] 'Superbugs in the supply chain – How pollution from antibiotics factories in India and China is fueling the global rise of drug-resistant infections', published by Changing Markets, October 2016. Source: https://epha.org/wp-content/uploads/2016/10/Superbugsinthesupplychain_CMreport.pdf

International bodies advocating sustainable production

United Nations

On September 21, 2016, the United Nations General Assembly issued a Political Declaration on AMR.

Among many other statements, the UNGA acknowledged that AMR is caused by residues of antimicrobials in soil, crops and water, and called for a multi-stakeholder approach to reduce it. In October, a research agenda was announced to collect evidence on the importance of antibiotic residues and resistant organisms in the environment.

Interagency Coordination Group on AMR

In September 2016, the United Nations, together with several partners (including the World Health Organization (WHO), the Food and Agriculture Organization (FAO) and the International Organization of Employers (IOE) of the United Nations), joined forces to set up the Interagency Coordination Group on AMR. The objective of the Group will be to provide practical guidance for approaches needed to ensure sustained effective global action to address antimicrobial resistance, including options to improve coordination, taking into account the WHO Global Action Plan on Antimicrobial Resistance.

Access to Medicine Foundation

In December 2016, the Access to Medicine Foundation started working on an AMR Benchmark to track how pharma companies are responding to increases in drug resistance. The companies will be ranked in an AMR Index, to be published in December 2017.

Investors

In 2016, based on a field study in India, global investors, such as Nordea[8] and BNP Paribas, raised concerns about the potential damage to global health and the environment caused by uncontrolled antibiotic discharges, demanding improved transparency and adequate waste management systems.

As Nordea Asset Management stated: "Pharma supply chains are as opaque as they are complex. There is a compelling body of research on the negative effects posed by pollution from antibiotics manufacturing plants in India. There is a need for transparency and strong environmental standards at every stage of the supply chain."

National Action Plans on AMR

In 2016, various countries shared their National Action Plans (NAPs) on AMR. China published its NAP in November 2016, which clearly shows the country is taking its responsibility seriously. India's NAP was in preparation in 2016, and will be published in April 2017. Both National Action Plans address the antibiotics pollution angle, which is an encouraging development.

National activities with DSP involvement

In January 2016, government delegations from the Netherlands, Sweden, and India visited DSP's Delft site, where DSP presented its Sustainable Antibiotics Program. DSP emphasized that the role of the industry should be part of the public debate on antibiotic resistance.

[8] 'Impacts of pharmaceutical pollution on communities and environment in India', published by Nordea, February 2016. Source: https://www.nordea.com/images/35-107206/impacts%201-20.pdf

In its National Action Plan, China aims to prevent and control environmental pollution caused by antimicrobials by:

- Controlling the selection and locating of antimicrobial manufacturing sites
- Carrying out strict environmental impact assessments on new, modified and expanded production projects
- Developing a pollutant indicator appraisal system
- Strengthening environmental legislation, regulation enforcement and monitoring technologies, as well as developing methods for treating water, soil, solid waste of antimicrobials and improving related standards
- Carrying out research into the environmental impact
- Studying the prevention and treatment of environmental pollution caused by antibacterial drugs
- Promoting antimicrobial waste reduction.

Throughout the year, DSP was actively involved in hosting meetings, seminars and presentations in India, raising the issue of AMR and putting the problem of pharmaceutical pollution on the political agenda. In October 2016, Prime Minister Modi of India spoke about AMR in his weekly radio show Man Ki Baat. In December 2016, together with the Neeti Foundation and the Dutch Embassy, DSP organized a multi-stakeholder panel discussion on the UN's Sustainable Development Goals in relation to AMR.

DSP's key achievements in 2016

Antimicrobial Activity Tests implemented at all our sites

To minimize any negative impact our operations may potentially have on the growing threat of AMR, we have implemented methodologies to detect antibiotic activity levels in our wastewater, as part of our Sustainable Antibiotics Program. Our tests are easy to use and have been frequently applied at all our sites since September 2016. Our current detection level is 50 parts per billion (equivalent to 50 mg per 1,000 liters based on Penicillin G). With the Environmental Working Group of the AMR Industry Alliance, we will define science-driven, risk-based targets for discharge concentrations with regard to antibiotics, as well as good-practice methods to reduce the environmental impact of manufacturing discharges.

Our 7-ADCA has contributed to more than 2.5 billion patient treatments

Celebrating 15 years of green 7-ADCA production

In 2016, DSP celebrated 15 years of green 7-ADCA production at our site in Delft. Our proprietary sustainable production process of 7-ADCA, a key intermediate for cephalosporin APIs, is leading to a better planet by significantly reducing CO_2 emissions compared to today's industry standard, which is based on chemical processes. To date, our process is the only combined fermentative and enzymatic route for manufacturing 7-ADCA worldwide.

What's more, the process has been regularly upgraded, making it even more sustainable. In addition, we minimize the release of the antimicrobial active ingredients into the environment by applying adequate wastewater treatment and carrying out frequent Antimicrobial Activity (AMA) tests on our effluent (see p. 38).

During the past 15 years, our intermediates have contributed to more than 2.5 billion patient treatments, and the process has led to the reduction of 1.5 million tons of CO_2 emissions, an equivalent of 350,000 flights around the world.

Frans Vlaar, BU Director of Europe/America, DSP: "Unlike common practice in today's industry, in which penicillin and chemical processes are used that require large volumes of solvents, our process is sustainable and environmentally friendly, resulting in a higher 7-ADCA product quality and reducing the product carbon footprint. I'm proud that at DSP we're taking our responsibility in the fight against AMR seriously. We need to take, use and especially make antibiotics responsibly in order to keep them effective."

Signatory of the Davos Declaration on AMR

In January 2016, along with some 100 other companies and trade associations, we signed a declaration at the World Economic Forum in Davos to undertake collective action to create a sustainable and predictable market for antibiotics, vaccines and diagnostics, and to coordinate activities to improve the prevention of infections, hygiene, stewardship and conservation measures.

In the Declaration, signatories call on governments to work with them to develop new and alternative market structures that provide more dependable and sustainable market models for antibiotics. Signatory companies also committed themselves to reduce the growth of antimicrobial resistance, to invest in R&D, and to improve access to high-quality antibiotics and vaccines.

Winner of the Cefic European Responsible Care Award

In 2016, DSP proudly received the prestigious Cefic Responsible Care Award in the Product Stewardship Category (see p. 35).

New member of the Pharmaceutical Supply Chain Initiative

In November 2016, DSP joined the Pharmaceutical Supply Chain Initiative (PSCI). The PSCI is a group of 24 pharmaceutical and healthcare companies who have joined forces to promote responsible supply chain management and better business conditions across the industry. Joining the PSCI enables DSP to play a leading role in establishing industry-wide guidelines that reach into the entire value chain to ensure antibiotics are produced responsibly and sustainably.

Frans Vlaar, BU Director of Europe/America at the 7-ADCA manufacturing site in Delft.

Driving force and signatory of the UN Industry Roadmap on AMR

DSP was one of the driving forces in establishing the UN Industry Roadmap for Progress on Combating AMR. This roadmap was presented at the UN General Assembly on September 21, 2016, in New York and signed by 13 leading pharmaceutical companies, including DSP. With the reduction of the environmental impact of antibiotics production as one of the four commitments in that Roadmap, this topic is now firmly on the agenda of leading pharmaceutical companies and others.

Four commitments

The Industry Roadmap for Progress on Combating Antimicrobial Resistance consists of four key commitments, which all signatories commit to delivering by 2020. These can be summarized as follows:

1. Reduce environmental impact
We will work to reduce the environmental impact from the production of antibiotics, promoting best practices in controlling the release of antibiotics into the environment, and demonstrating compliance with relevant standards throughout the supply chain.

2. Reduce unnecessary use
We will help governments and public health organizations to educate healthcare professionals and patients about the value and importance of using antibiotics appropriately, and to reduce the uncontrolled purchase of antibiotics.

3. Improve affordable access
We will find ways of making high-quality medicines (including antibiotics) more easily accessible for patients who need them, developing new, sustainable business models where necessary. We will also work to reduce the prevalence of substandard or counterfeit antibiotics in high-risk markets.

4. Encourage new ways of working
We will support new ways of working, such as open public/private collaboration to overcome scientific challenges, pre-competitive collaboration to share research costs, progress incentives, novel IP mechanisms and accelerated joint, global trials.

The original signatories to the Industry Roadmap
Allergan, AstraZeneca, Cipla, DSM Sinochem Pharmaceuticals, F. Hoffman-La Roche Ltd., GSK, Johnson & Johnson, Merck & Co., Inc., Novartis, Pfizer, Sanofi, Shionogi & Co. Ltd., Wockhardt.

2016: The Year of Truth

Interview with Lucas Wiarda – Sustainable Antibiotics

"In my view, 2016 will go down as the year in which we, as DSP, made a strong contribution to getting the issue of pharmaceutical pollution and its role in the spread of AMR firmly on the map – and making it a matter of public debate", says Lucas Wiarda, Director Marketing and Head of DSP's Sustainable Antibiotics Program. "The publication of the final report of the Review on AMR has made it crystal clear that the environmental angle to AMR can no longer be ignored. To many people, it has come as a shock that pharmaceutical companies, who were supposed to be providing us with lifesaving drugs, have actually been contributing to the spread of resistant bacteria."

Production pollution no longer a "hidden cause"

"Fortunately", says Lucas, "the Review on AMR has now led to the mobilization of the "good guys" within the industry. Several leading pharmaceutical companies, including DSP, have acknowledged the urgency of taking action. Among other things, this resulted in the publication of the UN Industry Roadmap in September 2016, and the recent launch of the AMR Industry Alliance. At the same time, we're now seeing traction in the public debate. All this means that environmental pollution caused by the manufacture of antibiotics is no longer a 'hidden cause' of AMR and is now firmly on the global agenda."

From commitment to action

In a sense, 2016 was the Year of Truth for the environmental side of AMR. Commitments were made by manufacturers, international agencies publicly recognized the problem, and activists, environmentalists, NGOs and universities are increasingly putting pressure on the industry. "I don't expect this traction to decrease anytime soon," says Lucas. "In fact, it will only get stronger. I expect that the European Commission's Update Plan on AMR, which will be presented in 2017, will also address the environmental angle of AMR. In addition, governments at local level, particularly in China and India, are expected to come up with measures in their National Action Plans."

The AMR Industry Alliance will play a crucial role going forward, says Lucas. "Now that we've made joint commitments to battle AMR, we'll focus on putting our plans into action in the years ahead. This will also include entering into a dialogue with other stakeholders, since we need their support too. Eventually, our goal will be to have the entire supply chain work in a responsible way. For manufacturing, this means using clean technologies, applying dedicated waste management technologies and facilities, and monitoring antimicrobial activity in waste streams. In short, we need a defined set of discharge controls and standards. Currently, the Industry Alliance includes only a small number of pharmaceutical companies. Together, we represent a mere 20% of the total antibiotics volume worldwide. The generic players, in particular, are underrepresented. So, clearly, we still have a lot of ground to cover."

Transparency

Now that the industry is defining metrics for "sustainable antibiotics", we also need a mechanism to distinguish the good from the bad. Labeling could play a role in increasing transparency in this regard. "It's important that the basic environmental criteria that products and raw materials need to meet if they're to be accepted as "responsible" should be made clearly visible," explains Lucas. "You can achieve this through self-regulation, formal legislation, or through labeling. One of the problems is that buying decisions for heavily commoditized generic antibiotics anywhere in the value chain are currently driven by the purchase price only. At DSP, we believe that sustainability criteria should also play a role in

sourcing decisions. Without labeling, you can't tell if a raw material or a product has been produced sustainably. Naturally, buyers automatically go for the cheapest. But the price does not represent the true costs and is often kept artificially low through 'hidden' non-compliances. This obviously needs to change, as society will pay the bill in the form of AMR for cheap but irresponsibly made antibiotics."

The years ahead will be crucial in turning around the threat of AMR, says Lucas. "DSP will continue to play its part through the many initiatives it has been driving and has joined. We've made a promising start, but there's still a long way to go."

Cefic European Responsible Care Award 2016

In 2016, we received the prestigious Cefic European Responsible Care Award in the Product Stewardship Category, for our work on Sustainable Antibiotics. Cefic (the European Chemical Industry Council) runs the award as part of its efforts to strengthen the Responsible Care initiative, the global industry's commitment to sustainability, and to encourage the use of best practices across Europe. Cefic's President presented the European Responsible Care Award to DSP on 7 October 2016 in Florence, Italy. The jury praised DSP's "well-rounded program, with impact throughout the value chain," adding that DSP is "very good in advocacy, and highest in this category."

"Our business is all about caring and being careful," says Lucas. "We make high-quality medicines to cure illnesses and save lives. I simply can't accept that irresponsible ingredient manufacturers are polluting the environment with antibiotics, making people sick at the point of production and – what is worse – contributing to one of the biggest health threats facing mankind: antimicrobial resistance. I'm therefore especially proud that our efforts to raise awareness for responsible manufacturing of antibiotics are being recognized by Cefic, since it is our industry that should stop buying, using and selling irresponsibly made antibiotics.

Innovation as a key driver

DSP was one of the first companies in the world to work out how to produce penicillin on an industrial scale so that it could become the twentieth-century's wonder drug.

DSP is a highly innovative company with a long history of technological ingenuity. For more than 140 years, our scientists have applied their knowledge and skills in fermentation and enzymatic chemistry to change the world for the better. We have a strong intellectual property position, with 500 individual patents in 80 patent families.

Today, we apply our biotechnological skills not only to develop new products but, increasingly, to develop more sustainable ways of making our products. These include using natural fermentation and enzymatic conversion rather than chemical solvents, economizing on the use of energy, resources and other raw materials, and minimizing our effect on the environment. Many of our "green" processes are patented, safeguarding our intellectual property against counterfeiting and dilution of quality.

We are continuously improving the productivity, efficacy and efficiency of our processes by fine-tuning the conditions under which fermentation takes place. This enables us to gain a higher yield from the glucose used as raw material. The yield is also increased through smart recycling of enzymes.

Our enzymatic processes are more efficacious and do not use hazardous chemicals

Over the years, we have extended our proprietary enzymatic technology platform, so that we can use it to make not only antibiotics but also statins. Our production processes for modern statins like Atorvastatin are more efficacious than those of our competitors and do not use any hazardous chemicals.

Active Pharmaceutical Ingredients

Our primary products are APIs (active pharmaceutical ingredients). These are "active" in that they trigger a desired pharmacological effect. Many of them belong to the beta-lactam antibiotics, such as the penicillin family. We are the technology leader in this field, using the most efficient and eco-friendly processes. But we continuously try to improve them, from beginning to end, increasing our efficiency in the use of raw materials, getting better yields on sugar, optimizing the performance of enzymes, developing new enzymes (case study at the right), increasing recovery yields, and recycling more. Our range of APIs that are made sustainably are sold under the brand name PureActives®, reflecting their purity.

Maximizing clean technology

We continuously try to increase the proportion of our products made using our proprietary, sustainable and environmentally friendly enzymatic technology. They bring our brand promise to life through superior quality, outstanding reliability, and leading sustainability performance. All our manufacturing sites use the best available technology and operate dedicated wastewater treatment plants, 24/7 throughout the year. Effluents are regularly sampled and checked for antimicrobial activity. In 2016, DSP celebrated 15 years of green production of our intermediate 7-ADCA, the key intermediate for cephalosporin APIs (see p. 32).

Wastewater treatment

In terms of volume, some 80-90% of all our waste streams is water. We thoroughly clean our wastewater flows in dedicated wastewater treatment plants (WWTPs) at all our sites, operating 24 hours a day, non-stop (see case study on p. 77).

Antimicrobial activity testing

We developed a robust, efficient, well-controlled and easy-to-use antimicrobial activity (AMA) test that detects even slight amounts of antibiotics (less than 50 parts per billion based on penicillin G). In 2016, we started regular monitoring of wastewater at all our sites (see p. 38).

Birth of a new enzyme: Elcolase

In 2016, DSP started using a new enzyme for improved performance in our enzymatic processes of producing semi-synthetic penicillins (SSPs) and cephalosporins (SSCs).

What is the role of enzymes?

Enzymes are proteins that act as catalysts: they make biological reactions happen faster. Unlike most chemical catalysts used in industrial processes, enzymes are very specific: they make targeted molecular conversions occur with fewer side reactions and fewer harmful side products.

Why develop a new enzyme?

Since the introduction of our enzymatic technology for the production of beta-lactam antibiotics in the 1990s, we have worked on optimizing the performance of our existing enzymes and development of new enzymes. We are always on the lookout for more "active and selective" enzymes that enable faster and more efficient processes.

We started screening for an enzyme with improved performance in the conversion of 6-APA and 7-ADCA into our beta-lactam penicillin and cephalosporin APIs. Through modeling and subsequent testing, we selected potential candidates that showed improved performance. The most promising ones were produced and tested on a larger scale.

The winner: Elcolase

The best candidate led to a new improved enzyme, which we called Elcolase. Elcolase offers a higher yield in the conversion to the beta-lactam antibiotic , and makes it possible to produce larger batch sizes. Thanks to strong collaboration between Operations and R&D, we were able to achieve successful global implementation of the new enzyme. In the last quarter of 2015, we introduced Elcolase at our production site in China, followed by those in Spain and India in 2016. In the first quarter of 2017, we also rolled it out to Mexico. Elcolase is now used at all our beta-lactam-producing sites around the globe.

AMA test: Keeping wastewater free of antimicrobial activity

One of the main ways antibiotics get into the environment is through polluted wastewater leaving factories where antibiotics are made. Since the 1980s, DSP has been working to counter this problem at its own sites by means of non-stop wastewater treatment plants. DSP has developed a very effective antimicrobial activity test (also known as AMA test) to ensure that there's no detectable antibiotic activity in our effluent before it flows back into public water. Herman Slijkhuis, Corporate R&D Advisor, explains how it works.

"One way of dealing with polluted wastewater is to search specifically for a given component that you suspect may be present and then remove it. This works well if only one product has to be tested for, but if multiple compounds with antibiotic activity are being produced within a company, conducting specific searches for each of the products can be complex, time consuming and expensive."

Smart adaptation

That is why DSP has developed its own AMA test. In fact, the test is an adaptation of the Delvotest®, a quick and easy-to-use test developed and marketed by DSM Food Specialties for detecting antibiotic residue in milk. Rather than looking for specific molecules, the AMA test takes a generic approach. It detects a broad spectrum of beta-lactam compounds including precursors and active ingredients, and gives a result within a few hours. What's more, it can detect an amount of antimicrobial activity (based on penicillin G) of 50 micrograms per liter (or 50 ppb).

Going for zero

"In 2016, we started implementing routine AMA testing at all our production sites on a weekly basis. At the same time, we're still working to optimize and expand the scope of these tests. Our aim is to achieve zero detectable antimicrobial activity not only in effluents, but in all of our waste streams. DSP is committed to achieving this sooner than the timeline indicated in the AMR Industry Roadmap, which means before 2020."

Unique enzymatic statin platform

Statins are among the world's top-selling drugs and currently the most frequently prescribed drugs for lowering "bad" cholesterol and raising patients' levels of "good" cholesterol. The main statins used in this fight against "bad" cholesterol are Atorvastatin and Rosuvastatin (see p. 50). Both drugs work in the same way. By blocking a particular enzyme, they help lower cholesterol, reduce the risk of heart attacks, and slow down the progression of cardiovascular disease.

One of the first three companies in the world to offer a generic Rosuvastatin under CEP

Atorvastatin became generic in 2011, and moving quickly, we became the first generics company to be granted a Certification of Suitability (CEP) for Atorvastatin in 2012. We were again quick off the mark in 2016, when the patent on Rosuvastatin expired. We were granted an update for our CEP for generic Rosuvastatin, which placed us as one of the first three companies in the world to offer a generic Rosuvastatin under CEP.

Rosuvastatin is made at our own facility in Toansa, India, using our unique fully backward integrated process. In line with our policy of making life easier for our customers, we have also developed a comprehensive portfolio of Atorvastatin and Rosuvastatin finished dosage formulations using our own API. This means we can offer

customers and marketing partners a one-stop shop for their statin needs, with more efficient registration and life-cycle management of their products.

We are currently working on the new statin Pitavastatin, which is believed to have fewer side-effects and be particularly effective in increasing “good” cholesterol.

Innovation in drug products

Thanks to the use of innovative compacting technology, Amoxicillin tablets, optionally including Clavulanic acid, can now be made more efficiently and cost-effectively using DSP’s Purimox® Compacted DC grade API. This technology no longer requires wet granulation and drying, saving significant amounts of time, energy and space (see case study at the right).

Purimox® Compacted DC grade saves time, energy and space in tablet production

With his team in the Netherlands and India, Bram Lardee, Senior Manager Drug Product Development, is responsible for turning our APIs (and those of customers) into the familiar tablets, capsules, sachets and suspensions that patients end up taking. The team has found a way of reducing the number of processing steps in making tablets. As a result, the product can be made faster and more sustainably.

A typical tablet starts life as a powder, a specific formulation of the active ingredient (medicine) for treatment of the patient. Each tablet must contain exactly the same quantity of the active ingredient. Other auxiliary materials, called excipients, are added to make sure the powder will compact together to form a tablet, which will ultimately disintegrate in the patient’s body to ensure the right availability of the active substance.

Traditionally, in order to improve the flow of the particles through the equipment and ensure even distribution of the various components throughout the tablet, the powder mix is granulated by wetting and drying to create larger particles.

This process, known as “wet granulation”, takes up a considerable amount of energy, particularly at the drying stage. By introducing our Purimox® DC grade, however, Bram and his team have managed to cut out several process steps. As a result, there’s no need for the energy-intensive drying step. Instead, dry mixing with the excipients takes place, after which the final mixture can be compressed directly into tablets. This saves time, energy and space, making the production process as a whole a lot more sustainable.

How we manage Q.R.S.

DSP's day-to-day management approach is guided by our brand promise of Quality, Reliability and Sustainability. We provide high-quality, reliable and sustainably produced pharmaceutical ingredients and drug products for people in need of healthcare. We do this by continuously exploring innovative technologies that positively impact patient care and environmental sustainability.

How we manage Quality. Reliability. Sustainability.

Quality

High quality of our products and services is an overall guiding principle and one of our three promises to customers. To make sure our products and manufacturing processes are as good and as sustainable as they can be, we have installed a global Quality Management System.

Building on our unique skills in fermentation, synthesis and biotechnology, we provide pharmaceutical ingredients and drug products based on our fully integrated global manufacturing capabilities, which meet the highest quality standards and the strictest sustainability criteria.

For us, quality means more than just compliance with Good Manufacturing Practices (GMP). We have a comprehensive set of Quality and Safety, Health and Environment (SHE) policies which we apply globally – not only to ourselves but also to our manufacturing partners.

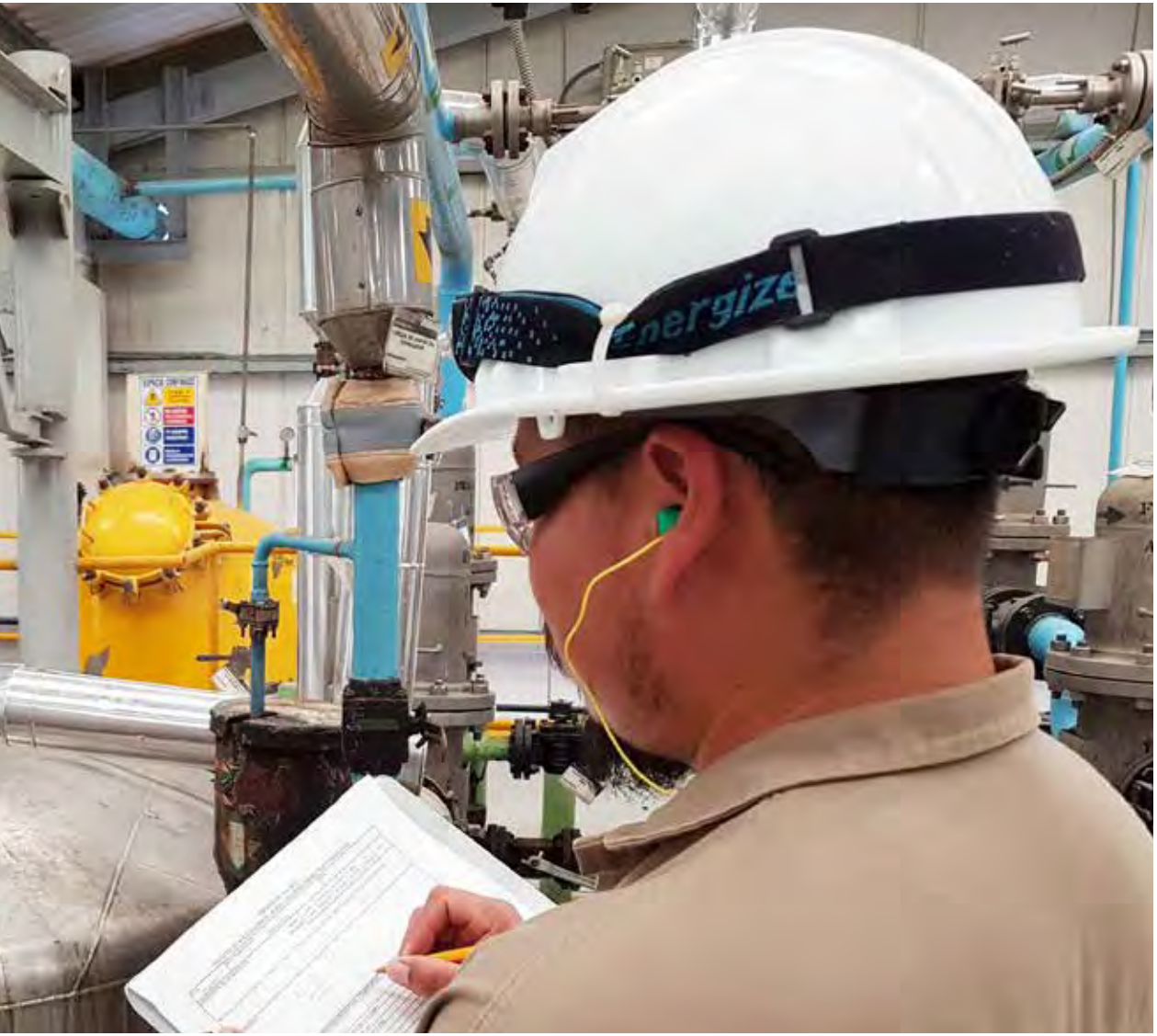
On the API side, this is supported by our membership in the Together for Sustainability initiative and PSCI. In Drug Products, we audit all our drug product manufacturing partners against a set range of criteria, ranging from SHE to GMP compliance. Combining these standards with our unique technology platform allows us to provide the world with life-saving medicines in a sustainable and responsible way.

Monitoring

To ensure we are at all times in continuous compliance with recent legislation and regulatory guidelines, our Quality Assurance Department conducts regular quality assessments. All relevant procedures and practices are updated to take account of any changes. In addition, pre-defined quality targets (KPIs), visible leadership qualities, and adherence to internal and international GMP are all subjected to regular audits, facilitated by the use of IT support tools, such as SAP, TrackWise and Electronic Document Management Systems. Understanding and awareness of quality requirements is tested periodically, using the DSP Learning Pyramid.

Quality culture

DSP embraces a ONE DSP approach, which facilitates the embedding and anchoring of a sustainable quality culture. The essence of this quality culture is encapsulated in our “Ten GMP Rules and Behaviors”. We focus on these to create continuous awareness of quality matters through a variety of media, including regular online sessions for shared learning, printed leaflets on SHE and GMP topics, and monthly Quality and SHE newsletters. We also provide continuous training in quality matters at all levels.



Management support systems

We use a set of highly advanced electronic systems to facilitate the effectiveness of our management and operations.

- A SAP-based infrastructure supports standardized business processes, such as purchasing, production, order-to-cash handling, finance and control, and quality management for raw materials, intermediates and DSP product release and distribution
- An Electronic Document Management System supports the management of the DSP business requirements and legal and compliance documents
- TrackWise, the world's leading Quality Management Software (QMS), is used at all our locations to record quality-related matters such as complaints, deviations and audits
- An Incident Reporting & Information System is in place for registration of, and learning from, Safety, Health and Environment (SHE) incidents
- We have several platforms in place for continuous improvement and sharing of best practices across DSP. Steered by these platforms, we use dedicated campaigns like "Time Out for Quality" and "Time Out for Safety" to keep awareness high and to keep improving (see p. 65)
- A purpose-built online system called "DSP Learning Pyramid" is used for planning and registration of employee training
- In 2016, we initiated the establishment of a Global Quality Manual (GQM) to facilitate global alignment on all our quality processes.

Reliability

Reliability means ensuring our customers can count on us to deliver the innovative solutions and high-quality products they need at the right time and place, and in the right quality and quantity.

Approximately 75% of our supply chain for key intermediates is fully backward integrated. The remaining 25% are with trusted suppliers with whom we have longstanding reliable supplier relationships. Customers can rest assured regarding the origin and traceability of our products, as well as the sustainability with which they have been processed and manufactured.

Our production is supported by multiple global plants and regional operations – all of which meet the highest local and international standards

Our comprehensive set of Quality and Safety, Health and Environment (SHE) policies, which we apply globally – not only to ourselves but also to our manufacturing partners – ensures freedom to operate and trust in our products and services: Quality by Design (ICHQ8, ICH Q11) and Quality Risk Management (ICH Q9) processes are implemented across the entire lifecycle of our products. Our R&D teams ensure that the quality-critical attributes of our processes are well defined and transferred from development to manufacturing following our project management process. By strictly adhering to our Quality Management System during the whole lifecycle of our products – covering R&D, Manufacturing and Supply Chain – we can guarantee our customers the highest reliability.

Sustainability

We seek to create sustainable value along the three dimensions of People, Planet and Profit. We are pioneers of the most eco-friendly technologies and production processes for sustainable APIs, such as our unique enzymatic technology used to manufacture our Sustainable Antibiotics, protected by 500 patented innovations in green technology.

We actively – and equally – pursue sustainability in the key areas of environmental quality, social responsibility and economic performance. In the long term, we believe you cannot achieve one without the other. Our Sustainable Antibiotics Program provides a comprehensive platform through which we address the serious global issue of Antimicrobial Resistance, and aim to increase the sustainability of our industry as a whole (see p. 28).

Our sustainability organization is represented by a three-tier board. The Sustainability Council, led by DSP's CEO, shapes and directs DSP's sustainability strategy. The Sustainability Board, represented by global heads, transforms the strategy into structured programs. Our Regional Sustainability Organization, consisting of business unit sustainability champions, along with local representatives, support global heads in implementing sustainability programs. They also drive and review the progress made on KPIs, and report back on a monthly basis.

Continuous improvement

Over the years, we have been engaged in various improvement initiatives aimed at improving efficiency and compliance, serving our three responsibilities of People, Planet and Profit. These were largely project-based and technical in nature, with a short-term focus, and they mainly involved project managers and professionals in the relevant focus areas.

In 2016, DSP embarked on a continuous improvement program aimed at changing the culture at DSP. It is called "DSP Integrated Continuous Improvement" (DICI), and it is designed to:

- Empower our organization to constantly evolve and improve
- Encourage people to strive for efficiency while maximizing value
- Continuously improve our culture.

DICI mainly focuses on creating vision and direction for business unit management, aligned with DSP's 2020 vision. Shop floor employees will be trained and fully empowered to identify and implement improvement opportunities, while site management supports and facilitates culture growth using a "Mindset and behavior" improvement program.

In 2016, DSP's site in Toansa, India, was selected to take part in the DICI pilot program, which led to the identification and implementation of various efficiency improvement and emission reduction projects (see p. 61).

In 2017, DICI will be further rolled out to other DSP sites. With full implementation in the coming years, this is expected to lead to production cost savings of 1% .

Living up to our promise of Quality

We pride ourselves on delivering the highest quality products. This not only requires the best quality in terms of resources and raw materials, but also high-quality manufacturing standards and procedures. To ensure compliance with both internal and external quality regulations and policies, we perform regular quality assessments at all our plants.

Our annual Global Quality Assurance of Good Manufacturing Practices (GMP) Audit Plan effectively helps to prepare our sites for continuous scrutiny by health authorities. For us as a pharmaceuticals manufacturer, compliance with all relevant authorities' principles and guidelines is essential. Such compliance is evidenced by written approvals and GMP certificates.

In November 2016, an internal quality assessment was performed at our Mexican site to check the status of improvement points resulting from audits in 2015. These had been flagged up by both local health authorities and DSP Global Quality Assurance. The overall outcome of the assessment was positive, as all the main issues had been addressed properly. The quality assessment has contributed to an increased focus on quality compliance and is expected to lead to improved performance in 2017. It was also an excellent preparation for the Brazilian health authority's inspection in December.

The effectiveness of our internal GMP Audit Plans is shown by the outcome of several inspections that were performed by various health authorities in the course of 2016:

- The Brazilian health authorities inspected our Mexican plant in Ramos Arizpe in December of 2016, with no observations to address. The inspection by Mexican health authorities resulted in a continuation of our GMP certificate.
- Our plant in Zibo, China, was scrutinized in July 2016 by the South Korean health authorities, from whom we received approval, with some points of improvement, all of which have since been addressed successfully.
- The Spanish health authorities inspected our site in Barcelona in July 2016, with some observations, which have been addressed accordingly, resulting in a renewal of our GMP certificate.
- In India, our site in Toansa underwent eight inspections from the Indian authorities in 2016 and three inspections from foreign health authorities (from Europe, Australia and South Korea). All of these were successful, with only minor observations from inspectors, which have since been addressed.

All our DSP sites and Contract Manufacturing Organizations (CMOs) have the relevant regulatory approval to cover global access in highly regulated markets, such as the US, Brazil, EU, Japan, Korea and Australia.

DSP's Quality and Regulatory Affairs teams after a succesful health authority plant audit in Ramos Arizpe, Mexico.

Assessing the effect of temperature fluctuations on product quality

Every country has different policies for registering pharmaceutical products. Before our products can be imported into a certain country, we need to comply with various standards and guidelines, including the standards for Good Distribution Practices (GDP). These also apply to the conditions under which our products are shipped, as there are many factors that may affect the quality of our products during shipment. One of these factors is temperature, which has been of growing relevance to the pharma industry.

As we promise best-in-class quality to our customers, we need to have full control of our distribution processes. This includes testing the potential effects of fluctuating temperatures during shipment on the quality of our products. That's why in 2016, DSP initiated a program

Several thermometers continuously measure the temperature our products are being exposed to

to monitor shipment conditions using the Data Logger method, which involves placing several thermometers inside our product containers. The thermometers continuously measure the temperature our products are being exposed to. The data are processed by a computerized system, which results in a temperature log from shipment departure to arrival. Results have shown that the temperature products are exposed to in a single shipment can fluctuate between –20°C and +60°C, depending on the region, the time of year, and the mode of transportation.

We will use the log data we collect as input for regular Cycling Stability Studies (CSS) on our products, which we designed in 2016. During a CSS, we measure changes in the quality of our products before and after shipment, as well as their resistance to extreme temperatures. The first of these studies will be performed in early 2017.

Sustainable supply chains

DSP applies backward-integrated technologies and manufacturing for its key materials, such as 6-APA and 7-ADCA. This helps us guarantee that these essential intermediates are produced to our own high standards of Quality, Reliability and Sustainability. We also operate a dual-sourcing strategy to make sure we always have economical and uninterrupted access to these materials.

DSP's Supplier Sustainability Program

To make sure our main suppliers do business in ways that align with our own values and vision regarding sustainability, they need to go through our Supplier Sustainability Program. This means that, before we do business with them, they need to officially agree to abide by the DSP Code of Conduct and undergo an assessment. Both our Code of Conduct and the assessment cover matters such as sustainable procurement, environment, labor practices, and fair business practices, as well as other areas covering the three sustainability dimensions of People, Planet, and Profit.

Together for Sustainability (TfS)

The assessment our suppliers undergo is the EcoVadis assessment developed by Together for Sustainability (TfS). This industry initiative, founded by six multinational chemical companies in 2011, has developed and implemented a global audit program for assessing and improving sustainability practices within the supply chains of the chemical industry. The results of assessments and audits are shared among TfS member companies on the EcoVadis platform. We joined the initiative in 2015.

Only if we look at the entire value chain can we create truly sustainable value for our customers and end-users, and the planet. To keep existing antibiotics effective now and in the future, we must take, use, and especially make them responsibly.

So far, TfS has carried out over 6,000 supplier assessments, and more than 700 audit reports are available on EcoVadis, performed by more than 300 qualified auditors. In 2015 and 2016, EcoVadis assessments were carried out at 27 of our suppliers (14 initiated by DSP), covering almost 70% of our third-party spend.

In addition, we proactively join TfS events together with our suppliers. Whenever an assessment score falls below the target level, we set up a Corrective Action Plan (CAP) together with the supplier, or schedule an audit to ensure that our picture of their sustainability performance is accurate.

Pharmaceutical Supply Chain Initiative (PSCI)

At the end of 2016, DSP actively joined the Pharmaceutical Supply Chain Initiative (PSCI) platform, which aims to create better social, economic, health, safety and environmental outcomes for all those involved in the pharmaceutical supply chain. This includes fair and safe work conditions and practices, responsible business practices and environmental sustainability, and the efficient use of resources.

Antimicrobial Resistance (AMR) survey

In 2017, DSP will carry out its first AMR survey with its API and intermediate suppliers. The aim will be to increase awareness of the environmental angle of AMR, particularly pollution due to irresponsible manufacturing. The survey will focus on the environmental management systems and waste management and discharge control practices applied by our suppliers and manufacturing partners.

ECO+ product and process design

DSP aims to provide customers with competitive products that deliver the best biotechnology benefits possible. ECO+ is our strategy for designing and developing them.

Launched in 2007, ECO+ is our program for the development of innovative products that have demonstrable ecological benefits compared to their chemically produced alternatives. This ECO+ concept was pioneered by DSM, one of our shareholders, and makes an important contribution to the environmental aspect of our sustainability agenda.

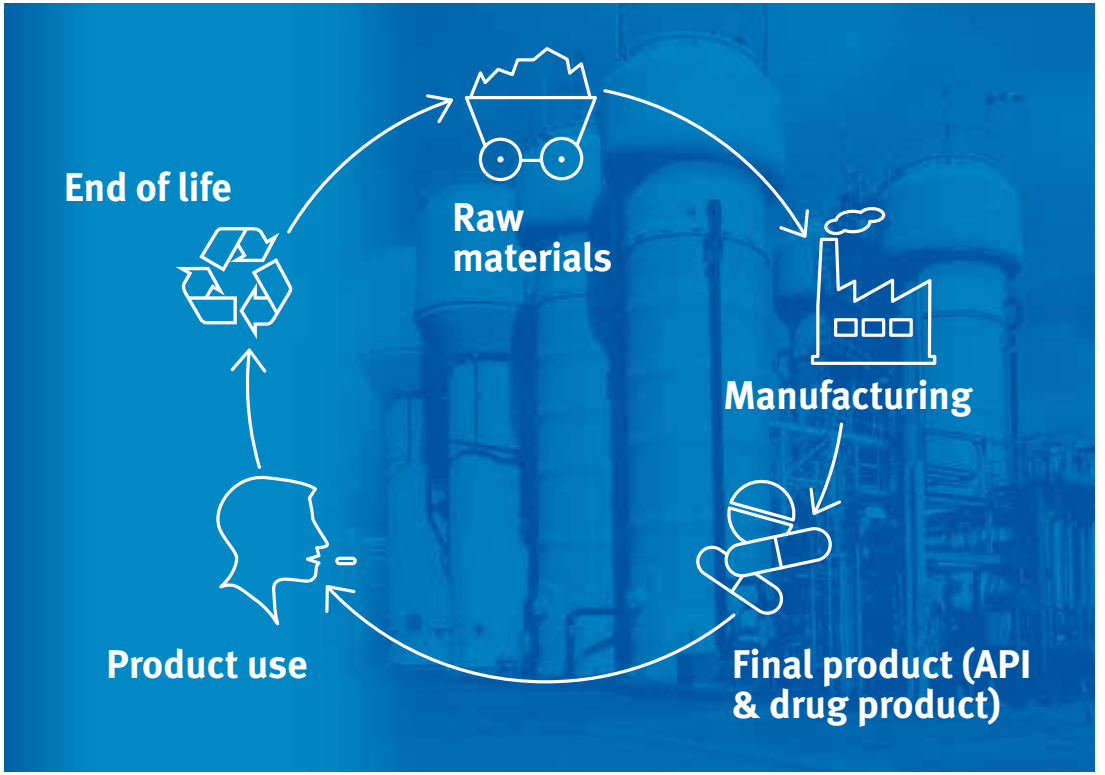
Benefits throughout the product life cycle

ECO+ benefits can be created at any stage of a product's life cycle, from raw materials through to manufacturing, potential re-use, and end-of-life disposal. They may include reduced use of natural resources, such as water or minerals (including metals), the reduction or valorization of waste, shelf-life preservation, yield improvements, energy savings, bio-based solutions, weight reductions, raw material efficiencies, and the elimination or removal of hazardous substances.

Life Cycle Assessment

The ECO+ framework uses a Life Cycle Assessment (LCA) methodology to measure the environmental benefits of each product. These calculations are based on ISO 14040, ISO 14044, and use best-in-class software. The main criterion is that ECO+ solutions must score significantly better on at least two of the three main categories of environmental impact: human health, ecosystem quality, and resource depletion. It must also score better on the weighted sum of all three categories.

Product life cycle



ReCiPe for assessing impact

The ReCiPe methodology for environmental impact assessment was developed by a consortium of respected companies and institutions in order to harmonize category indicators at the midpoint and endpoint level, and normalize them to the European reference value. To develop the best ECO+ propositions possible, our Marketing & Sales executives are closely aligned with researchers and developers in the program. At every stage of the value chain, our people work together with customers, suppliers, academia, NGOs and other stakeholders to determine which products the market most wants and needs.

Regulatory Affairs: securing safe and compliant drugs

A key part of being a sustainable company is being compliant with product and manufacturing regulations across the world. When, back in 2011, DSP began to incorporate drug products into its portfolio in addition to developing active pharmaceutical ingredients (APIs), these new products had to comply with stringent regulations in order to become commercially available.

DSP's Regulatory Affairs team ensures that our products are approved for global sales by regulatory authorities and consequently comply with the highest quality standards. In addition, the team plays an important part in helping to maintain and raise the quality of medicines around the world.

Regulation: raising quality standards

Before APIs or drug products can be used in Europe, they need to have been granted regulatory approval for Europe in the form of a Certificate of Suitability (CEP) for APIs and marketing authorization for drug products. This certificate, issued by the Certification of Substances Division of the European Directorate for the Quality of Medicines (EDQM), confirms that a given drug substance can be fully controlled by the standards (test methods and acceptance criteria) as displayed in the European Pharmacopoeia (Ph. Eur.). The procedures for gaining such approval can take a long time, but when it has been granted, the market is open to both ourselves and our customers.

Setting the standard

DSP has contributed to many reference standards in the world's two leading pharmacopoeias: the European Pharmacopoeia (Ph.Eur.) and USP (the U.S. Pharmacopeia). We proposed the reference standards for APIs like amoxicillin, ampicillin, nystatin, cephalexin, cefradine, and others. All of these are now accepted as the official reference standards in these pharmacopoeias.

Raising standards through expert groups

At DSP, one way we help to maintain and raise standards in pharmaceuticals internationally is by contributing to expert groups in the European Pharmacopoeia. DSP is a member of the expert group for antibiotics. This group establishes the minimum quality criteria an antibiotic needs to meet before it can be used on the European market. We also provide industry groups, such as Cefic (European Chemical Industry Council), with advice or feedback. In addition, we work closely with APIC (the Active Pharmaceutical Ingredients Committee), one of the sector groups of Cefic. APIC represents the European bulk pharmaceutical industry, and several DSP Regulatory Affairs and Quality managers participate in it. The organization regularly meets with regulatory authorities to discuss new draft guidelines on the quality of pharmaceuticals.

Our strong regulatory expertise securing safe and compliant drugs is one of DSP's key strengths.

ICH expert groups

APIC is also represented in some of the working groups of ICH, the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use. ICH's mission is to achieve greater harmonization worldwide, to ensure that safe, effective, and high-quality medicines are developed and registered in the most resource-efficient manner. To this end, it is drawing up new global quality guidelines. APIC contributes to the preparation of these guidelines.

Regulatory successes

In 2016, we had a number of regulatory successes. We issued 12 new regulatory submissions for APIs and maintained a further 91. Most notably, we submitted an ASMF (Active Substance Master File) for our new anti-fungal Caspofungin, which was approved as part of our marketing authorization application for the corresponding drug product. We also received a CEP for Rosuvastatin, produced in Toansa, India (see p. 50), and another for Cefaclor, produced at our facility in Zibo, China.

Supporting customers with one-stop shop for DSP's Rosuvastatin

Interview with Herman Slijkhuis and Rasjnish Chhabra – Rosuvastatin

In Europe, before an Active Pharmaceutical Ingredient (API) is used in drug applications, it needs regulatory approval, either as Active Substance Master File (ASMF) or in the form of a Certificate of suitability to the monograph of the European Pharmacopoeia (CEP). This guarantees that the product is made according to a specific process and complies with the highest European quality standards. DSP is one of the first three companies in the world to offer a generic Rosuvastatin API under CEP.

Moreover, we have registrations with almost all major authorities around the world. DSP's Rosuvastatin is manufactured at our own facility, in Toansa-Taraang, India, and follows a unique, proprietary process. Herman Slijkhuis (Corporate R&D advisor, DSP) and Rajnish Chhabra (Quality Assurance and Regulatory Affairs, DSP API) explain what makes this approach so special.

One of the three first companies in the world to receive a CEP for Rosuvastatin

Choosing reliability

After being the first company to receive a CEP for its Atorvastatin in 2012, DSP was once again a frontrunner with Rosuvastatin, receiving a CEP in early 2016 as one of the first three companies in the world. This CEP was updated when DSP started its own Rosuvastatin API production at its facility in Toansa-Taraang, India.

"With this we made sure we have full control of our production process," explains Herman. "This is particularly significant for our customers. Our proprietary production process is unique and our supply chain is fully backward integrated. This means we make our own key intermediates as well as our own side chain to produce Rosuvastatin. This offers our customers independence of third-party intermediate suppliers. At the same time, customers are assured of uninterrupted supplies, so they can meet their business objectives. In addition, they can rely on a high level of compliance assurance during audits and inspections."

Freedom to operate

Most production processes for Rosuvastatin are clouded by patents, which is a continuing challenge in the generic pharma industry, especially in regulated markets. "Technology patent situations are often unclear, and considerable delays can occur sorting these out," explains Rajnish. "Our customers can get round these problems by making use of our own unique manufacturing process. Our technology is internally protected by ten patent families, assuring our customers complete 'freedom to operate'. This scenario is also well supported by our modern, state-of-the-art and fully automated manufacturing facility in India, which complies with the most stringent

GMP standards. In essence, we provide customers with an easy path through both the complicated and strict regulatory environment and patent minefields that make many developing markets so difficult to work in.” .

Simplicity

DSP’s process for making modern statins is simple. “And that makes it more reliable,” says Herman. “It involves a highly efficient enzymatic coupling step, and uses a single molecular building block for early intermediates. This makes it easier for us to maximize efficiency, control quality effectively,

Offering our customers ‘freedom to operate’

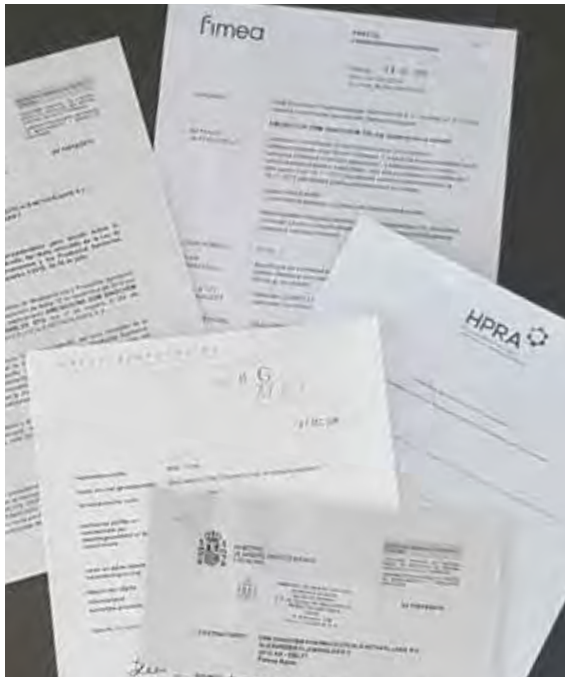
and ensure reliability of supply – in line with our brand promise,” he says. “For instance, DSP’s product quality is unrivaled, with an assay of more than 99% and stability at room temperature. We offer large batch sizes, significantly reducing costs of quality assurance and testing, and on top of that, in terms of sustainability, our approach eliminates unnecessary chemicals and provides a reduction in carbon footprint of up to 35%.”

One-stop shop

“Essentially,” says Rajnish, “we offer customers a “one-stop shop” for modern Rosuvastatin, delivering the highest quality. But perhaps most importantly, our technical support and services make life easier for our customers on all fronts – quality, reliability, sustainability and efficiency.”

Marketing authorizations

We received 112 marketing authorizations during the year (all in Europe). These were the result of excellent team work between many DSP functions, including Regulatory Affairs, R&D, Manufacturing and Marketing. Including the 112 new marketing authorizations, at the end of 2016, we had close to 200 marketing authorizations in total. These marketing authorizations are particularly significant for our Drug Products business, as they make it possible for our partners and customers to do business.



We supporting our partners and customers with marketing authorizations to enable them to do business.

Additional services

Our Regulatory Affairs department also offers customers additional services, such as assistance with their regulatory affairs strategy, operational support if changes need to be made, securing supply by adding more than one API supplier or Drug Product manufacturer, and facilitating expansion to new countries, such as the CIS countries.

New guidelines

During 2016, we continued to work on implementing several new sets of guidelines at DSP, making good progress, thanks to smooth cooperation between the Regulatory Affairs, API and Drug Products teams.

- **Elemental impurities.** The ICH has made it mandatory for manufacturers to investigate their products for the presence of elemental impurities (such as heavy metals), not only as remainders of process agents but also as pollutants (e.g., from water or reaction vessels). Full implementation should be complete at DSP by the end of 2017.

- **Genotoxic impurities.** The ICH also requires a risk assessment plus appropriate testing for genotoxic impurities (impurities that are potentially carcinogenic or may affect DNA). Implementation of corresponding guidance within DSP has been completed.

- **Serialization.** The third set of guidelines concerns serialization. This is the ability to track and trace a product throughout the supply chain, from manufacturer to patient. The purpose of these guidelines is to combat the falsifying (or counterfeiting) of drugs. Product packaging needs to be tamper-proof and bar-coded with all its unique details per saleable unit. With the deadline for implementation being 2017 in the USA and 2019 in the EU, we have already taken steps to set up a system that will help our customers to be fully prepared.

Success for cefaclor

In 2016, we were granted a Certification of suitability to the monograph of the European Pharmacopoeia (CEP) for our generic cefaclor API. Cefaclor is a second-generation cephalosporin antibiotic used to treat pneumonia, meningitis, and other infections. Part of our PureActives® range of enzymatic APIs, cefaclor is marketed by DSP under the name Puriclor® and produced at our facility in Zibo, China. It is the first time that a DSP API manufactured in China has received a CEP.

Puriclor® (cefaclor) is produced using our proprietary sustainable and environmentally friendly enzymatic technology. As a result, no solvents are needed during production, leading to greater purity.

Pharmacovigilance

When providing access to medical drugs, product safety for patients should be given the highest priority. DSP therefore has a pharmacovigilance system in place. Pharmacovigilance has been defined by the World Health Organization (WHO) as “the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-

related problem". DSP instructs all its employees on the basics of pharmacovigilance, in order to ensure the safety of those who use our medicines.

We provide the very latest drug information through implementation of Good Pharmacovigilance Practices (GPP), as issued by the European Medicines Agency, and by immediately adapting to new releases when necessary. This enables us to detect any potential safety issues that arise from literature screening, clinical studies, or other market reports. Relevant findings will subsequently be included in patient leaflets.

Labeling

All DSP drug products are labeled in accordance with regulatory requirements, such as the guideline on Summary of Product Characteristics (SmPC) and the latest Quality Review of Documents (QRD) templates. We also follow the Global Harmonized System (GHS) and Regulations for Classification, Labeling and Packaging (CLP).

Material Safety Data Sheets

We provide Material Safety Data Sheets (MSDS) for all drug substances as required, and have systems in place to keep these MSDS and our labels up to date with all changes in regulations and substance properties. In addition, we regularly screen the communications of relevant authorities to remain informed on new guidelines or regulations that might have an impact on the labeling of our products. The evaluation of these sources may result in the possible addition or amendment of a label warning, to ensure that our customers are properly informed. In the event that a safety information update is needed, we proactively inform our customers.

Drugs “on trial”

Medicinal drug products need to be effective. This means they must be manufactured in a cGMP-controlled environment and undergo thorough testing before being put on the market for human or animal use. Our molecules themselves undergo extensive testing and clinical studies before being integrated into our generic products.

Animal testing

For generic drug products, we refer to pre-clinical data from the literature and to pre-clinical studies performed by the innovator. These data may have been partially based on studies on animals.

Clinical trials

We sponsor clinical trials, such as bioequivalence studies, in several regions and continents, and always adhere to the highest global standards, even when local requirements are lower. The conventions and regulatory guidelines that we act in accordance with include:

- The Declaration of Helsinki, developed by the World Medical Association, which sets out the ethical principles on the protection of clinical trial subjects
- Current International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) principles of Good Clinical Practices
- Requirements of the countries in which studies take place
- Requirements of the country or region in which a study is submitted to obtain a marketing authorization, such as the ethical requirements of EU directives 2001/20/EC and 2005/28/EC.

We adhere to the highest global standards, even when local standards are lower

We ensure that all facilities and contract research organizations (CROs) involved in conducting clinical studies meet the necessary qualifications. They, in turn, are responsible for verifying study protocols, and coordinating the required licenses from ethical committees or relevant authorities. We retain an active monitoring and coordinating role throughout the clinical trial trajectory.

Patient privacy

With regard to patient privacy and the security norms of patient data generated from clinical trials, we fully respect and comply with the Declaration of Helsinki, the Good Pharmacovigilance Practice, Good Clinical Practices (GCPs) stipulated by the ICH, and any other applicable regulatory requirements. As a clinical study sponsor, we work only with CROs that are GCP-qualified and regularly audited by DSP Quality Assurance. The confidentiality of patient data during and after the clinical trial is clearly stipulated in the study protocol of each clinical trial.

Ready to respond

If any issues should arise, DSP has measures in place to ensure an immediate, effective response.

Product recall procedure

Fortunately, since we first started producing, we have never had to initiate a recall of enzymatic PureActives® pharmaceutical products from the market. In the unlikely event that a recall situation should arise, a written procedure is in place that specifies responsibilities and necessary actions. It clearly defines who should be involved in evaluating the information, how a recall should be initiated, and who should be informed.

As part of our recall strategy, we address the following items, together with our marketing partners:

- The depth of recall (which is defined by the material's degree of hazard and the extent of distribution)
- Whether a public warning is necessary based upon potential health risks
- When the situation is potentially serious or life-threatening enough to inform local, national and/or international authorities and seek their advice
- To what level and how often recall effectiveness checks are to be performed.

Our emergency plans are regularly reviewed and updated

When the API has already been converted into a drug product and distributed, the recall and safe disposal of the faulty material will be carried out in close cooperation with the relevant customer, wholesaler or distributor.

Emergency situations

All DSP sites have Emergency Response Programs (ERPs) in place designed to deal with calamities and emergency situations of various kinds. These cover the health and safety of our people and any possible impact on local communities and the public at large. The programs are regularly tested in mock drills.

The micro-organisms that we use in the production processes of our APIs are generally regarded as safe. In some laboratories where we may use micro-organisms from higher risk categories, there are dedicated permits and special requirements for their use and management, which are fully compliant and regularly audited. In the event of a global pandemic, we have comprehensive local response plans and a global coordination structure in place at each of our plants. These plans are regularly reviewed and updated.

People & Community

Our business is all about safeguarding people and their health. But clearly, we owe a special responsibility to those whose lives we affect every day – our employees, and the people who live in the neighborhood of our operations. Our commitment to our employees and the communities in which we operate is two-faceted: we aim to foster their development, performance and personal satisfaction, while also keeping them safe and sound.

Strengthening our ONE DSP culture

Our success at DSP is largely due to our people. That is why our DSP "People" vision is designed to ensure that we continue to attract, develop and retain passionate leaders and employees, people who deliver outstanding results in a responsible, ethical and sustainable manner. In this way, we aim to ensure continuity, high quality performance and a sustainable workforce.

Fundamentally, we seek to help our business leaders and employees to excel in everything they do. And we do this not only because it is rewarding for them, but also because we believe it helps us create the agile and high-performance organization we want to be. We believe the best way we can reach our goal is by working together with our employees in both their professional and personal development, resulting in mutual benefits. This joint approach results in a sense of shared purpose, leading to increased engagement, which shapes and strengthens our ONE DSP culture.

We seek to help every employee to excel in everything they do

Our ONE DSP cultural program focuses on four main themes: External Orientation, Accountability for Performance, Collaboration with Speed, and Inclusion & Diversity. The program acts as a backbone in reaching our growth ambitions.

Over the past few years, we have spread awareness of our ONE DSP cultural program by successfully implementing a number of initiatives. In 2016, we started taking these initiatives to a higher level by moving them closer to the business and integrating them with our core values of People, Planet and Profit and our brand promise of Quality. Reliability. Sustainability.

ONE DSP: four main themes

External Orientation
The pace of change today means we need, more than ever, to be aware of what is happening in society: emerging needs, social trends, and growing concerns.

Accountability for Performance
We believe we can make a significant contribution to solving some of the world's most pressing problems. We are keen to share responsibility for improving the world, while learning from our mistakes.

Collaboration with Speed
In today's highly connected world, collaboration and speed are important competitive advantages. That is why we encourage teamwork and networking both inside and outside the company.

Inclusion and Diversity
We acknowledge that working together in varied and balanced groups enables us to reach better decisions, arrive at more remarkable innovations, and interact in more productive ways.

Safety and Quality as part of our culture

In 2016, we integrated our ONE DSP cultural program with our Safety theme and brand promise of Quality. During the year, we organized two ONE DSP weeks on the theme of Safety, and two on the theme of Quality. Through integration with other themes, we increased understanding of the critical role of safety and quality in both our daily work and our journey towards excellence.

In the first half of 2016, we focused on Accountability and Collaboration in separate Safety and Quality weeks, with a very clear message: we are individually responsible for safety and quality, and by collaborating with our colleagues and teams, we can create the culture we strive for.

In the second half of 2016, we focused on Inclusion and External Orientation, with the objective of raising awareness of the idea that in building the right safety and quality culture, we must have both an "inside out" and an "outside in" approach. Inclusion helps us to value different perspectives and to learn from the everyday experiences of our colleagues. External orientation provides us with the knowledge, experience and practices of best-in-class organizations.

Talent development

Besides a strong focus on culture, we at DSP firmly believe that, in order to build an agile and high-performance organization, we need to nurture talent and stimulate development and growth.

We now have several initiatives in place to foster an environment in which talent can learn, grow and develop.

Each year, through our annual succession planning process, we identify the individuals with the highest potential across the organization, i.e., those who in our view are capable of growing into senior leadership positions. We invest in their leadership journey by offering them customized opportunities for development (such as assignments to broaden their skill set, global projects, and job rotations), as well as leadership development advice, mentoring and coaching.

We follow the 70:20:10 approach to building long-term and robust capabilities

In 2016, we successfully furthered our Short-Term International Rotation (STIR) program for identified potentials. The program provides young talent with global experience an opportunity to develop new skills and build capability to work in diverse cultures, in preparation for more senior roles. In 2016, we successfully arranged several Short-Term Rotations.

Based on this training philosophy, we focus on helping employees gain the competencies and leadership capabilities they need to contribute to the success of the business while also developing their own careers.

We follow the 70:20:10 approach to building long-term and robust capabilities: 70% through practical experience, 20% through coaching and mentoring, and 10% through training.

Short-Term International Rotation Program

The Short-Term International Rotation program (STIR) was designed specifically for our young talent. It aims to contribute to the growth journey of our potentials by giving them international experience, while enhancing their understanding of our business and processes across units and building their leadership capability.

Luis Coss started his career at DSP MLA as a Site Controller at our Mexican plant in Ramos Arizpe in 2014, where he later became Business Controller. “I first heard about the STIR program in 2015, and knew right away that this was something that I wanted to do,” he says. “I’m ambitious and always open to learning new things. I quickly realized that the STIR program would enable me to experience best practices in a new setting – not only working with a different team, but also seeing things from a different perspective in a different culture. In addition, it would give me a chance to expand my international network.”

As part of the STIR program, Luis joined the EA business unit in Rijswijk, the Netherlands in 2016. Since then, Luis has learned a lot about how financial processes are managed in a different environment. “It’s very diverse. For example, I’m currently learning how Operational Working Capital is managed, as well as which reporting styles are used and why. I’ve also found that my own experience, knowledge and network can be useful to my European and American colleagues. So it truly feels like a balanced exchange, where both parties benefit.”

“I’m ambitious and always open to learning new things”

Besides growing professionally, Luis says he has also grown on a personal level. “Being submerged in a different culture expands your perception on many things in life. Being away from my family for so long has made me realize even more how important family is. But learning about different values and ways of doing things has given me a different perspective. I’m sure that this will help me when connecting with people from different cultures in the future. I’m grateful for the opportunity I’ve been given, and would recommend it to all my colleagues.”

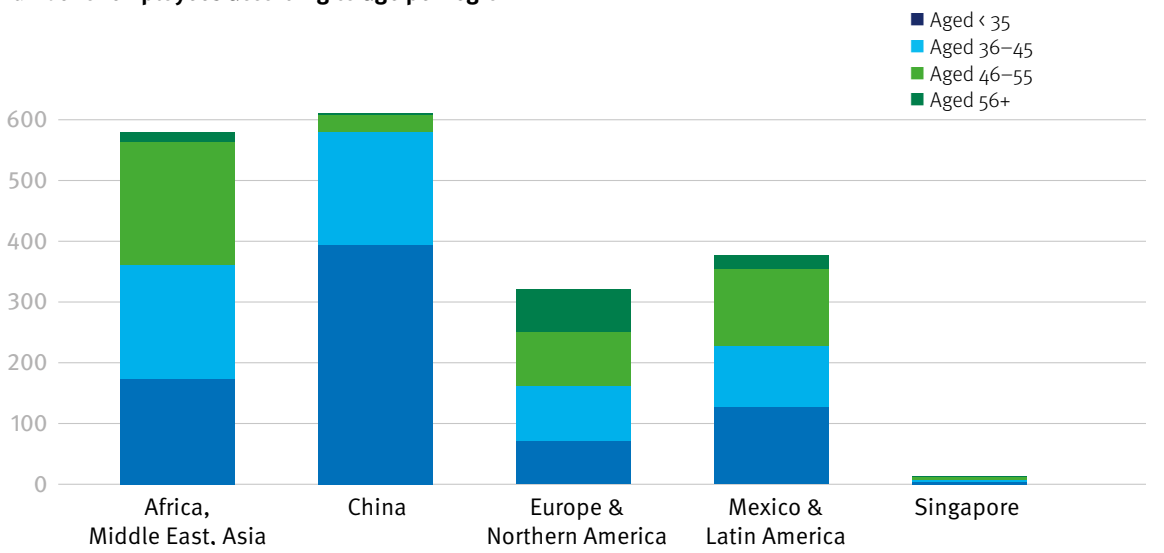
Who works at DSP?

At year-end 2016, the DSP Group employed **1,888** people globally.

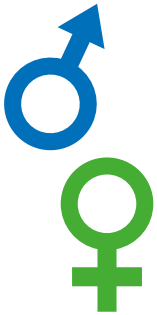
Women accounted for just over **19%** of the total.

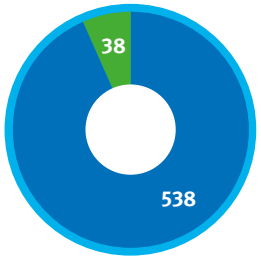
People under the age of 35 accounted for around **40%** of the total.

Number of employees according to age per region

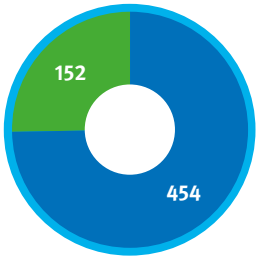


Number of employees according to gender per region

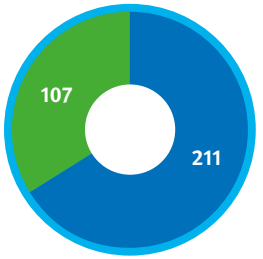




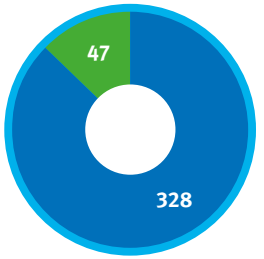
Africa, Middle East, Asia
576 employees



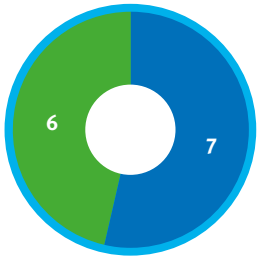
China
606 employees



Europe & Northern America
318 employees



Mexico & Latin America
375 employees



Singapore
13 employees

Integral Continuous Improvement at DSP

In 2016, we set up the DSP Integral Continuous Improvement (DICI) journey for operations (see p. 44). The aim of this journey is to maximize the performance of our operational areas and improve the efficiency of our processes.

The first step in the journey lays down a solid foundation for all employees involved. This step focuses on culture building and teamwork, involving shop-floor, plant and business unit management. With the foundation in place, the next step is to choose a specific subject (or pillar) for improvement, depending on the strategy and targets of the unit in question. There are six of these pillars: (1) Autonomous Maintenance, (2) Asset Care, (3) Set Up Time Reduction, (4) Quality, (5) Environmental Sustainability, and (6) Administrative Excellence. The DICI journey was first introduced as a pilot at our site in Toansa, India. The Toansa team decided to focus on “Set Up Time Reduction”.

The DICI journey acts in general as a catalyst for improvement, while also helping us to become a learning organization, as it builds the skills, capabilities and competencies needed for sustainable performance. The journey also provides tools and techniques for rewarding the right behavior, ensuring that all our people understand the benefit of investing in the continuous advancement of their various roles. Through regular pulse surveys, progress is measured and key learning points are addressed.

Before continuous development can become an integral part of our culture, many of our employees will need to adopt a different mindset and change some of their behavior. It was especially in this area that the Human Resources (HR) team in Toansa played an important role. They invested in communications and training by sending out newsletters, organizing workshops, publishing posters with key messages, setting up events, and distributing handy pocket cards with tips among employees. This was very much appreciated by employees and led to excellent results, such as an increase in production rate and a decrease in both changeover time as well as solvent consumption.

Our business units in the Netherlands and Mexico will set out on their DICI journey in 2017.

Employee Engagement Survey

The Employee Engagement Survey platform gives employees an opportunity to voice their opinions and highlight areas of strength and concern. An integral part of DSP's culture, the survey is held once a year.

In 2015, we added the Employee Engagement Pulse Survey (EEPS), a crucial halfway "snapshot" that allows us to measure progress on our strategic priorities.

In 2016, we decided to develop a custom-made DSP Employee Engagement Survey, one which was more relevant to DSP, our people and our specific journey. To help us in this process of discovery and improvement, we engaged the Korn Ferry Hay Group, a world leader in people consulting. The outcome was our own Employee Engagement Survey "ECHO – Every Colleague Has an Opinion", which we will conduct globally for the first time in 2017.

The objective of the survey is to obtain a clear direction for future initiatives aimed at making DSP a more effective place to work. Feedback will help us understand how our people feel about DSP and their job, and how can we improve together.

New Personnel Association in the Netherlands

Following the setup of personnel associations in other business units, we launched a Personnel Association for DSP employees based in the Netherlands. Social events are organized for all employees. As we have over 25 different nationalities working for DSP Netherlands, the events contribute to making people feel at home and learning about different cultures. Among other things, the personnel association organizes sports activities, cultural events, parties, and celebrations for children.

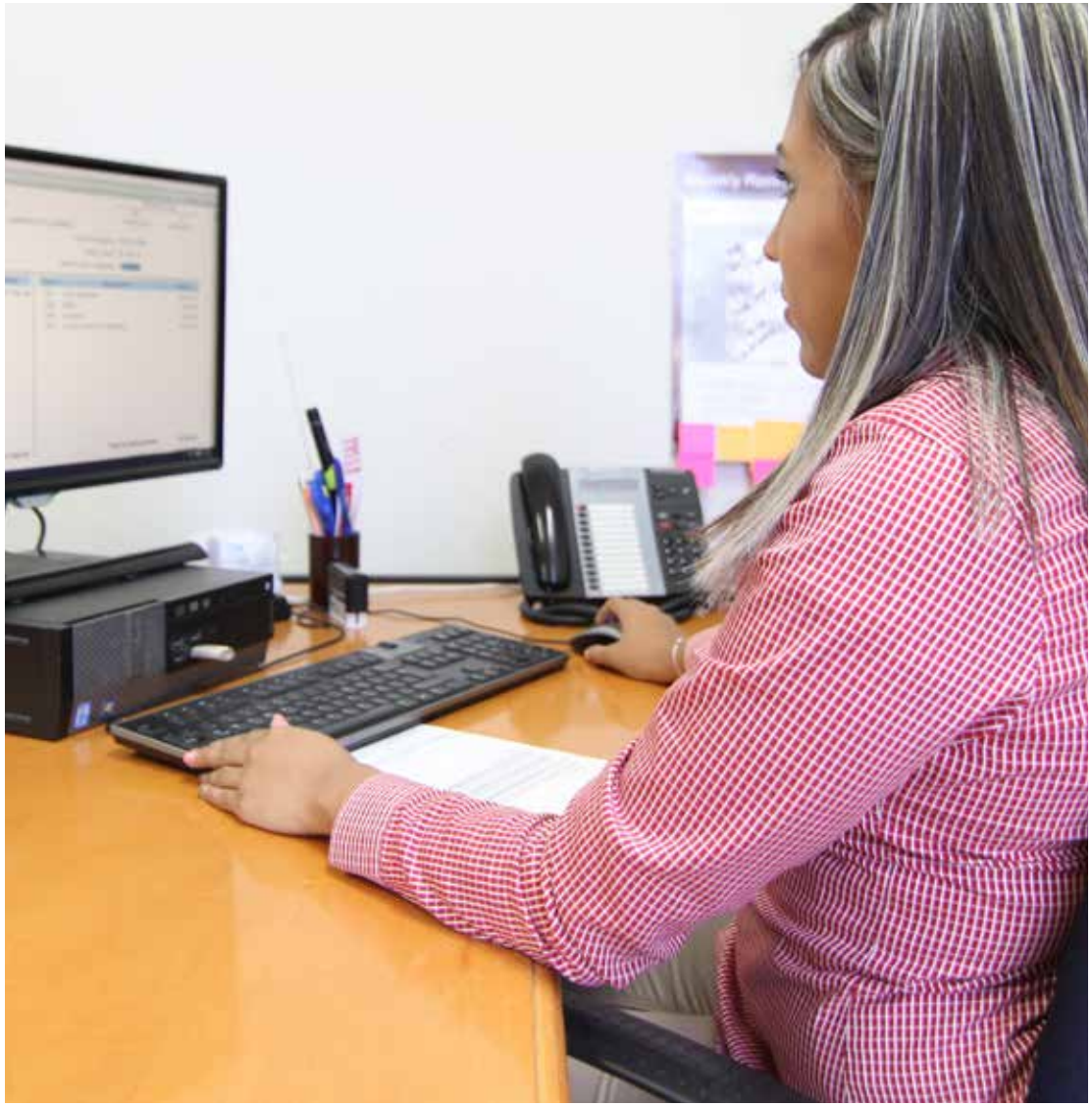
Competency building

Our DSP Behavioral Framework serves as a guideline in defining the behavior we expect from our established employees, new recruits and potentials growing into senior and leadership positions. At DSP AMEA (Asia, Middle East and Africa), we are striving to bring similar clarity and definition to the technical competencies people need to perform their roles and tasks as well as possible. Focusing on holistically developing both functional and behavioral competencies, we have introduced a Talent Competency Framework and an Annual Development Planner to support this objective.

To identify technical competencies required for each function and role within DSP AMEA, we started by developing an in-house program to create a Talent Competency Framework. The program covers all employees, and will help us to identify proficiency levels associated with each function and role, and eventually to design a strong competency framework. In order to ensure validity and consistency, proficiency levels are being verified by global leads for each function. Once completed, the competency framework will be used for both talent acquisition and talent development across AMEA, with the objective of implementing and using the framework across the entire DSP organization at a later stage.

Our Annual Development Planner focuses on structured development, and provides employees with opportunities to participate in professional leadership, competency and skill-building workshops throughout the year, in a cross-functional setting.

With these initiatives now in place, we are looking to attract, build and foster strong in-house talent, in line with DSP's culture and values and the functional capabilities the company needs.



Electronic payroll receipts for all employees in Mexico

Every week until 2016, our employees at Ramos Arizpe, Mexico, received manually printed payroll receipts. This meant processing more than 300 printed receipts per week, handling the prints and sorting them per employee supervisor. Naturally, this was a very time-consuming task for payroll administrators. Supervisors had to go to the HR department to personally pick up the receipts. When they had been processed, they were handed over to the employees individually.

The introduction and implementation of an electronic payroll application (an e-payment app) has meant that HR is now able to provide employees with their payroll receipts directly, without any intervention by supervisors.

The introduction of the e-payment app helps the environment by saving trees

Employees can now view and save their payroll receipts electronically, and print them on demand whenever they want to. The introduction of the e-payment app has not only saved our HR department and supervisors a lot of time and effort, it has also helped the environment by saving printing paper – and therefore also trees.

Safety and health

DSP's policies in the field of safety and wellness are derived historically from the Safety, Health and Environment (SHE) policies used by one of our shareholders, DSM. These extremely well-developed, best-practice policies are integrated throughout our operations at global, business unit (BU) and site level.

Process for an injury-free environment

Ensuring the highest safety standards across our global operations has always been a top priority. That's why we work to maintain and strengthen our safety culture and behavior through various projects, grouped under one management program with the slogan "Together, we're making DSP injury-free!"

The management program is based on three pillars: Process Safety, Life-Saving Rules and Behavior, and Time Out for Safety. These form the foundation of a permanent process to make DSP injury-free, a process that we are constantly updating by sharing information about incidents and near-misses at our sites. We also remain alert to opportunities for learning about useful, relevant practices seen outside DSP, which we could usefully apply internally. In this way, we are creating a living culture around safety awareness, with a continuous focus on improvement.

Life-Saving Rules

Our Life-Saving Rules are just that. No ifs, ands or buts – all our employees receive special training in the Life – Saving Rules, and are expected to follow these regulations at all times in their professional lives.

DSP's Life-Saving Rules

No drugs at work, smoking only in designated areas and no alcohol at work

Protect yourself against a fall when working at a height

If required, always work with a valid permit

Do not enter a danger zone where objects can fall

Test the quality of the internal atmosphere before entering a confined space

Comply with management of change when required

Lock out, tag out and try out before starting work on machines or equipment

Follow your journey management plan

Obtain authorization before line-breaking

Wear your seatbelt

Obtain authorization before overriding or disabling safety-critical equipment

Drive responsibly and comply with local laws. Do not use your mobile phone while driving (not even hands-free), and do not exceed speed limits. Avoid drinking and driving, always respecting legal limits

Performance in 2016

Since 2001 (when we did business within DSM as DSM Anti-Infectives), we have had a safety program in place and have been monitoring associated recordable injuries at DSP operations.

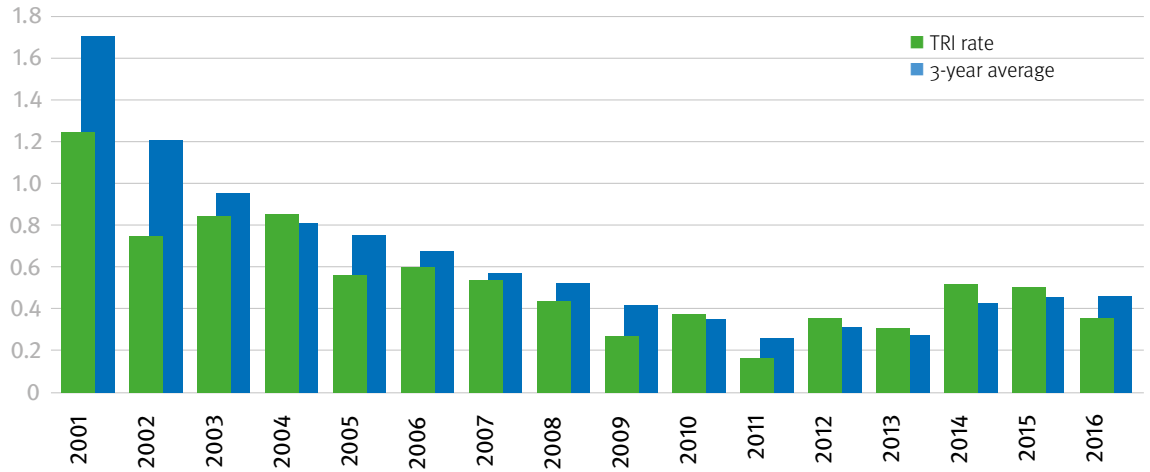
Unfortunately, although there was an improvement with respect to 2015, we did not meet our safety performance targets in 2016.

We achieved our best performance to date in 2011. In that year, six people were injured at work, compared to 47 in 2001, when we first started our safety program. We have been struggling since 2012 to maintain the excellent results of 2011.

With 9 injuries in 2016, DSP's major safety index, the Total Recordable Injury (TRI) rate, improved from 0.48 to 0.35. As before, many of the incidents involved were in the categories of "slips, trips, falls" or "caught, hit, trapped". One was classified as serious and was a clear violation of our company's key Life-Saving Rules. About 55% of the incidents were related to injuries to the hand. As a result, we have now launched several campaigns focusing on preventing such injuries.

Clearly, this performance is still far below what we want, as our ultimate aim is (naturally) zero injuries. In 2016, we continued our efforts to influence employee behavior. Our special focus this year was not only on actual incidents but also on potential incidents. This is because even incidents that do not involve any injury may still serve as important leading indicators of an accident "waiting to happen" – even a very serious one. That is why we also monitor such incidents that have a "higher potential" of risk or are highly likely to occur. We believe that monitoring leading indicators like this will ultimately enable us to improve our safety performance framework as a whole. At the start of 2016, we appointed one full-time Global Process Safety expert to support, coach and further guide our business towards improved safety.

TRI rate with regard to our own employees and contractors, regular and 3-year averages



Time Out for Quality and Safety

In response to a number of incidents in the summer of 2014, we launched a new safety awareness program called "Time Out for Safety" As part of the program, several sites took a real time-out and actually stopped production. For periods ranging from a few hours up to a whole day, the complete crew discussed the causes of specific incidents and how they could be avoided. This made a deep impression, and resulted in a variety of local follow-up actions.

In 2015, building on the success of our "Time Out for Safety" program, we extended our focus by including Quality as a focal point. Safety and Quality discipline teams worked together on influencing employee awareness and behavior, and promoted the "Time Out" concept as something employees should automatically think of every time they undertake something that puts either themselves or the quality of the product at risk.

In 2016, we continued with our quality and safety awareness program, now called "Time Out for Quality and Safety". Every six weeks, we sent out a newsletter to all employees with inspiring messages from DSP Management about local events, practices and learnings from incidents.

Leveraging local strengths

Our approach to health and wellness is primarily developed and run on a regional basis and at site level. This encourages the regions to develop local programs that are designed to meet their specific needs and aligned with local habits and culture. However, certain health-related regulations and requirements have been implemented across the whole of DSP.

Health Risk Assessments

The execution of Health Risk Assessments is mandatory at all our plants. These assessments provide the crucial basis for adequate control of a wide range of possible exposure factors. We also find it extremely important to ensure that our employees are physically well, so health checks are mandatory for them as well.

The local health programs generally address factors in the specific workplaces that could be detrimental to employees' physical well-being. However, they may also include lifestyle improvement monitoring and promotion activities. Examples of these efforts include:

- Ongoing campaigns to help people to quit smoking
- Increasing the availability of healthy food options in canteens
- Conducting on-site or off-site programs to encourage people to improve their fitness levels.

Ready for local issues

All our sites also have Emergency Response Programs (ERPs) in place. These are designed to deal with calamities and emergency situations, such as fires and other contingencies. They cover the health and safety of our people and any possible impact on local communities and the public at large. These are regularly tested and trained in mock drills.

Oral health is essential to general health and quality of life. Every year, dental checkup camps are organized for our employees in India to increase awareness of oral hygiene and oral health problems.

Legal compliance and whistleblower policy

We always strive for complete transparency and integrity. To this end, we have a whistleblower procedure called "DSP Alert", which has been in place since November 2013. It enables employees to report any concerns they may have about misconduct, and to do so in full confidentiality.

Our policy enables employees to report any concern they may have

The whistleblower procedure is just one of the measures in place to ensure that we always act in strict compliance with all relevant laws and regulations, as well with our own DSP requirements and DSP Code of Business Conduct. This compliance is already closely monitored on a daily basis. This is done from outside the company by the press, our business contacts, and the investment world.

A route that's always open

Internally, compliance is continuously monitored through work climate analyses, department meetings, consultative meetings, operational audits, complaint procedures and our appraisal systems. But despite all this monitoring, unacceptable conduct may still occur. And when it does, individual employees are often the first to notice that something is not quite right.

In accordance with our values, rule violations are generally discussed openly via the appropriate, designated channels. Initially directly with the persons involved, and subsequently, if necessary, with the management of the unit involved. In certain circumstances, however, an individual employee may not feel comfortable with this route, and prefer to report concerns to an independent DSP officer, or by reporting the incident online through our DSP intranet. The DSP Alert program makes this possible.

1250 | School desks donated

Contributing to people's lives

At DSP we also feel responsible for contributing to the sustainable development of society. We aim to add value to people's lives by providing economic, social and environmental benefits. We therefore continuously undertake new initiatives to improve people's lives wherever we can.

Free health awareness and aid

In 2016, the DSP AMEA team set up several initiatives to actively improve health awareness and provide aid in the surrounding areas of Toansa, India. These include a health center and an educational institution.

DSP company doctor Davinder Kaur visits the health center twice a week to give free consultation and medication to the people of Toansa and surrounding villages. One of the focus areas of the program is the health of schoolchildren and women. Regular interaction is ensured through counseling, and medical camps are organized at Toansa schools. The children receive free medicines as needed, and their parents are invited by the DSP healthcare team to attend sessions on children's healthcare.

At a medical camp organized at the local temple in Banna village for pilgrims coming into the area, the DSP healthcare team gave about 300 patients a medical check-up and provided them with any necessary medication free of charge.

MLA visited an elementary school to promote Earth Day with students, emphasizing that we are committed to protecting our planet and its communities.

Strengthening local education

We believe that every child has the right to be loved, cherished, and supported, and the right to receive proper education that empowers them and enables them to become self-sufficient.

In 2016, to strengthen local education, the DSP team in Toansa collaborated with District Administration SBS Nagar Punjab to work on the following projects:

- Renovation of 3 schools and one crèche
- 1,250 school desks
- 65 water filters and water coolers for several schools
- Free school notebooks and bags for children
- Free computers for the local middle school
- Provision of an instructor for physical training and exercise

The program received a lot of media attention, and the District Administration organized a special event to celebrate the DSP team's achievement.

Sanitation project

In 2016, DSP AMEA took the initiative of setting up environmentally friendly bio-toilets in and around its areas of operations. Altogether, 140 bio-toilets were placed in the village of Toansa and Bholewal – a clear step towards addressing the region's need for convenient sanitation facilities. The bio-toilets differ from conventional toilets in that they dispose of human waste in an eco-friendly manner, thus promoting environmental sustainability.


foto to be
replaced

Planet & Environment

We are dedicated to protecting the environment in everything we do. We work continuously to reduce energy use, greenhouse gas emissions and production waste at our facilities. In response to the threat of antibiotic resistance, we are also committed to ensuring that our production waste is free of antibiotic residue. And finally, we are dedicated to creating innovations that help customers improve their own environmental footprints.

Sustainability as a growth driver

We are convinced that sustainability, in the broadest sense of the word, can be a sound and successful growth driver. By working sustainably, we safeguard not only the quality and reliability of our products, our businesses and our brand, but also the well-being of the planet and all those who live on it.

Coping with antibiotic resistance

The well-being of people is particularly at risk in the face of antibiotic resistance, which can no longer be regarded as just a "threat". The Review on AMR (2016) confirms that antibiotic resistance is already causing hundreds of thousands of deaths every year, and it is estimated that, if we do not act now, by 2050, the number of lives lost each year will have risen to more than 10 million.

Independent research demonstrates that production practices in the pharmaceutical industry are playing a role in fueling this antibiotic resistance crisis. In this context, addressing environmental issues is not something that is "nice to do", it is an urgent need. Under the umbrella of our Sustainable Antibiotics Program, our proprietary green enzymatic technology platform and our ECO+ product program are playing a valuable role in enabling us to address these issues.

We were one of the first antibiotic producers to invest in our own state-of-the-art water treatment plant in the 1980s. Today we have such plants operating at all our sites around the globe.

Monitoring progress on our Sustainability Roadmap 2020

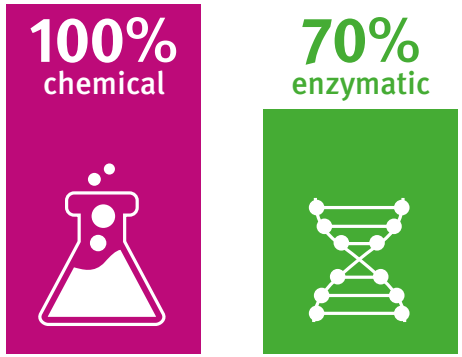
Internally, our additional efforts to offset environmental impacts have been established in an ambitious environmental roadmap for the period 2010–2020. Our progress along this path is monitored annually. DSP's Sustainability Roadmap 2020 includes targets for Key Performance Indicators (KPIs), which we are working towards by implementing sustainability projects and initiatives in the following areas:

- Energy efficiency and reducing harmful emissions
- Water efficiency and smarter water usage
- Antimicrobial activity testing and control in our waste streams
- Detecting and removing a broad range of antimicrobial activity in waste streams.

The enzymatic difference

New projects and initiatives at DSP are based largely on the implementation of new technologies. One of our major long-term projects of this type involves replacing chemical synthesis, wherever possible, by enzymatic bio-catalysis processes, which are entirely water-based. For example, since the 1990s, we have consistently worked – with great success – to replace our chemical processes by enzymatic antibiotic intermediates and APIs. Life Cycle Assessment (LCA) has confirmed that the environmental performance of our enzymatic products is superior to that of chemical products: specifically, upgrading to enzymatic processes reduces the carbon footprint of these products by an average of almost 30% and in some cases up to 65%.

Average % of carbon footprint of products

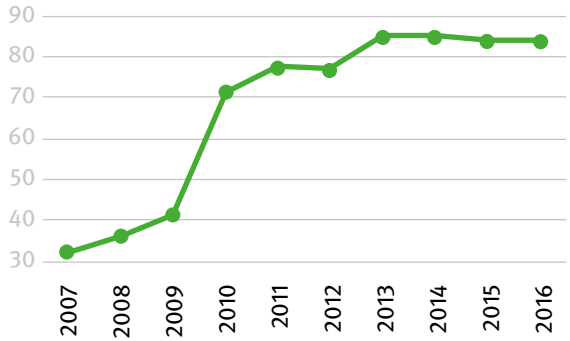


Enzymatic processes reduce the carbon footprint of antibiotic intermediates and APIs by an average of 30%.

Progress in 2016

Detailed information on progress made on specific environmental KPIs can be found below.

% Eco+ running business net sales 2007-2016



Our green alternative: ECO+

The ECO+ program is our ongoing drive to provide the market with greener products. We assess the green credentials of individual products using LCA. Such assessments clearly show that ECO+ products are associated with lower consumption of natural resources and energy use compared to their chemically produced alternatives. They also enjoy higher yield efficiency and raw materials efficiency. These factors benefit society at large, as they respond to major global issues, such as climate change, resource scarcity, human health, and the quality of the ecosystem. Nearly all our products have undergone LCA.

Wherever possible, we have replaced chemical synthesis by enzymatic bio-catalysis processes, eliminating polluting chemicals

Sales of ECO+ products as a percentage of net sales in 2016

In 2016, our sustainable ECO+ products accounted for 84% of net sales, maintaining last year's trend. In absolute terms, the total sales of ECO+ products increased. However, due to fluctuations in the market and continued demand for traditionally produced semi-synthetic penicillin (SSP) (with a bigger environmental footprint), the percentage of ECO+ products as share of the total portfolio decreased slightly.

Environmental monitoring approach

DSP is a rapidly growing company, with production sites around the world. We classify our sites into two types:

Type I sites are well-established, mature sites, with regular production cycles. They are monitored against our Sustainability Roadmap 2020 targets, and their performance is summarized in this report.

Type II sites are new (or relatively new) sites. They are monitored separately from Type I sites, as they cannot yet reasonably be expected to perform to the level specified in the plant design specifications, and their inclusion would skew the monitoring of progress against targets. Once production at a Type II site conforms to plant design specifications, the site is reclassified as Type I for the purposes of monitoring performance.

In 2016, our sites were classified as follows:

Type I
- Delft, The Netherlands
- Barcelona, Spain
- Ramos Arizpe, Mexico
- Toansa, India
- Zibo South, China
- Zibo North, China
- Yushu, China

Type II
- Toansa-Taraang, India

In the course of 2015, the sites in China at Zibo North and Yushu were reclassified from Type II to Type I, due to increasingly good performance during 2014 and 2015. The impact of this change can clearly be seen in our performance graphs for environmental KPIs (see pp. 76-78).

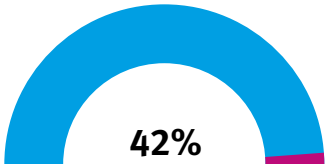
The Toansa-Taraang plant in India, has experienced large fluctuations in production since its opening in 2014, making it unreliable for monitoring and reporting purposes. It therefore remains classified as a Type II site.

Environmental monitoring targets

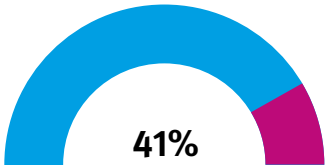
Our Sustainability Roadmap 2020 defines key targets for Type I sites. This roadmap and the progress made against those targets are reviewed each year. Currently, the main targets for 2020 are to reduce total usage (for production-corrected figures) by the percentages as shown under "Efficiency improvements by year end 2016".

Since the late 1990s, we have also been setting emission targets for Volatile Organic Compounds (VOCs). Since VOC targets are based on 5-year plans, they were tracked separately on the basis of the 2010–2015 targets. In 2017, we will be executing a materiality assessment to determine the key sustainability areas for DSP. As a result, an Integrated International Reporting Concept (IIRC), including an improvement plan, will be established. This will be the basis for defining the parameters that we will monitor. This may mean we will need to redefine the parameters that we monitor, setting new targets for 2020, and deciding whether to include other emissions (e.g., NOx, SO_2 and nitrogen) and waste among the parameters monitored.

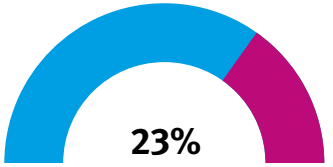
Efficiency improvements by year end 2016



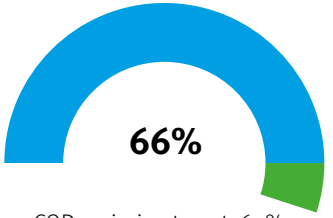
Energy consumption target: 43%
Achieved: 42%



CO_2 emission target: 49%
Achieved: 41%



Water consumption target: 33%
Achieved: 23%



COD emission target: 60%
Achieved: 66%

Materiality assessment

In the complexity of today's business, it is often difficult to focus precisely on those issues – economic, environmental and social – that are most important to employees, customers and other key stakeholders. That is why DSP, like many other advanced companies, is now conducting a "materiality assessment" to help it undertake this task. This is a formal exercise that guides us in reflecting on what is material in our situation, and then helps us in identifying and prioritizing the relevant issues. The outcome of the assessment shows us DSP's current position and its potential opportunities. It will help us to pursue our long-term Sustainable Antibiotics strategy, clarify our vision, monitor our KPIs and maintain our reporting standards. In so far as these material issues include factors that affect the decisions of our stakeholders, they also potentially merit inclusion in this report.

In conducting our materiality assessment, we are being assisted by True Price Consultancy. This social enterprise seeks to help build an economy that creates value for all. It does that by helping companies quantify, value, and improve their impact on society, thus providing insight into the associated risks and opportunities.

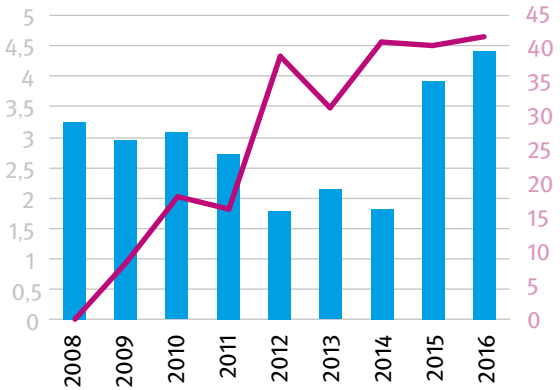
Energy consumption

As mentioned earlier, our Yushu and Zibo North sites were reclassified as Type I sites in 2015. This had a significant effect on our KPI performance. The high peaks in absolute figures in 2015 and 2016 were mainly due to the reclassification of Yushu, which has a high production capacity, and therefore high energy consumption.

In 2016, Yushu accounted for almost 45% of the total amount of energy consumed at all sites. The 10% energy efficiency improvement at Yushu compared to 2015 means DSP's overall performance has also improved. We aim to maintain this positive trend, so that we will achieve our target of 43% by 2020.

Energy consumption

Type I sites (including Yushu and Zibo North from 2015)



- Absolute energy consumption (per 1000 TJ/year)
- Relative energy efficiency improvement over the target period (%)

DSP's energy savings in 2016 were largely due to our success in increasing the proportion of our products made using our enzymatic technology platform. But important contributions were also made by implementing various energy-saving projects and energy-efficient technologies.

These included improving fermentation processes, using higher-efficiency air compressors, gas economizers and chillers, making better use of boilers, and installing additional energy meters for better monitoring and identification of improvement areas.

Extensive energy audit

In 2016, we conducted an extensive energy audit at all our production sites. Such audits provide useful insights into "hot spots" (where peaks of energy use occur), as well as opportunities for possible improvements in energy consumption. The audit covered mainly the consumption of electricity, gas, steam and coal. On the basis of the results of the audit, each site has prepared plans for sustainability projects, which will be evaluated and implemented in the course of 2017–2020. We already forecast an overall saving of 4% in absolute terms in overall energy consumption across all our production sites. The audit, along with proposed large-scale projects, contributed to a broader awareness of the use of energy, including hot spots. In addition, it revealed smart opportunities for further energy reduction with only small adjustments and for targeted investments in the manufacturing process.

Our enzymatic technology has made a substantial contribution to our energy efficiency improvement

Emissions to air and water

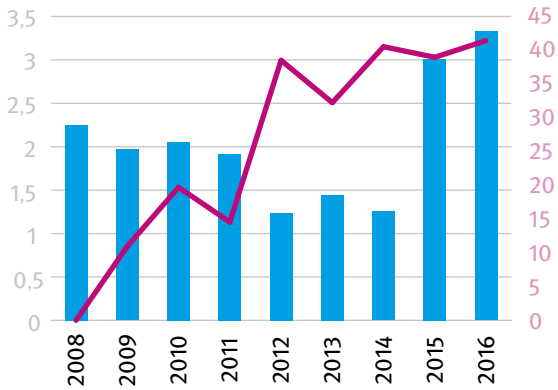
Emissions to air

CO_2 emissions

The amount of CO_2 (energy-related greenhouse gases) that we emit into the air is directly related to the amount of energy we consume at our production sites around the world. Our plant at Yushu, China, accounts for 54% of total CO_2 emissions across all sites. The relative significance of Yushu in overall CO_2 emissions is reflected in the chart below.

Since 2008, we have managed to reduce CO_2 emissions by 41% (up from 39% in 2015, including Yushu and Zibo North). Thanks to lower energy consumption at Yushu in 2015–2016, our overall CO_2 efficiency improved by 2%. These improvements at Yushu were largely due to two factors: successful efforts to increase the proportion of products we make using our enzymatic platform and the implementation of energy-saving projects.

CO_2 emissions
Type I sites (including Yushu and Zibo North from 2015)



- Absolute Greenhouse Gases (per 100,000 T/year)
- Relative CO_2 emissions efficiency improvement over the target period (%)

CO_2 Certificates to our dedicated customers

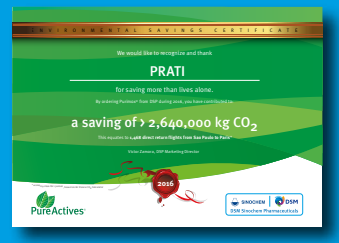
In 2016, we presented Environmental Savings Certificates to a selected group of customers to show how much CO_2 they had kept out of the atmosphere by purchasing from DSP. These certificates make our customers more aware of the tangible benefits of our enzymatically produced APIs, as well as of their own impact on the environment.

Collectively, the total CO_2 saved in 2016 is 233,734,000 kg, equivalent to 184,053 direct return flights from New York City to Paris.

234,000,000 kg CO_2=

184,000

return flights from New York City to Paris

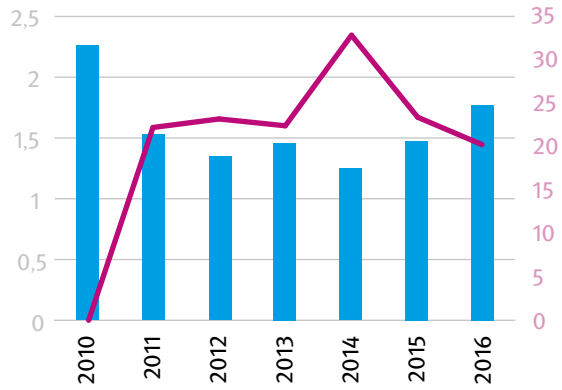


VOC emissions

The emission of Volatile Organic Compounds (VOCs) refers to the release of organic chemicals into the surrounding air. Organic chemicals that we presently use in our production processes are acetone, methanol, butanol, butylacetate, methylenechloride, isopropylalcohol, ethylacetate, hexane and cyclohexane. DSP has been setting targets for reducing VOC emissions since the late 1990s, based on five-year plans. This explains why they are tracked separately from the 2010–2020 targets defined in our Sustainability Roadmap 2020.

DSP's VOC emission levels are currently almost five times lower than they were in the year 2000, when we began monitoring. They are also 20% lower than they

VOC emissions
Type I sites (including Yushu and Zibo North from 2015)



- Absolute VOC emissions (per 1,000 T/year)
- Relative VOC emissions efficiency improvement over the target period (%)

were in 2010. The latter reduction is mainly due to the introduction of our enzymatic production process at Ramos Arizpe (Mexico) and at Zibo South (China) in 2009.

Operations at the fermentation site in Mexico were temporarily stopped in 2014, and restarted in 2015, giving rise to the volatility visible in the chart on the previous page. The increase in VOC emissions in 2016 (compared to 2015) was mainly due to a relative increase in demand for chemically produced products in 2015–2016. In fact, this has resulted in a decline (by 3%) in the relative efficiency improvement in 2016, in relation to 2015.

In the coming years, where possible, we plan to gradually convert the majority of our production lines to the enzymatic process. This way, together with process improvements at our sites in Toansa (India) and Ramos Arizpe (Mexico), we expect to improve our efficiency in terms of VOC emissions.

Our CO_2 emissions have been reduced by 41% since 2008

Emissions to water

Water consumption

Since 2008, the water efficiency at our Type I production sites has increased by 23%. Our improvement in water consumption is largely due to the optimization of production processes and production capacities. The peak in absolute consumption in 2015–2016 is due to the inclusion of figures of our sites in Yushu and Zibo North (China).

COD

Chemical Oxygen Demand (COD) is an indirect measure of the quantity of organic compounds in water. Our current COD emissions are 15 times lower than they were when we first started monitoring in 2000. Since 2010 alone, they have dropped by 66%. Our COD emission target for 2020 is 60%. In 2016, we already exceeded this by 6%.

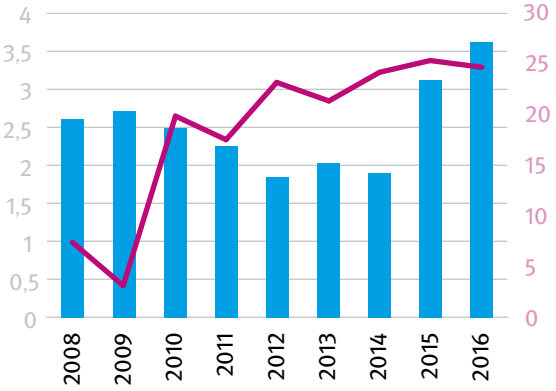
Most of this improvement was achieved by changing several of our production processes from chemical to enzymatic technology, and by implementing some targeted COD reduction projects. One of these reduction projects involved implementing more effective management of our wastewater treatment plant (WWTP) at our Delft site (the Netherlands), based on Lean Six Sigma sessions. This made a useful contribution to reducing our COD emissions throughout 2010–2016.

We are investing in renewable technologies and recycling projects that help us to further reduce our energy and water consumption. At our Delft site, we generate biogas from co-products that would otherwise be thrown away, and at our Toansa site, we reycle wastewater for reuse in the horticultural sector.

We exceeded our COD emission target in 2016

Water consumption

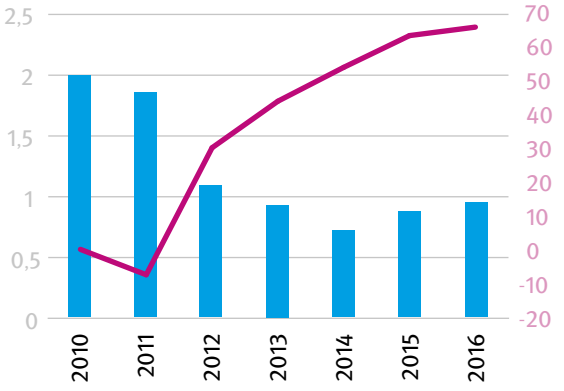
Type I sites (including Yushu and Zibo North from 2015)



- Absolute water consumption (per million m³/year)
- Relative water consumption efficiency improvement over the target period (%)

COD emissions

Type I sites (including Yushu and Zibo North from 2015)



- Absolute COD emissions (per 1,000 T/year)
- Relative COD emissions efficiency improvement (over the target period (%)

Wastewater treatment and discharge

Water is an essential raw material that is required in large quantities for the production of antibiotics. In order to discharge the resulting effluent water streams without harming the environment, the streams have to be thoroughly cleaned.

A breeding ground for resistance

DSP treats wastewater in dedicated wastewater treatment plants (WWTPs) before it leaves the site, but in the antibiotic production industry this is not always the case. It is common practice to send untreated wastewater streams to municipal or other common treatment facilities. Here, it is mixed with other industrial and household waste in a combined pool of pollutants. Recent studies show that such pollutant pools seriously encourage the emergence and spread of antibiotic resistance. Places where bacteria from the environment meet human pathogenic bacteria – as well as normal human flora bacteria that do not cause disease – are an ideal breeding ground for resistance. Resistant bacteria have been detected in high numbers in treatment plants that receive effluent waste streams from several sources.

Know your waste

"All our wastewater treatment plants are custom-designed to suit the production process in question, the products being made, and considering the location and effluent requirement of the factory," says Laura Blasco, DSP Corporate Technology & Manufacturing Advisor. "This precision approach, reflecting our professional R&D background as a company, is based on the principle of "know your waste", and on mastery of the specific skills required to operate continuously. In this way, we ensure that we are always compliant with the most stringent regulations and guidelines."

Pioneering wastewater treatment

DSP was one of the first antibiotic producers to invest in its own state-of-the-art water treatment plant in the 1980s. Over the decades, we have continued to invest in such facilities in other countries as well. Today, all of our sites have their own dedicated wastewater treatment facilities that effectively treat our wastewater. All wastewater (which makes up at least 80% of the waste) undergoes carefully executed pre-treatment, biological treatment and post-treatment before it leaves the site.

Testing for antimicrobial activity

As part of our Sustainable Antibiotics Program (see p. 28), we have also implemented methodologies to detect any remaining antibiotic activity in our wastewater. This way, we make sure none of our operations add to the growing threat of antimicrobial resistance (AMR). That is why

we have developed an easy-to-use test (see p. 38) to detect the presence of antimicrobial activity in effluent. We have carried out this test at all our sites every week since September 2016, and now have a purity level of less than 50 parts per billion (equivalent to 50 mg per 1,000 liters, based on Penicillin G).

Removing organic compounds

The quality of our wastewater is also measured in terms of chemical oxygen demand (COD), an indirect way of determining how much organic matter (such as food and beverage waste) is still in the water. Since 2010, our COD figure has fallen by 66% globally (see p. 78), which means that in 2016, we exceeded our emission target of 60% by 6%.

Earth Day celebrations in 2016

Every year, on April 22, we celebrate Earth Day. This event takes place across the globe and aims to encourage action and awareness with regard to the sustainability of our environment. Various local activities are organized at each location. By attending these events, employees can make individual commitments to reducing their ecological footprint at work and at home.

In 2016, our Earth Day celebrations were inspired by the Sustainable Development Goals (SDGs) defined by the United Nations. Out of these 17 goals, DSP chose four that are most relevant to our business vision and strategy. These were Responsible Production and Consumption, Climate Action, Clean Water and Sanitation, and Good Health and Well-being. Teams of employees were encouraged to challenge each other with a commitment that will contribute to one of these SDGs being achieved.

Earth Day activities organized at our sites included:

- Tree plantings
- Movies on AMR and global warming
- Distribution of reusable bags
- Posters with success stories on sustainability and sustainable antibiotics.

Employee commitments included:

- Reducing meat consumption
- Using reusable cups instead of disposable cups
- Recycling more
- Reducing printing by 50%
- Reducing the consumption of packaged food.

Trees for tomorrow

Trees play a vital role in the existence of our planet, as they help reduce CO_2 emissions, create oxygen, prevent erosion, and improve our overall quality of life when brought into our urban habitats. Due to rapid urbanization, however, more and more trees are being cut down. At DSP, we see it as part of our duty to society to help conserve the global tree population by ensuring the continuous planting of new trees. In 2016, the DSP team planted over 1,250 trees in the Toansa area of India.

Successful energy-saving program in Mexico

The penicillin G potassium salt plant of DSM Sinochem in Ramos Arizpe, Mexico, operates 24 hours a day, 365 days a year. In May 2016, as part of the plant's resource management program 'Project Jaguar', utilities manager Ricardo Martínez was put in charge of implementing a number of energy -saving initiatives.

Before year's end, the Ramos Arizpe plant was able to reduce its energy consumption per unit of penicillin G potassium salt by 20%. This positive result was achieved by implementing several Lean-inspired best practices, and excellent collaboration between the plant's utilities and fermentation team.

Initial audit

In order to highlight areas of inefficiency, a comprehensive internal audit of the plant's energy consumption was undertaken. This audit revealed several quick wins, such as the fact that three large industrial air compressors, which consumed close to 46% of the plant's total energy, could work more efficiently with cleaner filters.

Team efficiency

Inspired by Formula One pit stops, Ricardo implemented a competitive, single-minded approach to energy saving throughout the plant's 350-strong team. All team members were tasked with executing simple energy-saving best practices, such as not leaving machinery on standby, collectively making a significant difference. Ricardo also invested in enhancing the cross team's communications and defined clear roles and tasks, using the strengths of each worker.

Aligning team behavior

Because the Ramos Arizpe plant operates continuously, work is carried out in three eight-hour shifts. To align energy-saving behaviors throughout the team, communication channels were improved, including regular meetings with the plant's various groups, ensuring full alignment on energy-saving practices.

Superior equipment

The energy-saving drive has also involved the installation of new technical equipment. In particular, new, more efficient refrigerating units have recently been installed, which run on approximately 12% less energy than the old refrigerating units. New energy consumption control panels have also been installed on the air compressors, notifying technicians of any process faults.

2016 Highlights

In 2016, we made excellent progress in many areas. Some of the milestones in the year are highlighted in here.

We had a number of regulatory successes with CEPs for Rosuvastatin and Cefaclor, and an ASMF for our new Caspofungin. We continued our forward integration into drug products, resulting in 200 marketing authorizations by the end of the year.

Partly thanks to our efforts, the environmental impact of antibiotics production as an important cause of antimicrobial resistance gained increased attention. We were a driving force and signatory of the UNGA Industry Roadmap, and Cefic awarded our Sustainable Antibiotics Program with the European Responsible Care Award for Product Stewardship.

Routine AMA testing at all our sites

Offering Rosuvastatin API with CEP and finished dosage formulations with own API

Cefic Responsible Care Award for Product Stewardship

Stronger position as leader in sustainable antibiotics

United Nations General Assembly

Driving force and signatory of the Industry Roadmap on AMR

PSCI
PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

Membership of PSCI

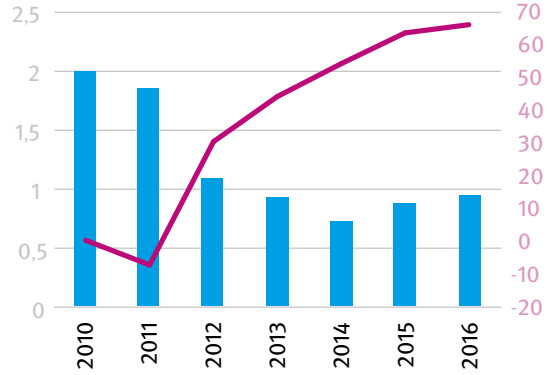
200 marketing authorizations

Multi-stakeholder engagement on irresponsible production causing AMR

84% net sales from ECO+ products

COD emissions

Type I sites (including Yushu and Zibo North from 2015)



Solid progress on our environmental monitoring targets

New improved enzyme Elcolase added to our enzymatic technology

For its sustainability reporting, DSM Sinochem Pharmaceuticals uses an approach inspired by GRI standardized guidelines and performance indicators.

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