

# Chemicals Knowledge Hub

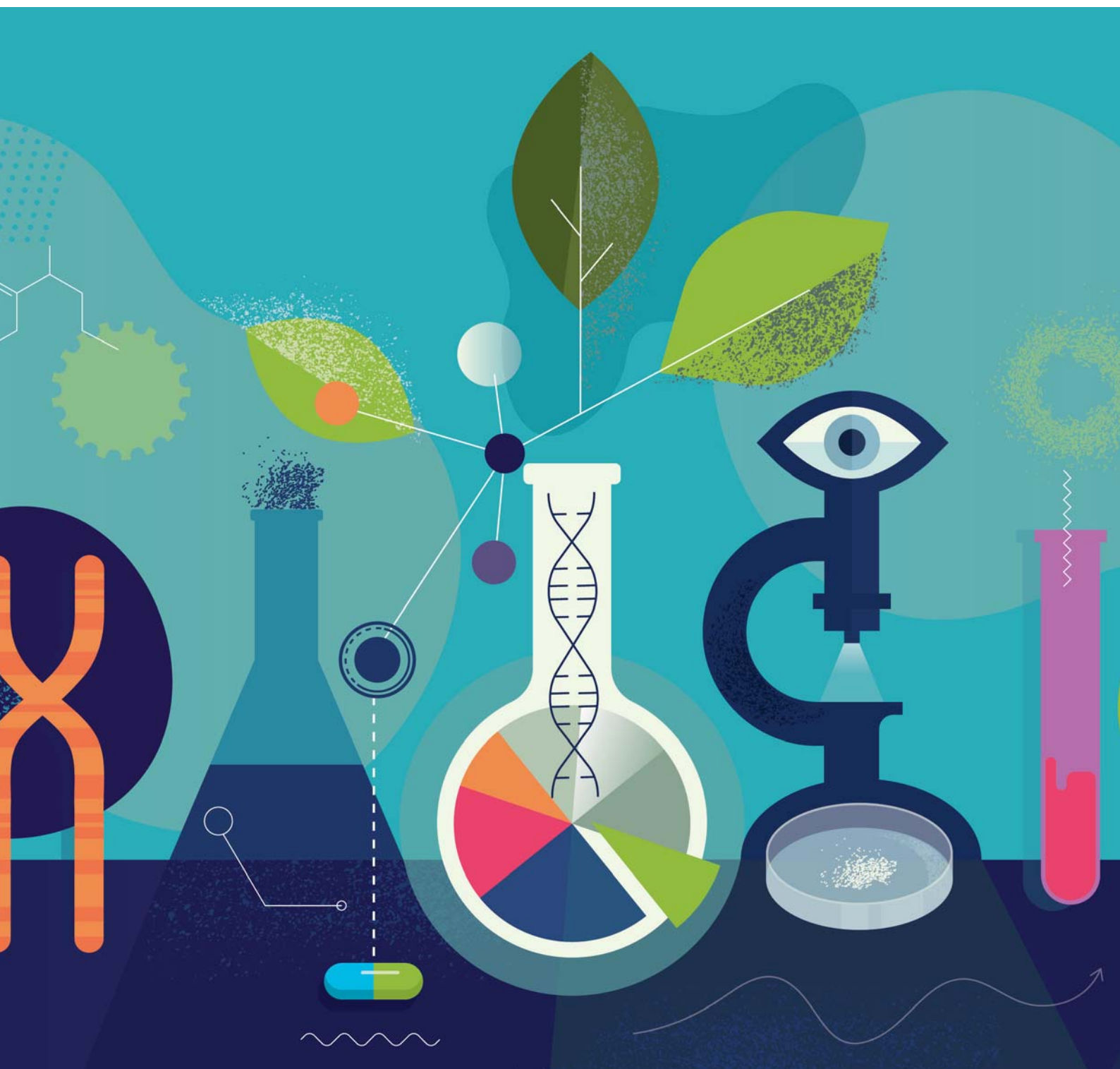
Connecting industry across the globe

Summer 2020

## INSIDE ...

- Life Sciences Focus
- Catalysis
- Topical Products
- Cosmetics
- Digital Technology
- Distribution
- Automotive Industry
- Water Treatment
- Contract Services

[www.chemicalsknowledgehub.com](http://www.chemicalsknowledgehub.com)





# Azelis expands its global presence into Latin America

**Azelis is thrilled to announce the acquisition of Megafarma, Mexico's premier specialty distributor for the pharma, food and veterinary industries.**

The addition of Megafarma into the Azelis global network strengthens our commitment to our valued principals and customers across Latin America, and is complementary to our strategy of sustainable organic growth. The transaction also creates a platform to build other market segments in Mexico, such as plastics, foam, CASE, personal care, and household & industrial cleaning.



Megafarma, headquartered in Mexico City, with offices in Guadalajara and Monterrey, represents some of the world's most renowned raw material producers and serves a large number of customers throughout all regions of Mexico.

**Innovation  
through  
formulation**

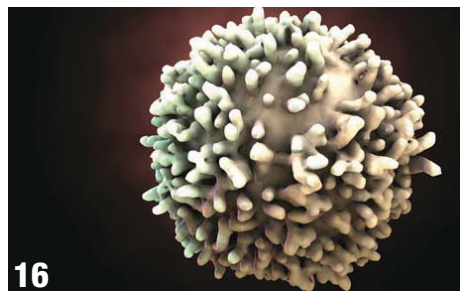
visit [azelis.com/americas](https://azelis.com/americas)  
[megafarma.com.mx](https://megafarma.com.mx)







6



16



22



24



33



36

<b>Welcome</b>	3
<b>Events</b>	
Events Calendar 2020	4-5
<b>Industry News</b>	6-14
<b>Life Sciences Focus: Drug Discovery</b>	16-17
Gene editing and gene modulation technologies support drug discovery	
<b>Life Sciences Focus: Drug Development</b>	18-19
Adopting a phase-appropriate approach to solid-state pharmaceutical chemistry	
<b>Life Sciences Focus: Drug Delivery</b>	20
The growing field of nanoencapsulation in pharmaceutical and cosmetics applications	
<b>Life Sciences Focus: Process Development</b>	22
Continuous manufacturing and the personalized medicine revolution	
<b>Life Sciences Focus: Biotherapeutics</b>	24
Avacta Group: in the forefront in the fight against coronavirus	
<b>Life Sciences Focus: Supply Chain Management</b>	26
Managing the triple threat - how Life Sciences can build pandemic-ready supply chains	
<b>Catalysis</b>	28
Biocatalysis – How secret should it be?	
The case for homogeneous ester hydrogenation	
<b>Topical Products</b>	33
Topical drug formulation: the challenges and new solutions	
<b>Cosmetics</b>	36
Eigenmann & Veronelli - Creating value for customers in chemical manufacture and distribution for more than 100 years	
Hi-tech cosmetics products and services give an individual look	
Capturing the essence of Africa	
<b>Digital Technology</b>	42
Building resilience with the digital twin	
<b>Distribution</b>	44
Azelis: innovative service provider on a global basis	
<b>Automotive Industry</b>	47
Let's drive forward to the future	
<b>Water Treatment</b>	50
Ozone and oxygen for sustainable odour and corrosion control	
<b>Contract Services</b>	55
Outsourcing as a key to success	
<b>Guidelines</b>	56
Do you have something to say?	

# Providing chemistry expertise to bring your therapeutics to life



Scientifically led and commercially minded, we are your dependable and trusted partner for innovation. We develop perfect-for-purpose chemistry solutions from lead optimisation through to product launch and life-cycle management. This enables our customers to create affordable, best-in-class small molecule therapeutics in an economically and environmentally sustainable way.

Discover more [catsci.com](https://catsci.com)

Get in touch [enquiries@catsci.com](mailto:enquiries@catsci.com)

BEYOND PROCESS CHEMISTRY

Welcome to the Summer 2020 issue of Chemicals Knowledge Hub. In this issue we have a strong focus on life sciences which is in anticipation of our new life sciences section. We are also delighted to bring you some great articles on pharmaceuticals and cosmetics, as well as our regular sections on distribution, water treatment and some insights into the automotive industry.

I'm delighted to announce the launch of CKH TV, the one-stop-shop for industry interviews and insights. This is your platform to showcase your products, services and expertise to the industry. This unique video content platform is the best place to be seen and see what's hot in the chemicals industry!

I want to thank most sincerely everyone who has shown

such faith in us throughout this year. Our editorial contributors, our advertisers, our readers and our partners – thank you all for helping us to be such a rapid success in the speciality chemicals communication arena. So please do stay with us, keep reading our news and articles, and let's see together what a thrilling future our industry will bring”.



Ellie Bruni

**Publishing Director**

**Chemicals Knowledge Hub (Global)**

#### PUBLISHING DIRECTOR

Ellie Bruni

T: +44 (0) 7872 516194 E: ellie.bruni@ckhglobal.org

#### ADVERTISING

Kenneth Carroll

T: +1 (610) 745-1426 E: ken.carroll@ckhglobal.org

Tom Scanlan

T: +1 (847) 624-8925 E: tom.scanlan@ckhglobal.org

Nadia Liefsoens

T: +32475593196 E: nadia@fivemedia.be

#### EDITORIAL CONTACT

Please send your news and suggestions for feature articles to the editorial team at [Editor@ckhglobal.org](mailto:Editor@ckhglobal.org)

Chemicals Knowledge Hub is published by BIBO Publishing SL Av. Diagonal, 409, 1st Floor, 08008, Barcelona, Spain

#### Disclaimer

BIBO Publishing SL will not be held responsible or liable for errors or omissions supplied or contained in this publication, although due care and attention are taken to ensure all content is accurate at the time of going to press. Speciality World Media Ltd also will not be held responsible for any false claims made by advertisers, or in articles contributed by external authors. The views and opinions expressed are not necessarily those of the Editor or BIBO Publishing SL.

#### Copyright

The contents of this publication are copyright © BIBO Publishing SL 2020. No part of this publication can be reproduced or transmitted in any form without the express permission of the publisher.

ISSN 2516-4481



## Don't miss the Autumn 2020 issue of CKH



**EDITORIAL: Ellie Bruni**

T: +44 (0) 7872 516194 E: ellie.bruni@ckhglobal.org

**ADVERTISING: Kenneth Carroll**

T: +1 (610) 745-1426 E: ken.carroll@ckhglobal.org

**Tom Scanlan**

T: +1 (847) 624-8925 E: tom.scanlan@ckhglobal.org

**Nadia Liefsoens**

T: +32 475 593196 E: nadia@fivemedia.be



# Events Calendar 2020

## CPhI Korea

26-28 August 2020 **NEW DATES!**

Seoul, Korea

[www.cphi.com/korea/](http://www.cphi.com/korea/)

## Adhesive and Bonding Expo VIRTUAL EVENT!

28 August 2020

[www.adhesivesandbondingexpo.com](http://www.adhesivesandbondingexpo.com)

## TIDES USA Oligonucleotide & Peptide Therapeutics VIRTUAL EVENT!

15-18 September 2020

<https://informaconnect.com/tides/>

## Festival of Pharma VIRTUAL EVENT!

16 October 2020

## MedTech Integrates VIRTUAL EVENT!

15 October 2020

[www.lifescienceintegrates.com](http://www.lifescienceintegrates.com)

## in-cosmetics Asia

3-5 November 2020

Bangkok, Thailand

<https://asia.in-cosmetics.com>

## CPhI South East Asia

4-6 November 2020 **NEW DATES!**

Muang Thong Thani, Thailand

[www.cphi.com/sea](http://www.cphi.com/sea)

## In cosmetics formulation summit

11-12 November 2020

London, United Kingdom

## TIDES EUROPE: Oligonucleotide & Peptide VIRTUAL EVENT!

10-13 November 2020

<https://informaconnect.com/tides-europe/>

## Chemspec Europe

11-12 November 2020 **NEW DATES!**

Cologne, Germany

[www.chemspeceurope.com](http://www.chemspeceurope.com)

## Bio Integrates

### VIRTUAL EVENT!

16 November 2020

[www.lifescienceintegrates.com](http://www.lifescienceintegrates.com)

## Pharma Integrates

### VIRTUAL EVENT!

17 November 2020

[www.lifescienceintegrates.com](http://www.lifescienceintegrates.com)

## CPhI India

25-27 November 2020

Delhi, India

<https://www.cphi.com/india/>

## CPhI China

16-18 December 2020

Shanghai, China

[www.cphi.com/china](http://www.cphi.com/china)

## APAC Biopolymer Summit 2020

16 – 17 September 2020

Kuala Lumpur,

Malaysia



### Speciality & Custom Chemicals America

9-11 February 2021

Fort Worth, USA

[www.chemicalsamerica.com/](http://www.chemicalsamerica.com/)

### DCAT Week 2021

22-25 March 2021

New York,

USA

<https://dcatweek.org/>

### CPhI middle east **NEW DATES!**

24-25 March 2021

Riyadh,

Saudi Arabia

[www.cphi.com/mea](http://www.cphi.com/mea)

### in-cosmetics global

13-15 April 2021 **NEW DATES!**

Barcelona,

Spain

[www.in-cosmetics.com/global/](http://www.in-cosmetics.com/global/)

### CPhI Japan

14-16 April 2021 **NEW DATES!**

Osaka, Japan

[www.cphi.com/japan](http://www.cphi.com/japan)

### CPhI North America

April 20-22, 2021 **NEW DATES!**

Philadelphia, USA

[www.cphi.com/northamerica](http://www.cphi.com/northamerica)

### Interphex

20-22 APRIL 2021 **NEW DATES!**

New York City, USA

[www.interphex.com/](http://www.interphex.com/)

### BIO International Convention

June 14-17, 2021

Boston, USA

<https://www.bio.org>

### in-cosmetics Korea

14-16 July 2021

Coex, Seoul, South Korea

<https://korea.in-cosmetics.com>

### Speciality & Agro Chemicals America

29 June-1 July 2021

Charleston, USA

[www.chemicalsamerica.com](http://www.chemicalsamerica.com)

### in-cosmetics Latin America

22-23 September 2021

Sao Paulo, Brasil

<https://latinamerica.in-cosmetics.com>

### CPhI worldwide

Autumn 2021

<https://www.cphi.com/Europe>

For more information about these and other events in the speciality chemicals industry, visit  
**[www.chemicalsknowledgehub.com/events](http://www.chemicalsknowledgehub.com/events)**



## Cambrex increases flexible manufacturing capacity at Karlskoga facility

US-headquartered pharmaceutical CDMO Cambrex is investing \$3.6 million at its Karlskoga, Sweden facility to increase flexible drug substance manufacturing capacity. The work, which will convert a previously customer-dedicated manufacturing train, will include an additional production line at 6 cubic metre scale being added at the site resulting in a 25 per cent capacity increase at the facility.

Engineering work for the expansion has already commenced at the facility and is expected to be completed by November this year. The work involves modification of an existing four-reactor configuration and the installation of



**Cambrex: investing in added flexible manufacturing capacity at its Karlskoga facility in Sweden.**

new holding tanks and a 4 square metre Hastelloy Rosemund filter.

"We are seeing continued growth in commercial-scale API manufacturing, and an ongoing trend for customers favouring high-

quality European and US partners, so we must ensure capacity is both flexible and available to be in a position to react quickly and effectively to customers' changing requirements," commented

Bjarne Sandberg, Managing Director, Cambrex Karlskoga. "This investment, as with others made by Cambrex across our global network, is in line with the company strategy of ensuring that the assets we can offer customers allow for the most cost-effective and efficient manufacturing."

Cambrex's site in Karlskoga employs more than 400 people and features a wide range of flexible manufacturing facilities, including four cGMP pilot plants and five full-scale commercial production units. In 2019, a new 600 square metre process and analytical development facility was added to the site, along with a 3,000 square metre logistics centre.



## BASF working toward circularity in recycling of mattresses

BASF has developed a chemical recycling process for used mattresses and is starting pilot tests at the company's Schwarzheide site in Brandenburg, Germany. The materials from old mattresses are to be recycled in such a way that they can be used for the production of new mattresses. "The target is to recover the raw materials with a quality comparable to that of non-recycled/virgin raw materials", said Shankara Keelapandal, Business Management Isocyanates Europe. The company says it is breaking

new ground and responding to the raised expectations regarding sustainability of the foam and mattress industry as well as those of consumers and that this is an important step to possibly re-enter post-consumer waste back into product lifecycles.

BASF's process breaks down the flexible polyurethane and delivers the initially used polyol. From there the company can produce new foam with a significantly lower carbon footprint, because fewer fossil resources are used.

## Piramal Pharma Solutions acquires solid dose facility from G&W Laboratories Inc

Piramal Enterprises Limited's Pharma Solutions (PPS) has entered into an agreement with G&W Laboratories Inc. to acquire G&W's solid oral dosage drug product manufacturing facility in Sellersville, Pennsylvania. Under the agreement, PEL, through one of its affiliates, would acquire at closing a 100 per cent stake in the entity that operates the facility and owns the related real estate.

The acquisition will add solid oral dosage form capabilities in North America to PPS's manufacturing portfolio: until now, the company's

capabilities in solid oral dosage forms were all located in the UK and India. The Sellersville site can also produce liquids, creams, and ointments, further expanding the PPS portfolio and the site also can support product and process development for solid oral dosage and oral liquids, including immediate release, modified release, chewable and sublingual solid oral dosage forms, solutions and suspensions in liquids. The site has received certifications from the FDA and the EMA.



**G&W Laboratories' Sellersville, Pennsylvania facility in the US will shortly be acquired by Piramal Pharma.**



# Global experts in nanotechnology and drug particle engineering

Nanoform is an innovative nanoparticle medicine enabling company that works with pharma and biotech partners to enhance drug effectiveness and targeting. Nanoform's Controlled Expansion of Supercritical Solutions (CESS®) technology produces nanoformed™ API particles with increased dissolution rates and improved bioavailability.

## See what small can do for you

We help drugs reach their full therapeutic potential by increasing the active surface area of API particles. CESS® Nanoforming™ produces uniform and stable nanoparticles, initiating an era of novel drug development and delivery applications that will transform the healthcare sector.

Before nanoforming™



40 µm

After nanoforming™



5 µm

Contact Nanoform to unlock the potential of your molecules

[nanoform.com](http://nanoform.com) | [info@nanoform.com](mailto:info@nanoform.com) | +358 29 370 0150

[@NanoformF](https://twitter.com/NanoformF) [in Nanoform](https://www.linkedin.com/company/nanoform)

 **nanoform**  
small is powerful



# SCIENTIFIC UPDATE

*We've got chemistry*



**VIRTUAL**  
Events Online

Scientific Update delivers conferences and training courses for industrial chemists and chemical engineers in chemical development, scale-up and many other specialist topics in organic chemistry.

## WEBINARS

Upcoming Webinars for industrial organic chemists on the following topics:

### **CRYSTALLISATION IN THE SALT-COCRYSTAL CONTINUUM: A TALE OF TWO MORPHOLOGIES**

Aug 12 2020 - 15:00 (BST), 16.00 (CEST), 10.00 (EDT), 7.00 (PDT)

### **SYNTHETIC ORGANIC ELECTROCHEMISTRY: BASIC CONCEPTS AND SCALE-UP**

Sept 16 2020 - 15:00 (BST), 16.00 (CEST), 10.00 (EDT), 7.00 (PDT)

## ONLINE TRAINING

We offer virtual training courses for industrial organic chemists on the following topics:

### **PRACTICAL MANAGEMENT OF IMPURITIES AND DEVELOPMENT OF EFFECTIVE AND COMPREHENSIVE CONTROL STRATEGIES**

September 22 - 30, 2020 | **ONLINE**

Dr Andrew Teasdale

### **SECRETS OF BATCH PROCESS SCALE UP**

Sept 28 - Oct 2, 2020 | **ONLINE**

## LIVE TRAINING



### **DESIGN OF EXPERIMENTS FOR CHEMISTS AND ENGINEERS**

Cologne, Germany  
Oct 5 - 6, 2020

### **UNDERSTANDING POLYMORPHISM & CRYSTALLIZATION ISSUES IN THE PHARMACEUTICAL INDUSTRY**

San Francisco, USA  
Oct 7-9, 2020  
Barcelona, Spain  
Oct 21-23, 2020

### **CHEMICAL DEVELOPMENT & SCALE-UP IN THE FINE CHEMICAL & PHARMACEUTICAL INDUSTRIES**

San Francisco, USA Oct 12-14, 2020  
Nice, France Oct 27-29, 2020

## VIRTUAL CONFERENCES

### OUR EXPERTISE

While we are unable to travel to hear the latest updates from our industry - we plan to provide highly focussed industrial conferences online with industrial case studies, virtual exhibitions and focussed 'discussion sessions'. Please contact us to present your work.

### COMING SOON

#### > **PROCESS ANALYTICAL TECHNOLOGIES**

Sept 21-22, 2020

#### > **THE SCALE UP OF CHEMICAL PROCESSES**

Oct 19-20, 2020

"Webinar organised superbly, presentation great, really well attended (570 at one point) and judging by the quantity and quality of questions it's generated a lot of interest. It's been a really great event to be involved in".

Lhasa Ltd



## LIVE CONFERENCES



We're still hoping to be able to resume our normal conference operations towards the end of the year and into 2021. Here are our planned events so far.

### **ORGANIC PROCESS RESEARCH & DEVELOPMENT**

Basel, Switzerland  
Dec 9-11, 2020  
New Orleans, USA  
Mar 9-11, 2021

### **MEDICINAL & BIOORGANIC CHEMISTRY**

Colorado, USA  
Jan 31 - Feb 4, 2021

**VISIT OUR WEBSITE TO BOOK AND CHECK ALL AVAILABILITY**

## LANXESS increasing its use of recycled raw materials for thermoplastics and composites

Speciality chemicals company LANXESS is increasingly making use of recycled raw materials in the production of its thermoplastic compounds and composites with the company's Durethan ECOBKV30H2.0, ECOBKV35H2.0 and ECOBKV60XF products as the most recent examples of product manufacturing being performed in line with this strategy. Recycled fibres manufactured from waste glass make up 30%, 35% and 60% by weight respectively of these three new polyamide 6 compounds and independent inspection company Ecocycle has awarded LANXESS an eco-loop certificate in accordance with ISO 14021:2016. The glass comes from waste left over from glass fibre production.

"We want to help make the switch from a throw-away society to a circular economy," stated Dr Guenter Margraf, global product manager at LANXESS's High Performance Materials (HPM) business unit. "Our goal is to make more and more of our plastic products sustainable so that we can make our growth less dependent on the consumption of finite resources, improve our carbon footprint and protect the environment."

HPM's primary target for the three new compounds is the automotive industry. "For instance, Durethan ECOBKV60XF offers exceptional strength and rigidity, which makes it suitable for manufacturing structural components such as front ends, pedal bearing brackets and A-, B- and C-pillars, as well as lightweight battery trays for electric vehicles," explains Margraf.

HPM is going to be gradually increasing the number of ECO product types certified in accordance with Ecocycle's mass balance method and is planning to launch a new polyamide 6 with a glass fibre content of 30% and a reduced carbon footprint. The caprolactam required to produce this more environmentally friendly polyamide 6 is based on a selection of petrochemical raw materials that support this aim. HPM is not currently using waste glass fibres from end-of-life components, but does view them as a particularly sustainable raw material for use in manufacturing new glass fibres. "Using waste glass cuts down on the use of resources as well, because it saves glass raw materials," says Margraf. "It also means there's no need to dispose of the waste glass."



**LANXESS using waste glass at its glass fibre production facility in Antwerp, Belgium. (Photo: LANXESS AG)**

## Catalent expands beauty and plant-based consumer health Softgel capabilities in Canada and Brazil

Delivery technologies specialist Catalent has completed a \$3.2 million expansion programme at its consumer health manufacturing facilities in Strathroy, Canada and Sorocaba, Brazil. The expansion projects include new softgel encapsulation lines at each site, dedicated to Catalent's proprietary Vegicaps® plant-based capsule and CosmoPod® twist-off capsule technologies. The company says the increased capacity will enable it to support its customers in North and Latin America to develop products for consumers seeking all-natural and plant-based vitamins, minerals and supplements using its Vegicaps capsule; and support those customers looking for innovative, easy-to-use, unit-dose beauty care products through its CosmoPod technology.

"We have seen increased consumer demand for greater product choice, with sales of

plant-based softgel technologies growing by more than 25% globally in recent years," commented Dr Aris Gennadios, President, Softgel & Oral Technologies, Catalent. "Additionally, Brazil has grown to become the world's fourth-largest market for beauty care products. While we have been supplying the North and Latin American markets with plant-based softgel capsules from our manufacturing sites in Italy and Germany, this investment allows us to provide local supply solutions to markets that complement existing capabilities in Europe."

Catalent's 110,000 square-foot facility in Strathroy, Ontario, and its 124,600 square-foot facility in Sorocaba, Brazil, both offer a broad range of integrated formulation, manufacturing, and packaging services to provide full-service turnkey solutions for the pharmaceutical, consumer health, and beauty industries.

## Almac Group launches Tempod 1000 to improve clinical site temperature data management

Almac Clinical Services has launched Tempod® 1000 as part of the company's site compliance and temperature management offering. Tempod 1000 is a USB device that captures and stores all clinical site temperature data and automatically identifies unreported excursions once uploaded into Almac's TempEZ Web-based temperature management software. Designed to remove the administrative burden of updating manual temperature logs, it also increases site compliance with reporting data and promotes best digital practice in clinical studies and patient safety, the company says, adding that manual methods of data capture have proved challenging

due to disruptions caused by the global pandemic. The Tempod 1000 automates the process by continually recording temperature data for drug products stored at clinical sites, providing sponsors and CRAs with full, remote visibility to ensure quality and integrity of the drug product.

Almac Clinical Services says that, in addition, Tempod 1000 will reduce the risk of missed patient visits due to unreported excursions, enable sponsors and CRAs to identify and resolve excursions remotely, speed-up CRA review time during site visits, and facilitate timely and efficient study close-outs and database locks.



## Biesterfeld opens new Lab and Innovation Centre

Speciality chemicals and product formulation company Biesterfeld is expanding its laboratory capacities in Hamburg, Germany with the opening of the Biesterfeld Lab and Innovation Centre. Covering a total area of 800 sq m, the premises will be used with immediate effect for application-related laboratory activities. These include the development of innovative and market-oriented formulations, carrying out of product tests and customer-specific project work. The Biesterfeld Group also has regional laboratories in Norway, Turkey and Poland.

An existing laboratory in Hamburg has been integrated into the new application laboratory to make the new Biesterfeld Lab and Innovation Centre. The premises also contains a conference room and a modern presentation and meeting area, which can be used for product launches and technical training sessions.

"In our application laboratories we develop tailored solutions to cater for the needs of our customers. An innovative formulation, for example, can be made market-ready through the addition of additives from our wide-ranging portfolio



**Biesterfeld is expanding its laboratory facilities in Hamburg, Germany to support product development.**

and thus support marketing work," comments Dr Lisa Nahrwold, Laboratory Manager at Biesterfeld Spezialchemie. "Alongside individual project work in accordance with customer requirements, the laboratory will be used to screen new raw materials from our partners and to conduct comparative studies. Comprehensive regulatory consulting rounds off our range of services."

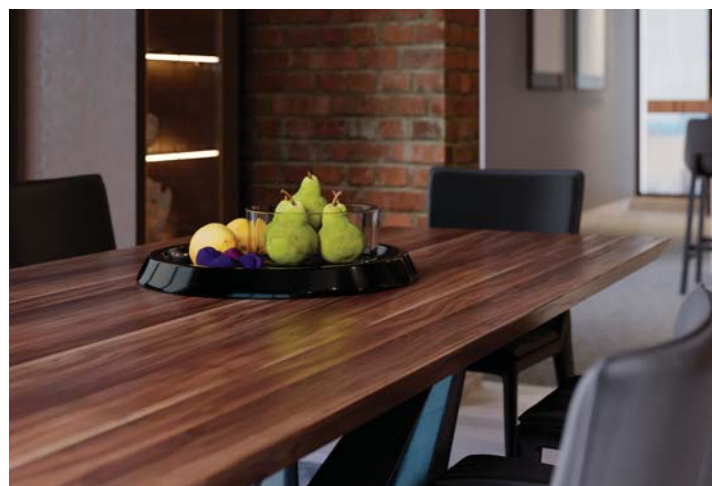
## Grace introduces novel matting agents for water-based wood coatings

Speciality silicas producer W. R. Grace & Co. has introduced two new premium matting agents especially designed for eco-friendly systems in water-based wood coatings: SYLOID AQ 800 silica and SYLOID AQ 880 silica. Specifically developed to ensure an extremely low-gloss finish, these new patent-pending speciality silicas have been designed to eliminate the typical water spots and stains that wood coatings manufacturers strive to avoid.

SYLOID AQ 800 and SYLOID AQ 880 silicas have been designed to offer superior matting properties

with high chemical resistance and clarity and the two silicas can be used alone or blended to achieve desired appearance and performance attributes. Grace says that SYLOID AQ silica series' proof-of-concept and extensive in-market beta tests have demonstrated "vast" performance improvements and formulation advantages over alternative matting agents.

The SYLOID AQ silica series has been designed to be simple to use, with low dusting properties and easier dispersibility, translating into shorter cycle times and potential cost savings.



**Grace's new SYLOID AQ 800 and SYLOID AQ 880 silica matting agents are designed to ensure an extremely low-gloss finish for wood coatings.**

## Syngenta Group launched to create global agtech market leader

Syngenta Group Co. Ltd. has announced the official launch of Syngenta Group as a single entity to create a new global leader in agricultural science and innovation that combines the strengths of Syngenta AG, headquartered in Switzerland, ADAMA, based in Israel, and the agricultural businesses of Sinochem, based in China. The new entity, headquartered in Switzerland, has

48,000 employees in more than 100 countries, and had sales of \$23 billion in 2019.

From its inception, Syngenta Group is the global market leader in crop protection, the global number three in seeds, the market leader in fertilizer in China and, with its Modern Agriculture Platform (MAP) Farmer Solution Centers, a leading agriculture services provider in China. The

Group offers comprehensive agronomic solutions and digital agricultural services, operating 15 key production sites.

Under its new structure, the organization encompasses four business units: Syngenta Crop Protection, led by Jon Parr based in Basel, Switzerland; Syngenta Seeds, led by Jeff Rowe based in Chicago, USA; ADAMA, led by Ignacio Dominguez based in

Airport City, Israel and Syngenta Group China, led by Hengde Qin based in Shanghai, China.

Erik Fyrwald, formerly CEO of Syngenta AG, becomes Syngenta Group CEO; Chen Lichtenstein, formerly CEO of ADAMA, becomes Syngenta Group CFO; Steve Landsman becomes Syngenta Group General Counsel, and Laure Roberts becomes Syngenta Group Chief Human Resources Officer.

## NOVA Chemicals and Enerkem collaborate on plastics recycling

Two Canadian companies are to collaborate on innovative technology to close the loop on recycling and drive a plastics circular economy. NOVA Chemicals Corporation, a leading producer of chemicals and plastic resins, and Enerkem Inc, a leading waste-to-renewable fuels and chemicals producer, have entered into a joint development agreement to explore turning non-recyclable and non-compostable municipal waste into ethylene, a basic building block for plastics. The companies will research advanced recycling technology to transform hard-to-recycle municipal waste, including items such as plastics, household waste, and construction materials, into ethylene at full



**Canadian companies NOVA Chemicals and Enerkem Inc have formed a joint development agreement to explore turning non-recyclable and non-compostable municipal waste into ethylene, a basic building block for plastics**

commercial scale. The companies say ethylene produced from waste would advance a plastics circular economy and help meet consumer brand goals for recycled content in packaging.

Advanced recycling technologies

are a necessary component of moving to zero plastic waste by creating valuable new feedstocks from post-use plastics that cannot be easily mechanically recycled and the quality of polymers produced with advanced recycling products is

indistinguishable from those made from 100 percent virgin, fossil-based feedstocks.

Enerkem is the first company in the world to produce renewable methanol and ethanol from non-recyclable, non-compostable municipal solid waste at full commercial scale. Its current technologies replace the use of fossil sources like petroleum and natural gas to produce sustainable fuels and chemicals that are used in a broad range of everyday products.

NOVA Chemicals is committed to enabling 100 per cent of plastics packaging is recyclable or recoverable by 2030; and 100 per cent of plastics packaging is re-used, recycled or recovered by 2040.

## Bionema secures Innovate UK grant to complete development of microencapsulation technology

Bionema Ltd, a leading UK-based biotechnology company, has received a grant from Innovate UK to support the company's continued development of its bioinsecticide microencapsulation formulation, which, the company says, delivers an effective alternative to chemical pesticides. This additional £98,000 Continuity Grant complements an initial £1.0 million in funding support from Innovate UK, the national funding agency that invests in science and research in the UK, and from the Welsh Government's SMART Cymru.

Dr Minshad Ansari, a world-leading biopesticide expert who leads Bionema's research team, commented: "The funding is helping the company to continue the development of its microencapsulation formulation and delivery systems, which is crucial to the development of effective biopesticide products," adding that

effective control of pests, such as western flower thrips, aphids, whitefly and spider mites, requires a robust formulation for targeted delivery. Currently, these pests are controlled by conventional chemical insecticides but some of them have now developed product resistance, while other products have been removed from the market, due to their harmful impact on the environment and human health. Ansari says that biopesticide formulation and its targeted delivery is a more stable and sustainable approach for controlling these pests which are causing billions of dollars of crop damage on a world-wide scale.

The Continuity Grant-funded project aims to develop a unique manufacturing process of proven microencapsulation formulation technology for next-generation bioinsecticide control. New microencapsulated products will



**Dr Minshad Ansari of Bionema: developing new microencapsulation formulation and delivery systems as the basis of increasingly effective biopesticide products.**

be registered and distributed across Europe, the US and Canada. Currently, trials are in place with several multi-national chemical companies and distributors to commercialize the technology.

The project team includes formulation experts from the School of Chemical Engineering at the

University of Birmingham and at Bionema. In addition to Bionema's research, development and commercial teams, Silsoe Spray Application Unit is also testing the product's large-scale applicability and Applied Insect Science, a regulatory service, is managing the registration of the product.

## Mergers & Aquisitions

### LANXESS completes acquisition of Brazilian biocide manufacturer IPEL

LANXESS has completed the acquisition of Brazilian biocides manufacturer Itibanyl Produtos Especiais Ltda. (IPEL). Headquartered in Jarinu, São Paulo, IPEL is one of Brazil's leading biocide manufacturers and generated sales in the lower double-digit million dollar range in 2018, with about 100 employees. IPEL generates the majority of its sales through biocides and speciality chemicals for the paints and coatings industry. The company's product portfolio also includes preservatives and fungicides for process control in water treatment as well as active ingredients for disinfection and cleaning agents.

### Gilead Sciences to acquire interest in Pionyr Immunotherapeutics

Gilead Sciences, Inc is to acquire a 49.9% equity interest in Pionyr Immunotherapeutics Inc for \$275 million with an exclusive option to purchase the remainder of Pionyr, a privately held company developing first-in-class cancer immunotherapies. Under the agreement, Pionyr's shareholders may receive up to an additional \$1.47 billion in option exercise fees and future milestone payments. Pionyr's Myeloid Tuning therapies have the potential to treat patients who currently do not benefit from checkpoint inhibitor therapies and the company's PY314 and PY159 candidates have demonstrated preclinical efficacy, suggesting potential in solid tumours in combination with established anti-PD(L)-1 agents. Pionyr plans to file investigational new drug (IND) applications with the FDA for both candidates in the third quarter of this year. Pending Phase 1b results from either candidate, or sooner if Gilead chooses, Gilead can exercise its exclusive option to acquire the remainder of Pionyr.

### KRAHN Chemie acquires Greek distributor

KRAHN Chemie GmbH has acquired a majority share of InterActive SA, headquartered in Athens, Greece. Through this strategic acquisition, the KRAHN Chemie Group has expanded its footprint not only in Europe but also to cover the Israeli market. InterActive SA was founded in 1990 and specializes in the distribution of lubricant additives in the Israeli, Greek and Cypriot markets, as well as scientific instruments for R&D and QC laboratories in the oil, pharma & chemical industries by representing international manufacturers.

### Eppendorf acquires centrifuge business of Koki Holdings Co, Ltd

Eppendorf AG and Koki Holdings Co, Ltd, have reached an agreement that Eppendorf will acquire the Japanese company's centrifuge business, including the premium himac brand. The acquisition marks a targeted step by Hamburg, Germany-based Eppendorf AG to expand its centrifuge business, solidifying its strong market position as one of the world's leading makers of high-end centrifuges for the pharmaceutical and life science industries as well as for academic and commercial research. Koki Holdings said that it will focus on developing its position as a comprehensive provider of power tools aiming to become a leading global company through strategic investment, accelerated technology and product development. Koki Holdings Co, Ltd, develops and produces ultracentrifuges and floor-standing centrifuges under the brand name himac.

## Catalent completes purchase of pharmaceutical packaging facility in Japan

Catalent has completed the purchase of Teva-Takeda Pharmaceuticals' packaging facility in Minakuchi, Shiga Prefecture, Japan. Operating in partnership with the company's existing Japanese clinical supply facility located in Kakegawa, the new 60,000-square-foot facility will provide customers with flexible clinical supply solutions, serving both local customers and global biotech and pharmaceutical companies. Catalent stated that the facility would play an important

role in its expanding Asia-Pacific network, working alongside two sites in China and one in Singapore to support customers' clinical trials across the region.

The facility will offer extensive clinical supply services including access to Catalent's FastChain demand-led supply services, primary and secondary packaging capabilities, and a range of temperature options for storage and distribution, as well as clinical returns and destruction services.

## SOCMA on-demand training for chemical operators

SOCMA, the Society of Chemical Manufacturers and Affiliates, reports that since its launch in January, 15 companies across 42 facilities have adopted its Chemical Operations Training Tool to train and refresh employees on standard operations and processes in chemical manufacturing and that SOCMA is now expanding this modernized training tool to non-member manufacturers.

"SOCMA developed this comprehensive programme with on-demand training in mind," said Joe

Dettinger, Senior Director, Compliance & Stewardship at SOCMA. "Having led EHS&S operations at a facility for many years, I understand the importance of thorough training and the need to safely onboard operators about the mechanics behind each process."

Companies that have implemented the modernized platform found the tool to be an efficient resource for both in-person and remote training. Further information can be found at [www.socma.org](http://www.socma.org)

## Eastman partners with IMCD Group to expand EMEA speciality plastics distribution network

Eastman Chemical is expanding and reinforcing its strategic partnership with IMCD Group for the distribution of its speciality plastics. The company offers the world's largest portfolio of thermoplastic polyester materials and IMCD will distribute these products over a wide range of markets and applications, including medical, consumer durables, cosmetics, personal care, and packaging, amongst others. Currently, IMCD distributes Eastman speciality plastics in Spain and Portugal and under the new distribution agreement, IMCD will

also start serving an expanded EMEA market comprised of more than 30 countries.

"IMCD is already a strategic partner in the distribution for various Eastman speciality materials, with demonstrated synergies and processes alignment," said Eastman sales director Oliver Osborne. "We believe this expanded partnership will ensure a smooth transition for our speciality plastics customers whose distribution arrangements with incumbent distribution partners finish at the end of July."



# When you Absolutely Need... FULL GMP!

Exclusively Manufactured in the USA

- Bulk GMP Buffers / Custom GMP Solutions
- Functional Excipients / NCEs
- Critical Process Chemicals



- Small Volume Support
- Critical Quality Attributes
- GMP Synthesis & Purification
- Heightened Regulatory Demands
- Full GMP Divp. & Regulatory Package



**Need it Full GMP?  
Key Ingredient Issues?  
Small Molecule Concerns?**

**For more information please contact: Paul DiMarco, Vice President**

**Ph: +1 610.599.3477 e-mail: [pdimarco@biospectra.us](mailto:pdimarco@biospectra.us)**

## MFG Chemical obtains ISO 9001: 2015 Certification for Pasadena, Texas plant

US-based speciality and custom chemical manufacturer MFG Chemical has achieved ISO 9001:2015 Certification for its 26.7 acre plant in Pasadena, Texas, completing certification for all four of the company's plants, the other three being located in Dalton, Georgia. MFG was one of the first chemical companies to achieve ISO 9001:2015 Certification, beginning in October of 2016, and has now been audited and certified four times.

ISO 9001 is the international standard that specifies requirements for a quality



**MFG Chemical's Pasadena, Texas facility: ISO 9001:15 Certification means that all four of the company's manufacturing facilities are now certified to this international quality management system standard.**

management system (QMS) and is used to demonstrate the ability

to consistently provide products and services that meet customer

and regulatory requirements. ISO 9001 is based on the plan-to-check-act methodology and provides a process-oriented approach to documentation and reviewing the activities. As part of the ISO9001:2015 certification process, MFG Chemical engaged in a rigorous audit of its business processes, as well as its product quality environments. The company said that by maintaining this level of certification, MFG Chemical is able to demonstrate a quality management system and continuous improvement of its products and services.

## New Solvay hydrogen peroxide dilution and packing plant in Vietnam

Solvay Peroxides Vietnam has started production at its new hydrogen peroxide dilution and packing plant at Phuc Long Industrial Zone in Long An Province, Vietnam. The facility is designed to reach 24,000 ton capacity per year to meet growing

local demand for international standard quality hydrogen peroxide for the textile industry and other applications. As the first Solvay industrial facility based in Vietnam, the plant was built and made operational in full alignment with the

group's HS&E standards and now high-quality hydrogen peroxides are being supplied by Solvay Peroxythai in Thailand and diluted and packed to meet Vietnamese customer requirements locally.

"With this new plant we are aiming

at better serving our customers in Vietnam," said Suthichai Srihawan, general manager of Solvay Peroxides Vietnam "To support sustainability and a circular economy, the use of returnable packaging has been implemented with our distributors and customers. This action allows customers to minimize the non-core operation of managing used packaging."

## People on the Move

**AMPAC Fine Chemicals (AFC)** has promoted **Dr Jeff Butler** to the position of President of the company. Dr Butler has performed in leadership roles of increasing responsibility at AFC, with his most previous position being Vice President of Project Management. In his new role, he is responsible for operations across all AFC US-based facilities. He holds a PhD in Chemistry from the University of California, Davis and conducted his post-doctoral research in chemistry at the University of Texas at Austin. He will continue to operate out of AFC's Rancho Cordova, California, USA facilities.



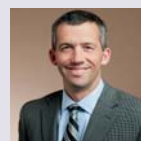
**Dr Jeff Butler**

**Pierre-Alain Ruffieux** will become Chief Executive Officer of **Lonza** effective November 1, 2020. He is currently Head of Global Pharma Technical Operations at Roche where he and his 12,000-strong team are responsible for all aspects of pharmaceutical commercial manufacturing and supply chain operations, technical, quality assurance and regulatory. Prior to that he held roles of increasing seniority at Novartis and has more than 20 years' experience in biopharmaceuticals.



**Pierre-Alain Ruffieux**

**Cambrex** has named **Tom Loewald** as its new Chief Executive Officer and a member of the company's Board of Directors effective September, 2020, the company being led in the interim by an Office of the CEO comprised of Wayne Hewett, Chairman of the Board, Robert Green, Executive Vice President and Chief Financial Officer, and Samantha Hanley, Senior Vice President and General Counsel. Loewald worked for 15-years at Thermo Fisher Scientific, where he served in several senior executive roles, including Chief Commercial Officer, President of the Analytical Instruments Group, President of the Laboratory Products Group, and President of the Laboratory Equipment Division. He currently serves as President of the Flexibles Division of ProAmpac, a leading flexible packaging manufacturer. Earlier in his career he held leadership positions at Tyco International and General Electric. Loewald currently serves on the Board of Directors of Harvard BioScience, a global developer, manufacturer and marketer of a broad range of solutions to advance life science.



**Tom Loewald**

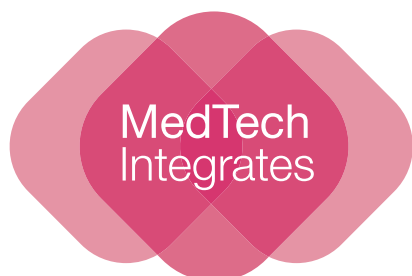


# Where transformation begins

Life Science Integrates is excited to announce that this year's three events : **MedTech Integrates 2020** on 15th October, **Bio Integrates 2020** on 16th November and **Pharma Integrates 2020** on 17th November, will be broadcast live on our new digital platform.

We will bring together Senior Leaders from across the Life Sciences, including industry, academia, government and regulators; providing you with a unique opportunity to be part of the conversations that set out the industry's challenges and identify effective strategies and solutions.

## Our events



### MedTech Integrates

 **LIVE ONLINE 15 October 2020**

Addressing the needs of the MedTech community to overcome the challenges needed to achieve a transformation of diagnostics and devices in healthcare.



### Bio Integrates

 **LIVE ONLINE 16 November 2020**

Focused on the biotech, start-up and emerging pharma sector addressing the needs of innovative companies that develop therapies of tomorrow.



### Pharma Integrates

 **LIVE ONLINE 17 November 2020**

Bringing together pharma and healthcare leaders to share insights and create debate on crucial topics that influence the future of patient outcomes.

**Register now and at each event benefit from real-time, face-to-face networking**

**1**  
day

**70+**  
speakers

**300+**  
senior industry  
executives

**We have 100 free tickets per event available for Chemicals Knowledge readers.**

**Register today for your chosen event on [www.lifescienceintegrates.com](http://www.lifescienceintegrates.com) and enter Promo Code CK100 when prompted.**

**[www.lifescienceintegrates.com](http://www.lifescienceintegrates.com)**



# Gene editing and gene modulation technologies support drug discovery

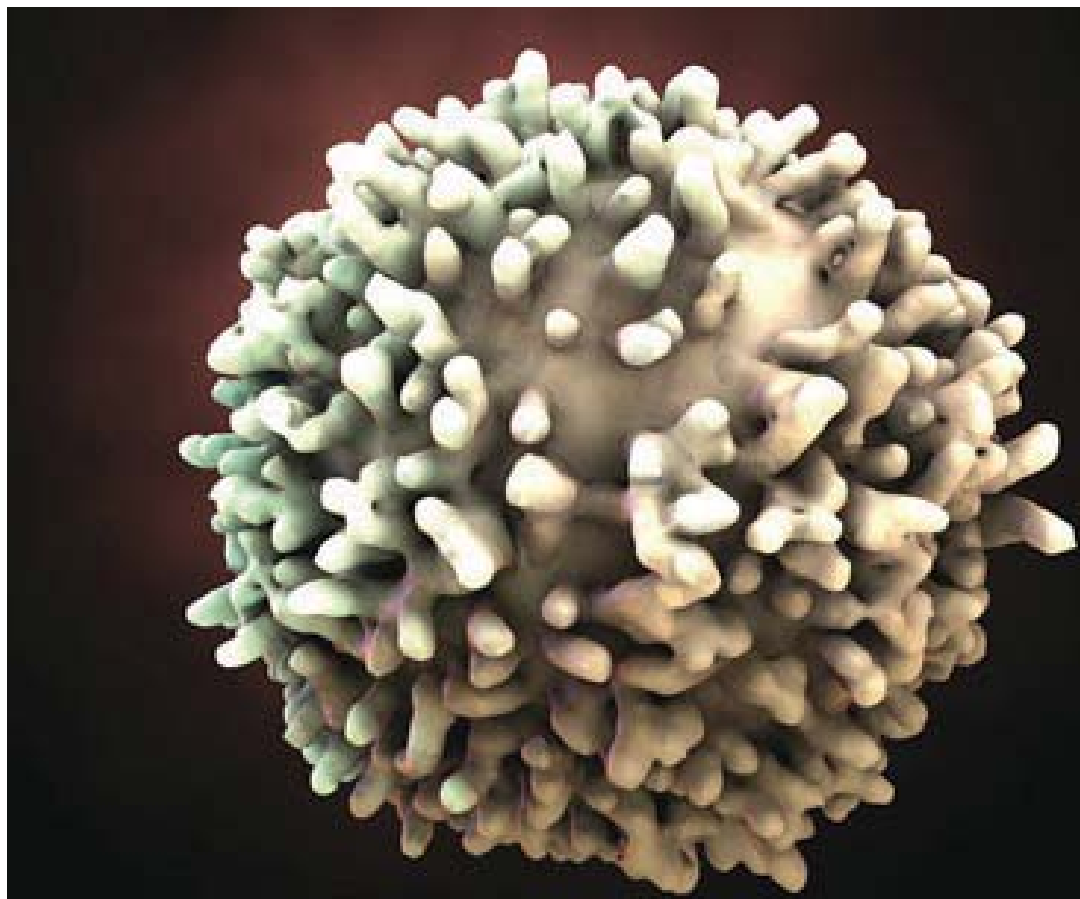
Horizon Discovery has developed a broad range of gene editing and gene modulation technologies that enable scientists to gain a greater understanding of gene function and apply this knowledge to the development of novel biotherapeutics, gene therapies and diagnostic workflows. This article reviews recent developments at the company.

Headquartered in Cambridge, UK and with offices in the US and Japan, Horizon Discovery Group plc specializes in the application of gene editing and gene modulation technologies that support drug discovery and development within the global life sciences sector, offering a portfolio of tools and services to help scientists gain a greater understanding of gene function, identify genetic drivers behind human disease and deliver biotherapeutics, cellular and gene therapies for precision medicine as well as for the development and validation of diagnostic workflows. The company's solutions are designed to enable almost any gene to be altered, or its function modulated, in human and other mammalian cell lines.

Its clients include leading academic institutes, global pharmaceutical and biotechnology companies and clinical diagnostic laboratories. Horizon says that its insight into the challenges faced by these organisations enables it to focus its efforts on the development of innovative solutions that not only differentiate its offering, but that also fuel development of the next wave of precision medicines.

## Gene knockout and gene activation studies

Earlier this month (July 2020), the company introduced its stably expressing Cas9 and dCas9-VPR cell lines to help accelerate gene knockout and gene activation experiments, respectively. The



**Horizon Discovery is now offering an arrayed CRISPR knockout screening service for primary human B cells, cells that are freshly isolated from donors and known to be difficult to study in the lab. Pictured is a B-lymphocyte antibody-producing immune cell. (Image from Shutterstock © Kateryna Kon)**

cell lines are optimized to work alongside the company's Edit-R predesigned synthetic single guide RNA (sgRNA) and CRISPRa guide RNA, offering researchers a complete solution to simplify and streamline CRISPR gene editing and modulation workflows.

Horizon's Cas9 and dCas9-VPR stable cell lines were generated using its Edit-R Lentiviral particles with a blasticidin resistance cassette and are provided in pooled

format. The cell lines are QC-verified and validated to ensure stable expression and functionality of Cas9 or dCas9-VPR endonuclease in a range of common cell backgrounds. Both cell lines are available in the same background to enable loss-of-function and gain-of-function studies to be performed in parallel without the need to engineer a cell line specifically for this purpose. Horizon says that removing the time-intensive

step of generating a stable cell line and the cost associated with purchasing a nuclease could help researchers increase R&D productivity and allow novice users to gain a better understanding of the CRISPR workflow.

## Production of highly complex proteins

In a separate recent development, in May of this year, biopharmaceuticals CDMO

**Horizon says that its insight into the challenges faced by these organisations enables it to focus its efforts on the development of innovative solutions that not only differentiate its offering, but that also fuel development of the next wave of precision medicines**

Rentschler Biopharma SE and Horizon signed a commercial licence agreement under which Horizon's cGMP-compliant CHOSOURCE platform will be used in combination with Rentschler Biopharma's novel in-house process for cell line development for difficult-to-express proteins. Horizon's gene-edited glutamine synthetase (GS) knockout CHO K1 cGMP-compliant cell line will complement Rentschler Biopharma's existing service offering, providing a royalty-free, state-of-the-art alternative for the production of highly complex

proteins to support researchers from early drug development through to commercial manufacturing.

The two companies say that by entering into the agreement, they aim to empower organisations of all sizes, from large pharmaceutical companies to clinical stage biotechs and early-stage startups, to drive efficiencies in biotherapeutic manufacturing and that Rentschler Biopharma's integrated platform process, together with Horizon's cell line, will provide innovative and tailored solutions to translate complex medical research into new biopharmaceuticals, elevating the standard of protein expression and allowing clients to access a robust and flexible approach for designer protein therapeutics from concept to market.

#### **Immunotherapy development**

Horizon had earlier announced that the CHOSOURCE platform had played a key role in generating a stable cell line for the development of an immunotherapy for autoimmune diseases with pharmaceutical-grade, stable CHO cells delivering high yields of monoclonal antibody for LAG-3 immunotherapy, enabling Immutep and Batavia Biosciences to reach an important milestone in the preclinical development of the compound. The company's

gene-edited GS knockout CHO K1 cell line expression system, offered by Batavia Biosciences as part of its STEP-mAb service, was used to generate a high yielding cell line for Immutep's IMP761 product candidate, an agonist antibody targeting the immune checkpoint lymphocyte activation gene LAG-3 which controls the signaling between specific immune cells, T cells and antigen-presenting cells responsible for the adaptive immune response, making it a promising focus for novel cancer therapies or for the treatment of autoimmune conditions such as inflammatory bowel diseases, rheumatoid arthritis, and multiple sclerosis.

In yet another CHOSOURCE platform development, Horizon announced in April this year that it was offering special licensing terms to facilitate rapid access to the CHOSOURCE for the development of COVID-19-related therapeutics and diagnostics. Horizon is already a key supplier for COVID-19-related research as a provider of tools and services to academia and industry in their efforts in the pandemic.

#### **Arrayed CRISPR knockout screening service**

Also in April, Horizon announced the addition to its cell-based screening services of an arrayed CRISPR knockout screening service for primary human

B cells, cells that are freshly isolated from donors and known to be difficult to study in the lab. One advantage of working with these cells, however, is that it brings scientists one step closer to healthy or diseased micro-environments, enabling them to better understand disease etiology and therapeutic mechanisms and thereby advance drug discovery and development programmes.

Horizon has already applied its gene editing and cell culture expertise to maintain the viability of primary human T cells to enable functional genomic screens and has been delivering data-rich information to customers working in drug discovery and development. Horizon says the new B cell screening service, the first of its kind in the market, will enable researchers to identify genes that affect the function of B cells and examine how this impacts other immune cell types, particularly in infectious diseases, cancer, and auto-immune disorders, such as COVID-19, Burkitt's lymphoma and multiple sclerosis, respectively.

**Further information**  
**Horizon Discovery plc**  
**Cambridge, UK**  
**Ph: +44-1223-976160**  
**E: [technical@horizondiscovery.com](mailto:technical@horizondiscovery.com)**  
**W: [www.horizondiscovery.com](http://www.horizondiscovery.com)**

**Get recognized  
for your achievements  
ENTRIES NOW OPEN**

**Ethical Innovation  
Awards 2021**

**CPhI north america®**  
entr@ ICSE #FDF bio@ Amity I-mec

**Chemicals  
Knowledge**

# Adopting a phase-appropriate approach to solid-state pharmaceutical chemistry

**Dr Julian Northen, research manager at Onyx Scientific, explains how a more phase-appropriate approach to solid-state chemistry may present an effective option for drug development teams in assuring the physical properties of drug products and ensuring optimal drug performance.**

The majority of today's marketed drugs are administered as solids, making solid-state chemistry a critical component of pharmaceutical research and development. The solid-state structure of drug compounds and their relationship to the drug formulation requires full consideration to provide assurance of the physical properties of the drug product. A thorough understanding of the compatibility of the chosen solid phase with drug product excipients in the solid state (relative to chemical and form stability) is also required to avoid the unwanted changes that can occur in pharmaceutical preparations.

Solid form screening and selection is important at all stages of drug development. However, with increasing demands on developers to balance cost pressures with the need for fast progression, especially in the early stages, the industry is calling for more appropriate strategies that pay attention to the specific requirements at different stages in the product lifecycle.

## The advantages of collaboration

There is a growing realization from pharmaceutical developers that active pharmaceutical ingredient (API) development and manufacturing requires a more interactive approach with collaborative input from multiple groups, including medicinal chemists, solid form scientists, development chemists, and formulation scientists. Considering input, objectives and deliverables from different parties can aid the adoption of a more phase-appropriate approach that will provide developers with a 'road map' to ensure screening activities become increasingly comprehensive as the needs and technical requirements at each development stage evolve. The increased understanding that will be gained through having more individuals and capabilities involved in the process may result in considerable time savings when it comes to selection. If the right studies have



**Dr Julian Northen, research manager at Onyx Scientific**

been conducted using the right materials and in a logical order, progression to first-in-human studies can be more efficiently achieved.

Despite the advantages of adopting this type of approach already being understood, there still exists a culture of solid form selection that is less robust. For example, it is not uncommon for a drug developer to adopt a form or version based solely on it being an easy way to isolate a clean solid, or on the chemistry naturally delivering the salt or polymorphic form.

## Meeting requirements at different stages of development

No two drug candidates are the same and the solid-form strategies required for any single API will vary over the course of its development. The adoption of a phase-appropriate and inclusive approach can enable a more predictive pathway that will enable solid form studies to progress in a way that ensures specific objectives are achieved at different stages.

## Discovery and lead optimization

Starting at the discovery and lead optimization stage, a robust set of physiochemical

parameters should be identified as markers for the competing analogues in play. This can include a simple response to changes in pH and solubility, Log P, presentation form (oil, solid, amorphous, crystalline), and whether a salt can form and aid in isolation/development.

## Early development

During early development, a robust assessment of the various solid form versions and candidates, such as salt versus API, should be carried out. This may encompass solubility across a range of pH, solid stability, solution stability, crystallinity, and thermal properties. The choices must also deliver against chemical development needs, including robustness of process, purge of impurity, and process efficiency. Additionally, an understanding of how the various presentations of each version may influence the drug product is also required, for instance powder flow, bulk density and morphology for simple solid dose formulations.

The information will provide development groups with options to consider as material transitions through Phase 1. For example, the most soluble salt may not always deliver the best option or approximation of bioavailability. Dissolution rate and propensity toward disproportionation and the kinetics of the process will need to be considered along with pharmacokinetic (PK) evaluations that support and enable selection. Ideally, the selected version will be maintained through to commercial manufacture.

## Late phase

During late-phase development it is critical to challenge the process in place versus the necessary specification to ensure that the solid form of choice delivers routinely against all performance targets. The process would normally encompass a broader polymorphism study. This may or may not identify competing versions that will provide additional protection from an intellectual property (IP) standpoint. This



process can also ensure that as scale increases and the route becomes fixed along with the impurity profile, no new forms emerge to derail the development programme and subsequently lead to costly delays. At this point, a process risk assessment should also be introduced supported by a robust form and crystallization development programme. From a worst-case-scenario perspective, the absence of such a thorough evaluation may mean that developers could see the emergence of new stable forms post-release and commercial manufacture.

### Final thought

The identification of an ideal solid form of an API not only improves the PK profile of a drug but can result in more streamlined manufacturing workflows and increased product stability. The collaborative approach created by having multiple groups work together (medicinal chemists, solid form scientists, development chemists, and formulation scientists) cannot be underestimated, and the importance of solid-state considerations at all stages of development programmes is becoming more widely acknowledged. Changes in impurity profiles, processing conditions and excipients can influence the solid form of the API and require careful monitoring throughout the drug

**There is a growing realization from pharmaceutical developers that active pharmaceutical ingredient (API) development and manufacturing requires a more interactive approach with collaborative input from multiple groups, including medicinal chemists, solid form scientists, development chemists, and formulation scientists**

development lifecycle.

The solid form of an API will have a significant impact on drug development activities; therefore, appropriately placed studies will help to develop an extensive understanding of the solid form

landscape and provide the aforementioned 'road map' for development, avoiding unwanted solid form transformations. Building a strategy for solid-state that is phase-appropriate and considers the necessary requirements at the right time can be a useful tool in establishing a more efficient and cost-effective path to market.

**AT: +44-(0)191 5166507**

**E: Julian.northern@onyxipca.com**

### About the Author

**Jules Northern, Research Manager, Onyx Scientific.** As Research Manager, Jules Northern is Onyx's resident expert in solid-state chemistry development, covering screening, crystallization and candidate selection. With more than 15 years' experience in the field, he drives Onyx's solid-state group and integrates with lead optimization services including process and development (PR&D) projects for Phase 1 studies through to Phase 3/commercial API development and manufacturing.



# La mesta

CHIMIE FINE

WE ARE NOW



## FSSC 22000

CERTIFIED !

FOOD SAFETY SYSTEM CERTIFICATION

FSSC 22000 V4.1



CERTIFICATE OF REGISTRATION  
N° FR18/81842904  
For food aromatic  
substances for industry

La Mesta Chimie Fine is a Custom Manufacturing Organization located in France. Since 1971, we have been developing and manufacturing sophisticated products for Pharma, Cosmetics, Flavors & Fragrances industries using original technologies.

www.la-mesta.com

# The growing field of nanoencapsulation in pharmaceutical and cosmetics applications

Nanotechnology is helping to drive technology and product development in many different fields including in the pharmaceutical and cosmetics industries. Both these fields need to utilize the latest formulation technologies and there is now a growing trend of using nanoencapsulation methods across both industries to better improve the characteristics of the products on offer to the general public. Liam Critchley reports.

## What is nanoencapsulation?

Nanoencapsulation, simply put, is the encapsulation of an active ingredient – be it a drug in pharmaceutical applications or water, ie moisture enhancer, in cosmetic applications – within a nanosized carrier vessel. These carrier vessels are often termed nanocarriers (a general term) and there a number of different types that can be used depending on the application and the desired effect. Nanoencapsulation is similar to other encapsulation methods however with the main difference being that the encapsulation and release of the active ingredient occurs at the nano-level.

The encapsulant, ie the active ingredient inside the core of the nanocarrier, can be a solid, a liquid or a gas. Nanocarriers typically fall into one of three categories: inorganic nanocarriers, organic nanocarriers and solid drug nanoparticles, with the latter being used only for pharmaceutical applications. The nanocarrier is a shell that protects the active core material from the local environment until released—which is often a controlled diffusion release in response to an external stimulus, such as shear forces, a change in pH, or enzymatic action.

## Types of nanocarrier

Inorganic materials were the first types of nanocarrier developed, as their synthesis is typically more straightforward, but they have

limited biocompatibility (which can be overcome by functionalizing the surface with organic molecules) and they struggle to be broken down and excreted by the body—this being the main issue with their use. Some of the main examples over the years have included gold nanoparticles, iron oxide nanomaterials, mesoporous nanosilica and metal-organic frameworks (MOFs). Carbon nanotubes have also been trialled, and while they are technically organic in chemical makeup (due to being made of carbon), their properties are more reminiscent of the inorganic nanocarriers than they are of the organic nanocarrier class.

Organic nanocarriers are now widely established and most of the work in this area revolves around polymer- and lipid-based nanocarriers, such as liposomes, as well as dendrimer architectures, as their biocompatibility is much better than that of inorganic materials and they can be broken down by the body much more easily after use. Solid drug nanoparticles are not as widely explored but their use is growing. These solid drug nanoparticles are only comprised of the drug of interest, the nanoparticle is simply a nanoscale form of the drug packed into a template/suspension. Because they are comprised of already approved drugs, there are not as many regulatory barriers to overcome, so while these systems are not yet as widespread as other



**While much of the focus of nanoencapsulation and nanocarriers has been around pharmaceuticals and drug delivery systems, there are some areas within the cosmetics industry where they are also used. Some of the more common examples include delivering moisture in oil-based ointments and creams to increase the hydrating properties of the product**



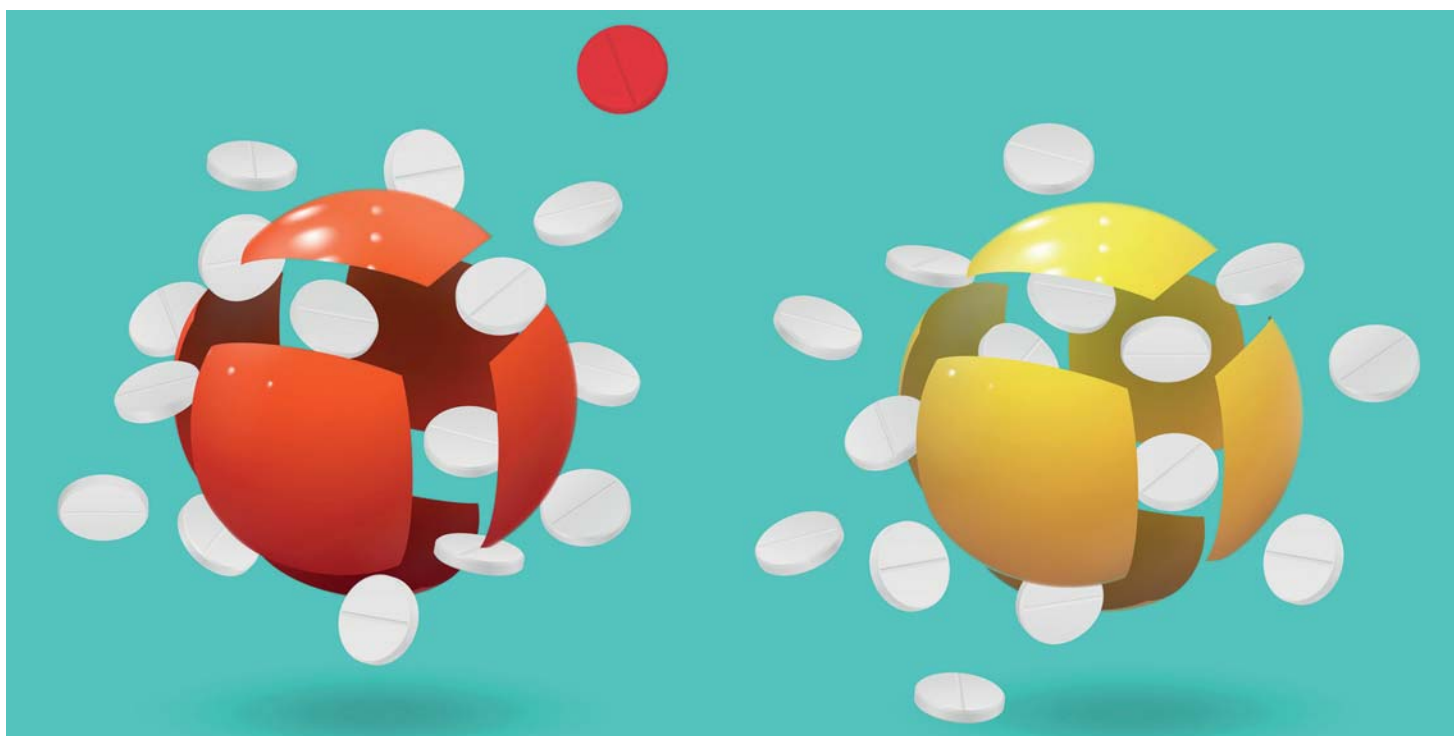
organic nanocarriers, their use is likely to increase.

## Nanoencapsulation in pharmaceutical applications

Organic nanocarriers and solid drug nanoparticles are the more common options in pharmaceutical applications because they have better biocompatibility than inorganic nanocarriers: inorganic nanocarriers were the first to be trialled but have been phased out

in favour of biologically compatible materials. Nanocarriers are typically used as drug delivery vessels to deliver an active drug to a target area and release it. This method has become an effective way of enabling a drug to be delivered to the right area while being protected until it reaches this intended area, meaning that the drug will not decompose en route, nor will it target the wrong area of the body. This also means that drugs that would otherwise be too toxic to administer can be encapsulated and delivered safely without affecting the healthy cells of the body, widening the scope of possible therapies available to a patient over those available using other drug delivery routes.

How the nanocarrier carries and delivers the drug depends on each specific type. In general, inorganic nanocarriers and liposomes, ie the more spherical delivery systems, will uptake the drug into their core, attach to the target of interest via surface groups and release the payload. Dendrimer-based systems will usually have the drug molecules covalently linked within the dendrimer and the drug will be cleaved when the dendrimer binds to its target site. Solid drug nanoparticles offer something completely different: the active drug molecules within the solid drug nanoparticle suspension are slowly released over 1 to 6 months, thus drug nanoparticles are seen as a controlled way to tackle drug dosing compliance



**Abstract representation of drugs encapsulated in nanocarriers.** (Image © iStock.com / writerfantast)

issues with patients because regular administrations of the drug are not required.

### Nanoencapsulation in cosmetic applications

While much of the focus of nanoencapsulation and nanocarriers has been around pharmaceuticals and drug delivery systems, there are some areas within the cosmetics industry where they are also used. Some of the more common examples include delivering moisture in oil-based ointments and creams to increase the hydrating properties of the product. There are a number of commercial products that use nanocarriers to add such hydration properties to formulations and hydrate the skin when applied.

Another common nanoencapsulation approach is to encapsulate fragrances, where the nanocarrier vessel breaks upon application, releasing the fragrance and making it last longer. There are also many unstable cosmetic compounds, such as hydroquinone — a compound that is used to lighten skin — that oxidize rapidly in oxygen and moisture. By encapsulating such molecules, they can be applied on the skin and not undergo any unfavourable chemical reactions before they perform their intended function.

There is also a growing trend to use nanocarriers to deliver cosmeceuticals — a cross-over area of pharmaceuticals and cosmetics that applies both therapeutic and cosmetic benefits

to the surface they are applied on. A range of nanocarriers are in use in this interdisciplinary field, including liposomes and other lipid-based carriers, niosomes and nanoemulsions, to name a few. These nanoencapsulation methods play a wide role in the cosmeceutical area, including hair care products for treating grey hair and hair loss (as well as other hair serums), anti-wrinkle creams, and in sunscreens. Identik, Origem, Nirvel, Chanel, Dior, Estée Lauder, Decorte and Sesderma are just a few of the big-name brands that currently utilize nanoencapsulation technologies to enhance their products.

### In summary

Overall, a number of companies

across the pharmaceutical and cosmetic sectors are now starting to utilize and reap the benefits of nanoencapsulation methods, and nanotechnology in general. It is likely that this trend will continue, and there will be more products in both sectors utilizing nanoencapsulation methods and other nanotechnology-based systems in the years to come.

**Author:**  
**Liam Critchley**  
**Freelance Chemistry and Nanotechnology Writer**  
**E: [liam\\_critchley@hotmail.com](mailto:liam_critchley@hotmail.com)**  
**in: <https://www.linkedin.com/in/liam-critchley-nanowriter/>**  
**t: [https://twitter.com/LC\\_nanowriter](https://twitter.com/LC_nanowriter)**



## NEW! Connecting industry across the globe

Enquire now!  
[info@ckhglobal.org](mailto:info@ckhglobal.org)





# Continuous manufacturing and the personalized medicine revolution

As the pharmaceutical industry moves towards the development of personalized medicines, manufacturing processes must adapt to match demand. This article explores how continuous manufacturing, combined with digital technologies, is providing the flexibility to produce on-demand, specific therapies for small patient populations.

No two people are exactly alike and, as a consequence, the vast majority of drugs are effective in just 30-50% of the population. [1] In spite of this, two patients with completely different pathologies will often be prescribed the same treatment for a given illness. Advances in genomics and biomarker identification in recent years have driven the pharmaceutical industry away from a 'one size fits all' trial-and-error approach to medicine.

Increasingly, the focus is on creating therapies that are specially tailored to the patient. Biomarker research constitutes an important part of the personalized medicine revolution, allowing medical professionals to predict disease progression, identify the class of drugs that a patient will respond to best and create a customized treatment plan. In order for patients to fully benefit from personalized medicine, however, the whole pharmaceutical industry must adapt its processes to enable specialized drugs to be manufactured and distributed in smaller volumes than is currently the norm. From reconfiguring supply chains to implementing new technologies, such as continuous manufacturing and artificial intelligence (AI), it is clear that a number of changes are on the horizon.

## The manufacturing process is evolving to meet demand

Advances in continuous manufacturing technologies have emerged as one solution to the challenge of manufacturing drugs cost-effectively on a relatively small scale. In contrast to traditional



**Dr Gareth Jenkins, CSO, Arcinova**

batch manufacturing, in which drugs are manufactured through a stepwise process, continuous manufacturing is more flexible and allows drugs to be manufactured non-stop as reagents and solvent continuously flow through a reactor. When applied to the production of personalized medicines, the benefits offered by continuous flow are manifold.

For example, continuous manufacturing often eliminates the need for chemical engineers to develop a series of ever-larger, specialized reactors to accommodate scaled-up production – which can be highly labour intensive. Instead, drug manufacture can be tailored to demand. If a personalized medicine is targeted at only a small percentage of patients, fewer or smaller reactors need to be dedicated to the task of manufacturing it. Equally, if demand goes up, it is a simple matter to run the process for longer, or devote more reactors in parallel to the production of that particular drug. This capability can help to accelerate the drug to commercial

manufacture and deliver it into the hands of patients more quickly.

In addition, continuous manufacturing technology enables chemical engineers to safely access much more challenging reaction conditions, including hazardous reagents and extreme temperatures. Using continuous manufacturing can enable chemists and chemical engineers to produce a wider range of molecules and unlock new synthesis routes to complex personalized medicines. Furthermore, a continuous process also lends itself to continuous monitoring, which can help increase confidence in product quality.

Finally, continuous manufacturing can facilitate a reduction in the requirement for high volumes of organic solvents. This not only improves cost-effectiveness, but also reduces waste. As the industry moves towards greener manufacturing principles, this important environmental benefit can help drug manufacturers to reduce the footprint associated with drug production.

## Reconfiguring supply chains

The current pharmaceutical supply chain is based around delivering large quantities of a given drug for widespread use. Switching to small-scale production of more specialized drugs presents logistical challenges. Creating personalized medicines on a small scale means manufacturers will not be able to benefit from the economies of scale, and it is expected that CDMOs that have invested in cost-effective solutions such as continuous manufacturing technology will have an advantage in this area.

Another challenge is ensuring that specialized drugs are correctly delivered to the intended patients, despite the increased complexity of a supply chain that involves shipping customized products directly to specific individuals. Consequently, as the personalized medicine sector grows, logistics providers may adopt techniques that will improve efficiency and visibility to prevent any errors of this sort from arising. To this end, advanced GPS tracking and automatic alarm systems, should the delivery go off-track, may be of benefit in future. [2]

## AI, Pharma 4.0 and the future of drug manufacture

Pharma 4.0, a popular buzzword for the incorporation of the latest digital advances (such as self-learning machines and smart data management) into processes within the pharmaceutical industry, offers up numerous exciting opportunities for personalized medicine manufacture. In particular, the increasing level of automation can facilitate the creation of intelligent networks across the development pipeline. Machines may be able to predict failures, and trigger essential maintenance automatically, to sidestep issues before they arise. [3]

Currently, production managers can spend significant amounts of time troubleshooting quality control errors that occur during manufacture. For example, if the raw materials used are of insufficient quality, using traditional methods this may not be detected until the batch of product had been completed. Continuous manufacturing combined with

automated monitoring and artificial intelligence can mitigate this by providing real-time information on all aspects of drug manufacture. This will not only help to increase efficiency by reducing the time spent investigating the cause of any issues that arise, but will also reassure manufacturers that the drugs fully meet all of the stringent GMP regulations set out. [3,4]

### Continuous manufacturing paves the way for the personalized medicine revolution

As researchers continue to expand our knowledge of how an individual's molecular biology influences their response to a given drug, personalized medicine opens up new horizons for the medical field. In an industry accustomed to producing drugs on a large scale for widespread use, however, continuous manufacturing, combined with advances in AI and automation, has emerged as a solution to the practical challenges associated with manufacturing customized therapies on a small scale. By offering chemical



engineers the flexibility to adjust production to meet demand, access new synthetic routes and continuously monitor quality, in the future it is expected that the technology will continue to establish itself in Pharma, helping patients obtain access to vital treatments.

#### REFERENCES

1. <https://www.phcal-journal.com/your-rps/what-impact-will-personalised-medicine-have-on-pharmacy/20201328/article?firstPass=false>
2. <https://www.su.haivive.com/news/personalized-medicine-cold-chain-logistics-growth/434060/>
3. <https://www.phceutical-technology.com/contractors/machines-labelling/dividella2/>

[pressreleases/pharma-4-0-enabling-factory-future/](#)

4. <https://www.pharmaceuticalprocessingworld.com/pharma-4-0-industry-4-0-applied-to-pharmaceutical-manufacturing/>

**Author:**  
**Dr Gareth Jenkins, CSO, Arcinova**  
**E: [info@arcinova.com](mailto:info@arcinova.com)**

# Kaneka

## FLOW CHEMISTRY



- ✓ R&D, SCALE-UP AND MANUFACTURING
- ✓ FDA INSPECTED
- ✓ GMP
- ✓ PROVEN MANUFACTURING EXPERIENCE
- ✓ SCALE-UP EXPERTISE
- ✓ ROBUST CHEMISTRY DESIGN
- ✓ ENZYMATIC TRANSFORMATIONS IN FLOW

Contact: [Stephen.Drake@kaneka.com](mailto:Stephen.Drake@kaneka.com).

Visit: [www.Kaneka.co.jp](http://www.Kaneka.co.jp)

# Avacta Group: in the forefront in the fight against coronavirus

**Novel cancer immunotherapies specialist Avacta Group has joined the fight against coronavirus by developing a rapid antigen test for the SARS-COV-2 spike protein in collaboration with Cytiva. In the meantime, the company continues to progress its anti-cancer drug candidates through preclinical development and into the clinic.**

**A**vacta Group is a Cambridge, UK-based company developing novel cancer immunotherapies by combining two proprietary platforms, Affimer biotherapeutics and tumour targeted chemotherapies. With this approach, the company aims to address the lack of a durable response to current immunotherapies experienced by most patients and in the near term is supporting this research from revenues generated by developing Affimer reagents for diagnostics, bioprocessing and research at a separate business unit based in Wetherby, UK.

## Alternative to antibodies

The Affimer platform is an alternative to antibodies and has been designed to address many of the negative performance issues of antibodies, principally: the time taken, and the reliance on an animal's immune response, to generate new antibodies; poor specificity in many cases; large size; and cost. The company's other technology platform, its proprietary targeted chemotherapy approach, releases active drug only in the tumour, thereby limiting systemic exposure and improving the overall safety and therapeutic potential of these powerful anti-cancer treatments. By combining the two platforms, Avacta is building a wholly owned pipeline of novel cancer therapies with the aim of creating effective treatments for all cancer patients including those who do not respond to existing immunotherapies. The company



**Dr Alastair Smith, Chief Executive, Avacta Group: “very encouraged” by the positive data from the company’s first SARS-COV-2 (coronavirus) spike protein rapid antigen test devices being developed in collaboration with Cytiva.**

expects to take its first drug, a targeted form of the standard-of-care Doxorubicin, into the clinic shortly (mid-2020) and to follow on with an IND/CTA submission for the first Affimer programme, a PD-L1 antagonist, in Q4 2020.

## Coronavirus: developing a rapid antigen test

Avacta is also very active in fight against coronavirus/COVID-19 disease through its rapid antigen test development partnership with Cytiva (formerly GE Healthcare Life Sciences) and recently announced positive initial data for the first Affimer-based rapid test strips for the SARS-COV-2 (coronavirus/COVID-19 disease) spike protein.

In mid-May, Avacta provided Affimer reagents that are specific to the SARS-COV-2 spike protein to Cytiva which has now developed the first lateral flow test strips using these reagents. The data show that the test strips detect the spike protein in model samples at concentrations within the clinical range found in saliva of patients with COVID-19 and work is now continuing on refining the test strip design, optimizing its performance, and establishing the best detection limit possible in order to generate the highest sensitivity in the final rapid test product.

Following the optimization of the lateral flow test by Cytiva, the design will then be transferred

to manufacturing partners in the UK. These manufacturers are currently being selected by Avacta and are working with the company to compress manufacturing, clinical validation and regulatory timelines in order to bring a product to market as quickly as possible.

Dr. Alastair Smith, Chief Executive of Avacta Group, commented: “I am delighted with the progress made by our partners at Cytiva and very encouraged by the positive data from the first test devices. We now need to optimize the test performance to achieve the best possible limit of detection as this will ultimately play a significant factor in determining the clinical



sensitivity of the test.

"This is a really positive step and we aim to have completed the optimization very soon so that we can begin the transfer to manufacturers. I will be updating the market on progress in due course."

### New cell and gene therapies

In a completely separate development, Avacta and Daewoong recently put in place a collaboration and licence agreement with their joint venture company AffyXell Therapeutics to develop Affimer proteins to be used by AffyXell for the generation of new cell and gene therapies. Avacta and AffyXell are now working together on developing Affimer proteins against a range of targets which, when produced by mesenchymal stem cells (MSCs), are intended to inhibit inflammatory and autoimmune

**Avacta is building a wholly owned pipeline of novel cancer therapies with the aim of creating effective treatments for all cancer patients including those who do not respond to existing immunotherapies**

pathways and improve the overall efficacy of MSCs, creating a next generation of stem cell therapies. The initial focus for AffyXell will be on inflammatory and autoimmune diseases, while in the longer term there is potential for AffyXell to

address oncology uses for these Affimer-enabled cell and gene therapies.

Under the terms of the collaboration and licence agreement, Avacta's research and development costs associated with generation of the Affimer proteins will be funded by AffyXell. In addition, Avacta will retain the rights to commercialize the Affimer proteins outside of the field of cell therapies.

Dr Smith commented: "The potential for AffyXell's new class of cell therapies, which can be applied to a wide range of inflammatory and autoimmune diseases, is enormous. We are therefore very excited by the opportunity to be part of this new venture and to demonstrate the power of Affimer proteins in the field of engineered cell therapies."

"Our objective is for these cell therapies to finally fully address diseases, such as inflammatory

bowel diseases and multiple sclerosis, as well as other autoimmune diseases, such as chronic obstructive pulmonary disease," he continued. "From a commercial perspective, the global stem cell market is expected to be worth \$16 billion by 2025. AffyXell has a unique opportunity to combine two world-class technologies, Avacta's Affimer antibody mimetic platform and Daewoong's proprietary technology for generating 'off-the-shelf' allogeneic MSC therapies to create the next generation of stem cell therapies. We believe that this has the potential to create substantial value for stakeholders in the near future."

**Further information**  
**Avacta Group**  
**Whittlesford**  
**Cambridge, UK**  
**E: [affimers@avacta.com](mailto:affimers@avacta.com)**

# The Ethical Innovation Awards 2021

April 2021

Philadelphia, PA, USA

Pennsylvania, Convention Centre

General enquiries: [awards@ckhglobal.org](mailto:awards@ckhglobal.org)

Sponsorship enquiries:

Ellie Bruni | [ellie.bruni@ckhglobal.org](mailto:ellie.bruni@ckhglobal.org)

Ken Carroll | [ken.carroll@ckhglobal.org](mailto:ken.carroll@ckhglobal.org)

Tom Scanlan | [tom.scanlan@ckhglobal.org](mailto:tom.scanlan@ckhglobal.org)



 **CPHI** north america®



*Global pharmaceutical product supply disruption caused by the coronavirus pandemic can be overcome through the adoption of new supply chain systems.*

(Image from Pixabay)

# Managing the triple threat - how Life Sciences can build pandemic-ready supply chains

Bill DuBois, Director of Product and Marketing Content at Kinaxis, demonstrates how the normal supply chain management issues of working in a highly regulated environment with products that have limited lifespans and the consequent need to supply products to patients quickly have been exacerbated by the current COVID-19 crisis and explains how this 'triple threat' can be managed for successful product delivery through 'pandemic-ready' supply chains.

Supply chain planning in life sciences has always been complex. It is a highly regulated sector; pharmaceuticals products typically have limited life spans, and supply chains are often based on functional silos. Planning cycles can sometimes extend over 5-10 years. Excess inventory can also be a problem but the overriding concern is getting products quickly out to end users to keep them well.

These issues are exacerbated by the current crisis. This is no single demand spike. COVID-19 has been disrupting supply chains for months. In the US, as early as February, Senator Josh Hawley warned: "The coronavirus outbreak in China has highlighted severe and longstanding weaknesses in our medical supply chain. This

is more than unfortunate; it's a danger to public health."

Certainly, the pandemic has raised serious questions of life sciences supply chains globally. Here are three main areas to consider as we navigate uncharted territory:

## # 1 Demand is volatile

We have seen spikes in demand around key products such as ventilators, masks, gowns and test kits. There is also a need to hurry through therapeutics and vaccines as well as temporary testing and hospital facilities.

At the same time, there are demand slides. At the outset of the pandemic we saw an initial run on medicines which has now subsided. Today, with travel limited and people self-isolating, the

items seeing demand cliffs are extensive. This, coupled with spikes in demand, make current plans and forecasting methods of little value. Businesses will need to have good visibility across the chain to see the real picture on the ground and they will need to have tools in place to enable them to adjust their approach accordingly.

## #2 Supply shortages are inevitable

The life sciences supply chain is struggling to deliver medications to patients across the world. Moreover, panic buying of medicines directly related to the symptoms of COVID-19 has led to shortages in pharmacies. Supply from manufacturing facilities in China has been hit hard and is only now beginning to recover





***'Pandemic'-ready supply chain systems ensure worldwide medical product supply.***

and India had export restrictions in place on 24 active pharmaceutical ingredients (API) and formulations for a month from early March to early April.

Both scenarios contributed to supply chain delays and dealing with such disruption is not easy, longer lead times being inevitable. And it is not straightforward to identify and switch to alternative suppliers. There would need to be a review of contractual liabilities, quality issues or regulation impacts.

### # 3 Recovery is an unknown

It's anybody's guess when things will return to normal. The unknown is the biggest difference between the COVID-19 pandemic and other major supply chain disruptions such as hurricanes and tornados, for example. With COVID-19, it is not one problem and there is no end date and supply chains must continue to deal with the normal complexities as well as issues like Brexit, tariffs and ongoing weather events. This is on top of an ongoing global crisis that appears to be here for the long-haul.

### Managing the triple threat

Response and risk management will be a hot topic in boardrooms moving forwards as companies take lessons learned to up their supply chain response processes. It is vital that businesses and their supply chains are able to rapidly address the challenges of the ongoing crisis. As supply chains focus on a response, surprise is the new norm. It seems like things are changing daily, even hourly, but that

does not negate the importance of planning.

A prerequisite for a solution will be strong collaboration capabilities. Collaborating at the speed needed to respond to today's pandemic is predicated on the assumption you have a single place to collect data, simultaneously execute multiple supply chain functions, and collaborate across the globe. Having a single source of truth that everyone can rely on is key. Planning, responding and risk management processes will need to ask and answer multiple questions at lightning speed, they will therefore have to have good visibility across the supply chain and work with data they can rely on.

The more unknowns there are, the more questions there are for the supply chain. What if regulations change? What is the impact on delivery, revenue and margin? What if a supplier is not back online for another two months or so? You need to be able to run different scenarios, analyze their likely impact, make sure you get answers that you have confidence in, often and fast, and share them for collaborative resolution.

### 'Pandemic-ready' supply chains

Coming out of recovery there may be new requirements placed on the life sciences supply chain. There will be new visibility requirements, for example. The Sarbanes-Oxley Act of 2002 laid down requirements on how US companies reported financials. Moving forwards, we are likely to have something similar for reporting on the supply chain.

Health officials across the world will be looking for visibility of details of manufacturing

capacities for essential drugs and devices to protect vital medicines and manufacturers will need to report on imminent shortages of life-saving medical devices to the relevant authorities. This may require life sciences companies to bring together supply chain data into a single source and turn that data into information that could stand up in court.

Complex issues around demand volatility, supply constraints and recovery dates represent serious challenges for any supply chain manager across life sciences. Hopefully the word 'recovery' will generate some optimism. History teaches us about the resilience of humanity and its endeavours. In the meantime, we can 'pandemic ready' our supply chains so we become experts at response and risk management and take the decisions in the boardroom that help drive a positive future.

**E: [Kinaxis@whiteoaks.co.uk](mailto:Kinaxis@whiteoaks.co.uk)**

### About the Author

#### **Bill Dubois, Director of Product and Marketing Content, Kinaxis**

Bill DuBois has worked for more than 20 years with Kinaxis in a number of roles including his current position as Director of Product and Marketing Content. Prior to his move to Marketing, DuBois was a Senior Business Consultant providing pre-sales support to the Kinaxis sales team. This included developing and delivering 'stand-out' product demonstrations, delivering ROI analysis and conducting pilot projects for prospective customers.

Prior to joining Kinaxis, DuBois gained 12 years of manufacturing, supply chain and 'Lean' experience while with Boeing of Canada. He holds APICS CPIM certification and, as a qualified APICS instructor, has developed and delivered APICS courses in material planning, master scheduling, capacity management and just-in-time. He has also developed and delivered Lean education and training packages for all levels of personnel.

DuBois studied Electronics Technology at Algonquin College in Ottawa, Ontario, Canada and is the host of Canada's Stevie Award-winning Late Late Supply Chain Show.





# Biocatalysis – How secret should it be?

Professor Tom Moody (VP Technology Development and Commercialisation), Dr Steve Taylor and Dr Stefan Mix (Head of Biocatalysis) highlight how Almac is approaching state-of-the-art technology development and how they guide their customers through the process of deciding how to best protect their commercial interests in relation to biocatalysis.

The pharmaceutical, health care and associated chemical industries are strategically outsourcing more and more of their activities. Recent trends indicate that this is not slowing down when it comes to procurement of advanced intermediates and building blocks for their speciality chemical products. In many cases, biocatalytic processes lie at the core of such product manufacture, bringing not just their green credentials but tangible economic benefits, too, through route shortening, reducing energy requirements and a reduction in reagent and solvent use.

The service sector is changing rapidly to meet customer demands in relation to quality, security of supply, timelines and cost, with opportunities arising for companies that can deliver on these. Quality, customer care and delivery are now baseline expectations and demonstration of additional added value with its associated intellectual property at the right price is taking centre-stage. A key question that customers are now asking is whether a process should be patented or whether it should be kept secret as industrial know-how.

## The rise and rise of biocatalysis

The synthetic attractiveness of enzyme technology stems from being able to use it for catalysis of many types of chemical reactions, and especially the unequalled ability of enzymes to recognize subtle differences in molecular shape. This, all under conditions that may be no more daunting than those found in a typical kitchen. Such impressive versatility is illustrated in Figure 1 using a hypothetical molecule.

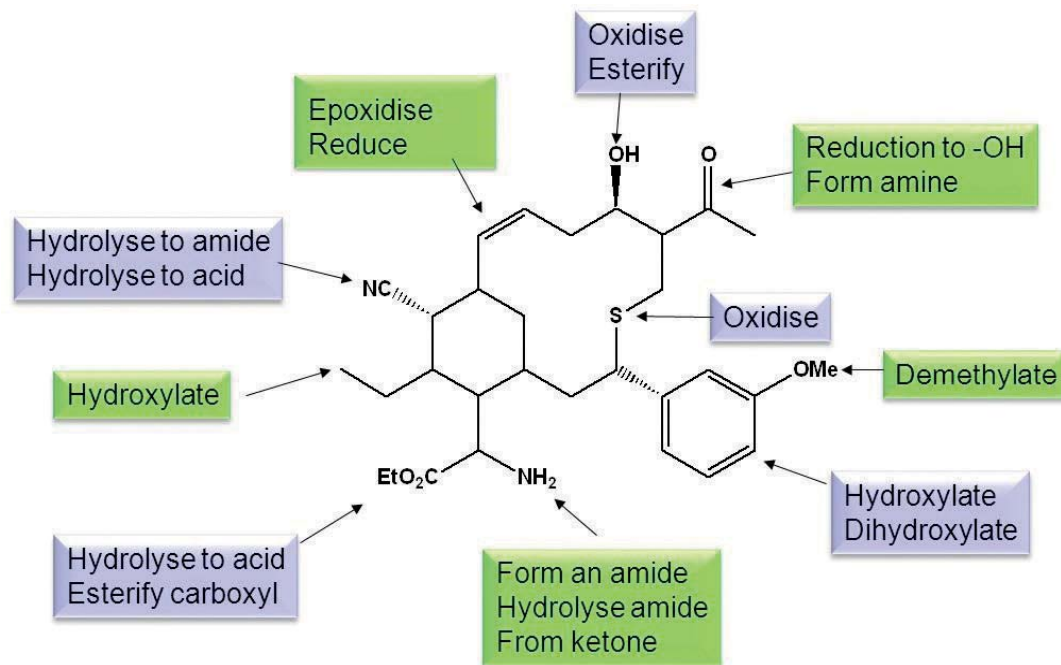


Figure 1 – An illustration of enzyme versatility.

Biocatalysis was once the preserve of specialists working with limited in-house collections of enzymes and cultures. A revolution in molecular biology has enabled the rapid development of much larger and more diverse enzyme collections at Almac and other companies, and has also enabled astonishing improvements in enzyme process performance to be realized. This has elevated biocatalysis from a niche to a widely applied mainstream technology, relevant to a diverse range of chemical transformations.

The reason for the surge in the application of this green technology, in our view, is simply that success breeds success. Unlike ten years ago, we now have a suite of supporting technologies that can really make a difference in enzyme development, such as bioinformatics, enzyme evolution and high throughput screening, as well as substrate and process engineering. Figure 2 highlights the options for driving bioprocessing

from enzyme selection (enzymes are derived from metagenomics, bioinformatics, protein engineering and in silico design), process optimization (process and substrate engineering, DOE, application of process intensification tools such as ultrasound and continuous flow, and enzyme immobilization) and actual delivery of API (GMP or non-GMP), advanced intermediate or fine chemical.

Inevitably, developing and exploiting cutting-edge biocatalysis technologies generates intellectual property and is accompanied by a need to protect, where possible, the processes and products surrounding it. It is useful to consider how patenting attitudes have changed as the technology has evolved and expanded in recent years.

## The changing landscape of IP strategy in biocatalysis

In the early days of biocatalysis it was enough to simply patent an enzyme catalyzed reaction without too much definition of the enzyme

beyond its basic classification such as dehydrogenase or nitrilase. So, a claim could be very broad as in the following example taken from EP0332379B1, granted in 1996.

“A process for the production of an L- $\alpha$ -amino acid which comprises causing a microorganism having enantioselective nitrile-hydrolyzing activity to act at a pH in the range of 8-12 on one or more  $\alpha$ -aminonitrile compounds represented by the following general formula.....”

Such an unspecific claim would be unacceptable today, since it quickly became common knowledge that enzymes are extremely powerful and versatile catalysts. It is no longer surprising or considered inventive that an unspecified biocatalyst might perform a certain biotransformation, even if it had never been demonstrated or published.

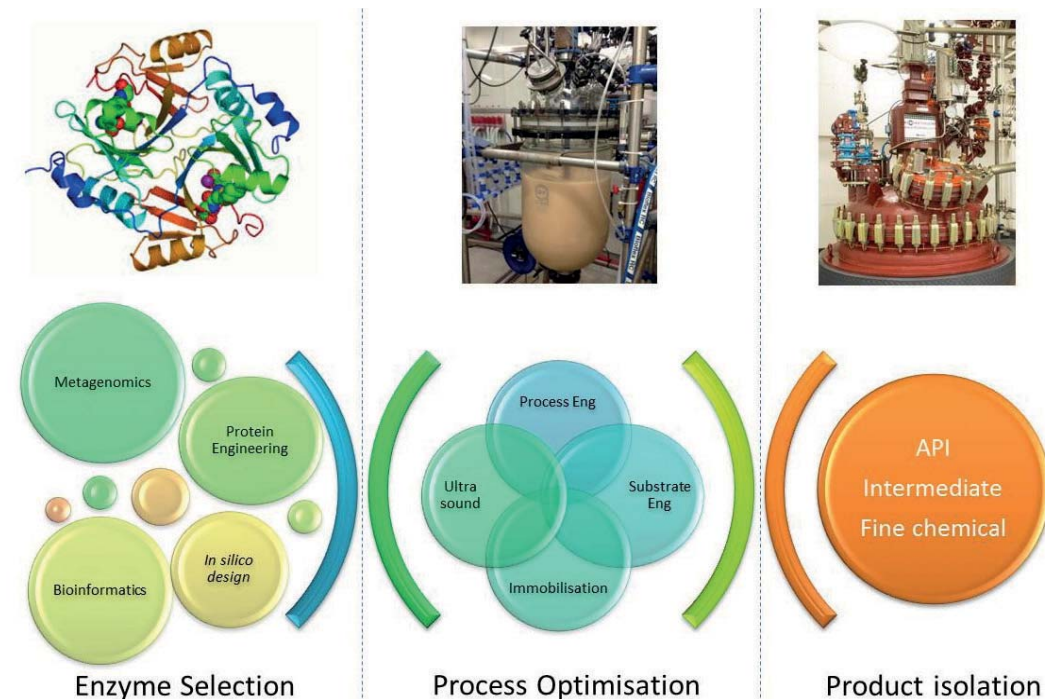
With biocatalysis in its embryonic years, cloning, expression and sequencing technology was driving a revolution in the health

care sector, and biocatalysis - as an offshoot of this - was a major beneficiary. The amount of searchable enzyme sequence data that was readily available increased rapidly and exponentially, and this inevitably influenced IP strategy. Homology claims became the centre of attention for a period of time in an attempt to capture as many wild-type enzymes as possible, whose sequences were known, for a process of interest. Thus, typical claim language would refer to an enzyme sequence and any derivatives of the enzyme to a certain level of homology in protein sequence. It was realised, however, that claiming all enzymes to a level of 80% homology to the discovered enzyme often yielded little protection since enzymes with much lower levels of homology could be just as effective for a given biotransformation.

Meanwhile, enzyme engineering and evolution technology became a widely practised technology, thus introducing another level of complexity to the landscape. In the formative years of this technology, the focus of attention turned towards broadly protecting enzymes and engineered mutants in patent claims with less regard for any particular intended use. This had the unintended consequence of revealing much about the underlying technology and approach involved, disclosing how subtle changes in enzyme structure were able to influence catalyst performance. Furthermore, it fired up an argument as to whether a biocatalytic process should be patented at all for fear of teaching others about the underlying technology. This is aside from the ongoing concerns of others' regard for respecting intellectual property rights.

Today a strong biocatalysis patent will most likely combine three elements into its main claims to give the assignee the best chance of securing a competitive advantage:

- First, it will have a reaction focus, defining the core reaction that is of commercial interest together



**Figure 2 – Enzyme selection to product isolation.**

with varying amounts of detail on the reaction conditions required for the biocatalytic reaction to occur.

- Second, there will be enzyme/catalyst definition to describe the origin of the enzyme/catalyst, which can be either the commercial source or the sequence data elsewhere in the patent. If the sequence is given, there may be an attempt to capture homologues by a traditional claim of percentage sequence identity to the originating sequence.
- Third, and critically, there will be definition of changes that have been made to the engineered or wild-type enzyme sequence that endows the enzyme with properties that enhance its performance to a level where its use allows the reaction of interest to become viable. This immediately raises the bar for others to find something similar and change, for example, an enzyme of lower homology in other ways at the sequence level, since it is now prior art and has been shown to be possible.

When these three elements are combined, the patent application has a good chance of satisfying three key requirements:

commercial value, novelty and inventiveness. This last requirement of inventiveness is of course the hardest to satisfy. If an assignee can argue that their target reaction is greatly improved and enabled through deliberate and inventive choice or design of the enzyme, then they have the best chance of securing a granted patent. It should be noted that a mere sequence of an enzyme (standard enzyme catalysis) is no longer patentable, may it be a wild type or even an engineered enzyme within a screening kit. For the process to be both novel and inventive, the application must show or demonstrate reasons why the enzyme is superior or enables the specific A to B transformation which would not have been obvious to anyone skilled in the art. This means that the selected enzyme from a commercial kit needs to be further engineered for the A to B transformation to identify a new sequence that has superior enabling power to allow the transformation to work commercially.

### Choose the IP strategy that suits best

The options for the customer are as follows:

1. Substance of matter patent –

this is the best for the customer as they control their end product (independent of the technology used to synthesize it).

2. Process patent – protects their A to B transformation, whether using an enzyme or not. This is the easiest patent to file, however it may be harder to get granted in the future due to meeting novelty and inventiveness criteria. The enzyme can simply be stated in the patent as the commercial code just like any other chemical reagent.

3. Process patent with sequence and homology claims. To get this granted, the divulged sequence will need to be designed for the specific A to B transformation and show both novelty and inventiveness. Simply taking a wild type or engineered enzyme sequence from a commercial kit is not enough to be novel and inventive and therefore not patentable in its own right. It is best to go for option 2 above by not showing the sequence to the world.
4. New catalysis for a said enzyme, eg an unexpected reaction not known for being catalyzed by an enzyme in prior art. This is probably the best and tightest patent.


When claims are broad, the patent becomes very hard to police. If it is a very specific reaction, good commercial planning needs to be

assessed to ascertain if return on investment is achievable.


For all the above points, the customer needs to assess the commercial landscape and what their shareholders expect as key milestones in the company's lifespan and their product development. However, even where the chances of securing a strong patent appear to be good, in all of this there is still a healthy debate needed for every biocatalytic process as to whether to keep it as a trade secret or embark on a patent filing.

What we see at Almac is different customers have different concerns and/or objectives. Some companies may have little concern about how an intermediate is synthesized since their value is captured and secured in the drug substance of matter's patent and they would like suppliers to compete to make intermediates for their drugs at the lowest possible cost.

Other companies though, may have different priorities and pressures, for example emanating from venture capital investment and related stakeholders. Process technology for making their drugs and/or intermediates may be much



**With biocatalysis in its embryonic years, cloning, expression and sequencing technology was driving a revolution in the health care sector, and biocatalysis - as an offshoot of this - was a major beneficiary.**



more important to these companies.

Often companies that are keen to protect the developed enzyme processes as much as possible, (especially where such processes are wrapped up in critical pathways) do so for company development and the need to increase shareholder value.

Companies must ascertain what creates the most value, eg is speed of process development and product delivery or commercial protection key at this point?; Is this intermediate

important to a family of valuable compounds or are there multiple technologies available to make the product?; Is there assurance that the enzyme (or technology) will be available at scale if needed?; or is there freedom to operate, etc.

For processes enabled by extensive and costly enzyme and process engineering programmes, filing a patent protecting the novel design is most common, particularly in contested market spaces, so as to prevent others from doing the same. A simple publication in a scientific journal would also have the effect of securing permanent access to the technology while avoiding hefty fees. However, this also enables access by others, and is therefore chosen when this is not deemed problematic. Examples have arisen, for example, from Big Pharma research into future generics space, or from API maker's inventions towards improved supply with key raw materials and building blocks.

A number of factors therefore need to be weighed up in the argument for or against secrecy. Can a good case for inventiveness really be made? Is a competitor likely to find a similar process and obtain a

patent themselves? Does it make sense to reveal the sequence of a catalyst and how it was improved? Is the life-time cost of the patent justified? These are just some of the questions that need to be considered.

### In conclusion

The proven ability of biocatalytic technology to produce hard cost savings for pre-existing processes or to provide economical access to NCEs in the pharmaceutical sector ensures increased investment year on year in this area. With the use of this cutting-edge technology comes much opportunity for intellectual property generation and this needs careful evaluation in the context of how this is exploited. Almac's approach is to listen carefully to customer needs and to follow the best path forward that takes account of the numerous risk factors at play. Some cases merit patent application whilst others favour a trade secrecy approach, or the opposite – publication in a journal.

### Further information

**E: [tom.moody@almacgroup.com](mailto:tom.moody@almacgroup.com)**

## About the Authors

**Professor Tom Moody** graduated from The Queen's University of Belfast with a 1st Class BSc (Hons) in chemistry in June 1998 before returning to gain a PhD in Physical Organic chemistry in December 2001. He has also completed a Masters in Business graduating with distinction in July 2007 specializing in business strategy. His work has earned him numerous accolades and he is co-author and author of more than 90 publications and patents. He is currently VP Technology Development and Commercialisation for Arran and Almac in Ireland and works in the area of Chemistry & Biocatalysis and its application towards the synthesis of chiral molecules, metabolites and labelled compounds. He is responsible for managing a multi-disciplinary team of both chemists and biologists to obtain commercially useful biocatalysts and their intended applications, developing biocatalytic processes from mg to tonne scale manufacture including development of fermentation processes to yield the desired biocatalyst. He has been a scientific leader and problem solver in >50 commercial projects in the past three years and acts as a consultant in the area of biocatalyst development for pharmaceutical and biotech companies. He is also an honorary Professor at Queen's University of Belfast in the area of

biocatalysis. He may be contacted at [tom.moody@almacgroup.com](mailto:tom.moody@almacgroup.com).

**Dr Stefan Mix** was born in Berlin, Germany, where he completed his secondary education. After graduating with a Diploma in chemistry, he received his doctorate in 2004 from the Technical University of Berlin after working in the group of Professor Siegfried Blechert on stereoselective synthetic methodology and olefin metathesis. He is the author of several publications, and has been working with Almac Group since 2005. He has gained broad industrial experience including in applications of biocatalysis, crystallization development, process development for chiral building blocks and APIs, and technology transfer to manufacturing network partners. He may be contacted at [stefan.mix@almacgroup.com](mailto:stefan.mix@almacgroup.com)

**Dr Steve Tayloris** an experienced practitioner of biocatalysis having spent many years allied to the pharmaceutical industry developing enzyme catalyzed processes for small biotech companies through to global chemical companies. He has worked with Almac Sciences for more than 15 years since the inception of the biocatalysis group. In addition to working with Almac, he has interests in projects to biotransform and repurpose natural products for use in cosmetic, food and drug industries through his work for Celbius Ltd.



# The case for homogeneous ester hydrogenation

Authors: Dr Antonio Zanolli-Gerosa, R&D Director at Johnson Matthey and Dr Lucy Milner, NBD Manager at Johnson Matthey

A revolution in homogeneous hydrogenation catalysis is in full swing. This has been triggered by a renewed enthusiasm for operationally simple, cost-effective and sustainable transformations and is supported by the continuous evolution of more active, chemoselective and efficient catalyst families. Amongst the emerging transformations, homogeneous ester hydrogenation (EH) using ruthenium-based catalysts has now become an exciting and industrially viable addition to the catalytic toolbox. Dr Antonio Zanolli-Gerosa, R&D Director, and Dr Lucy Milner, NBD Manager, discuss the reasons that should, and will, lead to an ever-increasing implementation of this technology.

At the beginning, innovations in the homogeneous ester hydrogenation (EH) field have largely been driven by the flavours & fragrances industry. This is motivated by their high number of primary alcohol targets which require robust, selective and economical manufacture. As such, large players including Firmenich, Takasago, Givaudan and DSM have all developed proprietary technology in this field.

Building on its track record as a trusted and innovative catalyst supplier, Johnson Matthey has licensed a world-leading class of EH catalysts and made the technology accessible for all of the company's fine chemicals customers. Examples of such catalysts, developed by Professor Dmitri Gusev of Wilfrid Laurier University's research group, are illustrated in Figure 1.

As with any emerging technology, effective propagation into new markets can only occur when a product meets the unique demands of each user. The most valuable benefits for each stakeholder will depend both on the industry and their role within the development chain (Figure 2).

Applications within the pharmaceutical industry require the catalyst to be tolerant of diverse and complex functionalities, ideally operating at low pressure to allow easy outsourcing of the route to CMOs. Applications in the agrochemical, flavour and fragrances, fine and commodity chemical industries will face additional pressure on factors such as process



Figure 2: The value in using homogeneous EH from discovery to launch.

efficiency, low catalyst loadings and, desirably, catalyst recyclability. All end-users require safe and reproducible chemistry, selective processes and simple reaction work-ups – all of which are key benefits offered by homogeneous EH catalysis.

## Why should industry use homogeneous ester hydrogenation?

### The economic case

The fine chemicals industry has been using hydride reductions for many decades and most chemists are familiar with the technology from lab-scale experiments to large-scale applications. Bulk prices of the most common hydride reagents can range anywhere between €5 and €20 per kilogram. Even considering stoichiometric (or higher) molar ratios, this appears cheap compared to the headline price tag of a homogeneous catalyst. However, in an optimized process, only a minimal amount of catalyst is required for converting large amounts of starting material to product. A rough estimate for the point where an EH catalytic process becomes more competitive than a hydride process (purely looking at the cost of reagents) sits around the catalyst molar ratio of 10,000/1. This threshold, which has been achieved and surpassed on several targets, will be lower in the case of high-value substrates (eg chiral substrates) or where the catalytic route provides significantly enhanced selectivity or yield. Besides this very basic cost model, a more sophisticated analysis should include the cost savings associated with simpler work-up and much-reduced waste generation.

### Safety, simplicity and sustainability

Any chemist who has run hydride reductions can intuitively appreciate the advantages of avoiding the handling of hazardous reagents and the complex, exothermic work-up (think  $\text{LiAlH}_4$ ), which produces several times the reaction volume in organic and contaminated aqueous waste. In lab-

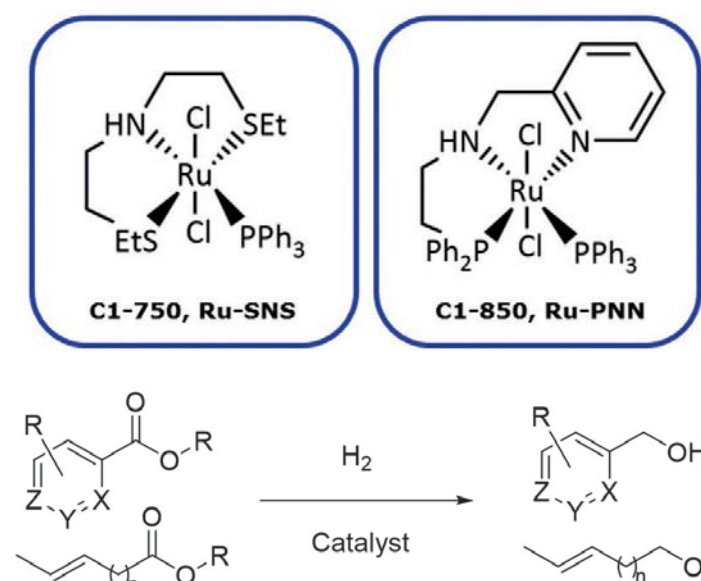


Figure 1: Typical Gusev catalysts as developed by the research group of Professor Dmitri Gusev at Wilfrid Laurier University.

scale reactions, the risks can be (generally) safely managed and, in absolute terms, waste generation is minimal, but the process safety hazards and environmental impacts increase significantly upon scale-up. An optimized homogeneous EH process provides selective and quantitative (> 95%) conversion to the desired alcohol under controlled conditions and the catalyst can be removed by a simple precipitation step using a co-solvent or by distillation.

Johnson Matthey's survey of hydride reductions of esters reported in *Org. Proc. Res. Dev.* confirms poor environmental metrics and E-factor values in the 30 to >100 range are common. Even with the difficulty of making exact like-for-like comparisons, JM estimates that similar transformations with homogeneous hydrogenation catalysts would reduce the sustainability metrics by a factor of five- to tenfold. As the pharmaceutical industry faces mounting pressure to achieve sustainability, the use of simpler catalytic processes is an unmissable opportunity to minimize the environmental impact of operations and improve green credentials. As highlighted in Figure 3, the possibility of using many of the simpler substrates 'neat' can further increase process efficiency.

Despite the requirement to operate under hydrogen pressure, the benefits offered by the enhanced safety, simplicity and sustainability of homogeneous EH catalysts far outweigh the initial investment to explore this new technology. JM's in-house R&D teams have demonstrated efficient turnover at hydrogen pressures as low as 5 bar, well within the pressure capabilities of most CMOs. The application of continuous flow technology, where higher pressure can be operated with a limited equipment footprint, will be another viable alternative.

### A bright outlook

Homogeneous EH catalysis has a bright future in the fine chemicals industry, however, one major hurdle to its uptake is the 'human factor'; in an industry where time pressure is overwhelming, chemists tend to rely on trusted, established technology, even when more effective alternatives become available. However, as molecules continue to become more structurally complex, environmental regulations continue to tighten, and health and safety policies become more stringent, the case for considering improved catalytic routes will become imperative. Johnson Matthey's role in the homogeneous EH journey is twofold; first, to provide rapid access to high-quality, best-in-class technology and, second, to offer its extensive in-house expertise to support customer uptake optimization of EH within their specific processes.

### Further information

E: [pharma@matthey.com](mailto:pharma@matthey.com)

#### References

##### Gusev catalysts

- Gusev et al. *Angew. Chem. Int. Ed.* 2013, 52, 2538  
 Gusev et al. *Organometallics* 2012, 31, 5239  
 Zanotti-Gerosa et al., *Chimica Oggi*, July/August 2019, 37(4)

##### Reviews on EH

- Clarke *Catal. Sci. Technol.* 2012, 2, 241  
 Ikariya et al. *ACS Catal.* 2012, 2, 1718  
 Beller et al. *Org. Process Res. Dev.* 2014, 18, 289  
 Pidko et al. *Chem. Soc. Rev.* 2015, 44, 3808  
 Dub et al. *Nat. Rev. Chem.* 2018, 2, 396  
 Pidko et al. *Chem. Soc. Rev.* 2018, 47, 1459

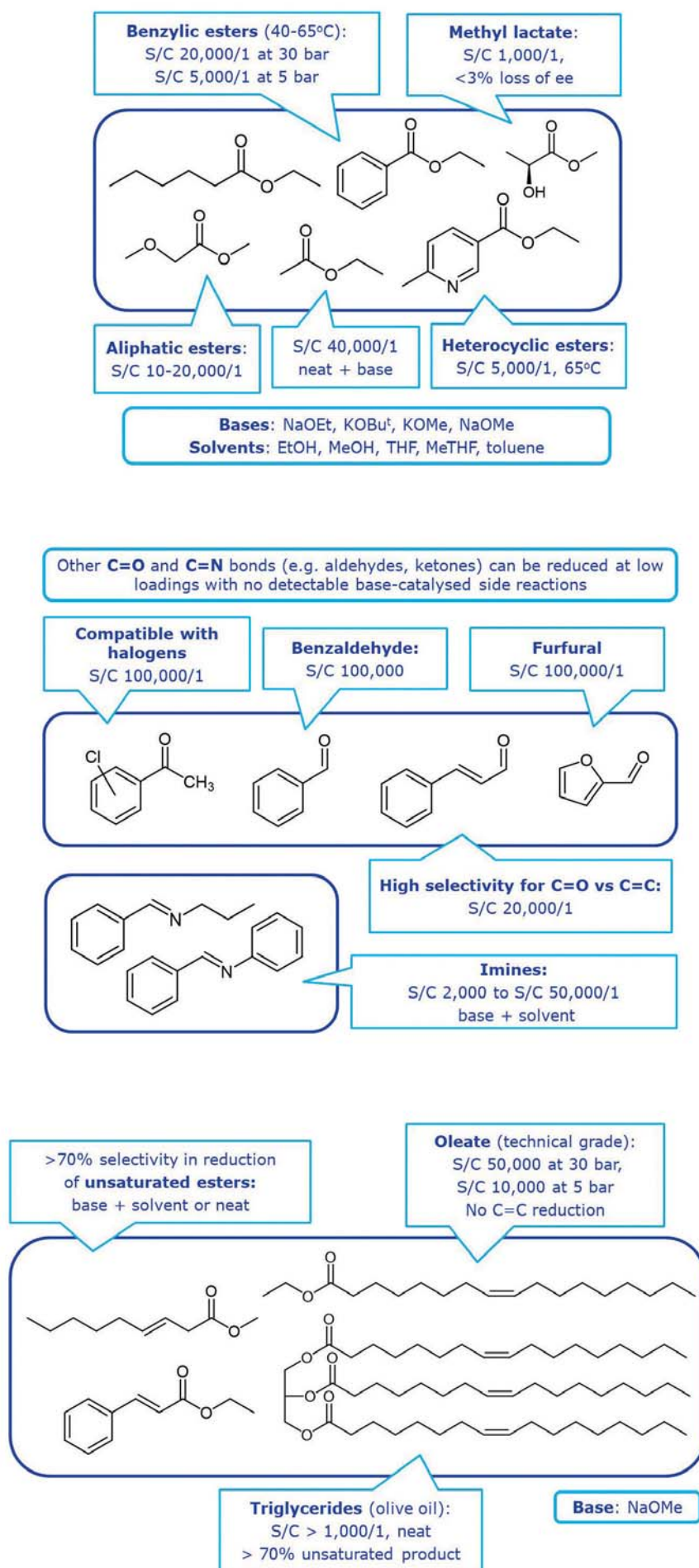


Figure 3: Substrate scope, molar substrate to catalyst loading (S/C), selectivity.

# Topical drug formulation: the challenges and new solutions

By Ralph Landau, Head of Development, Cambrex Whippany, Cambrex Corporation

Drug product formulation is a complex endeavour and every formulation presents unique development and manufacturing challenges that will vary based on the type of drug and the method of administration. Here, the particular challenges facing formulators of topical drugs are discussed and ways of addressing these are presented.

Topical drugs are prescription or over-the-counter (OTC) dermatological drugs or pain medicines that are manufactured as lotions, creams, foams, solutions, suspensions or gels. They are classed as a semi-solid drug product based on their composition of water, oil, the active pharmaceutical ingredient (API) and other ingredients such as thickening or gelling agents, emulsifiers, preservatives, antioxidants and solvents. This type of formulation is particularly challenging because it requires specific consistency and stability, and aligning the mechanism of action and sensory characteristics can be challenging. In addition, like liquid formulations, topical drugs are typically less stable and have a shorter shelf life than solid dosage forms.

The mechanism of action pertains to the intended use of the topical, and whether it is meant to treat the surface of the skin by penetrating to a certain layer of the dermis, or into muscle tissues, as with pain-relieving drugs. A topical should be easy to apply and have a composition appropriate to the needs of the product. From a sensory perspective, a topical should have a good texture (also known as skin feel), appearance and smell that should not change during the documented shelf life of the product.

## Getting into the skin

Topical formulations can be applied to treat a range of dermatological indications including dermatitis, eczema, pain, psoriasis, antimicrobial treatment/infection,



Ralph Landau

diabetic ulcers and acne.

In addition to an appropriate composition and texture, a topical should be easy to apply and not cause irritation. While this may sound simple, it requires a concentrated development work focused on five key physical characteristics:

1. Homogeneity
2. Particle distribution
3. Grittiness
4. Spreadability (ease of application vs tendency to drip)
5. Need for surfactants

The viscosity of a topical has a strong impact on skin feel and will help to determine how a topical is classified, in addition to all five of the key physical characteristics listed. Ointments are made without an aqueous phase and have the thickest feel of all the topical drug types. Gels are made without an organic phase and tend to have the lightest feel. Creams and lotions are emulsions, the only real difference between them being their viscosity, creams being thicker than lotions.

The choice between formulating a product as an ointment, lotion, cream or gel is driven by the indication, including what area of the body is being treated and the frequency of application. It can also be driven by market forces. For example, just as a tablet is not considered equivalent to a capsule, the various types of topical dosages are also considered to be different from each other, which means a generic of 'Brand A's' lotion could not fill a prescription for 'Brand A's' cream. Therefore many companies will introduce topical line extensions in a new topical dosage form in order to remain exclusive. Determining whether the API needs to act on the skin surface or whether it should be absorbed into the skin is critical in the choice of formulation as there are ingredients that encourage or discourage penetration.

## Quality process for quality products

Drug product formulation success relies on batch-to-batch consistency and the reliability of the process and of the product. Somewhat unique to topical drugs is the property of viscosity. Many processing factors can affect the final viscosity, including mixing speed and duration as well as small changes in composition, particularly of thickening agents. Viscosity is a critical variable to control in topicals because it is related to drug delivery rate.

When manufacturing bulk powder for tablets or capsules, the time of mixing (for example in a V-blender) has very little

**A topical should be easy to apply and have a composition appropriate to the needs of the product. From a sensory perspective, a topical should have a good texture (also known as skin feel), appearance and smell that should not change during the documented shelf life of the product**

impact if the mixing is continued an extra hour after homogeneity is achieved. However, semi-solids can experience significant viscosity changes (shear-thinning or shear thickening phenomena) if process variables are not tightly controlled. Whether working with prescription topical drugs or OTC products, there is a need to achieve the exact same texture, viscosity and homogeneity across batches. This not only affects the clinical performance of products, but also affects the patient experience when the patient applies the topical. Products with variable viscosity tend to receive more customer complaints.

Even the smallest of details can impact the critical quality attributes



for topical products, highlighting the importance of documentation and managing the process closely from the start. Material sourcing will have just as much impact as working with the right equipment and testing methods.

### Topical formulation technicalities

Successful process design requires extensive analysis and preparation prior to implementation. Important variables in topical formulation will require experimentation and innovative solutions. Some of the most crucial elements to consider are:

- Identifying/profiling the API
- Optimal concentration of viscosity agents
- Degradation of APIs depending on formulation composition
- Appropriate filler and preservative ingredients
- Sterile filtration requirements (for sterile topicals, e.g. sterile ointments) and temperature impact
- Packaging preferences
- Storage and transportation

Once the drug needs are defined and a topical formulation is selected, the focus moves to process planning and implementation. The right equipment is imperative for manufacturing steps, including mixers, emulsifiers, mills, and agitators. Scale-up is a major hurdle for semi-solids because liquid systems exhibit more variability regarding mixing and mixing environments and often change when transferring from lab to plant, much more so than in solid dosage form processes. Temperature control is also critical due to its effects on viscosity and other properties.

Some formulations with the same exact composition can have different density and viscosity simply due to the path taken during manufacture, for example longer mix times or temperature excursions. To achieve the

temperature ranges required during manufacturing, jacketed vessels can be employed, heating or cooling as needed. With automation advances, there are now electronic recipes available to control temperature and mixing speeds. In principle, the run being completed today can be an exact replicate of what was done yesterday using this approach, which is very useful for semi-solids.

In-process sampling and characterization is employed to confirm that the manufacturing run is progressing within specification, typically when the bulk semi-solid is made and prior to filling into bottles or tubes. In some cases, specific samples during bulk manufacture are needed (for example, to assure pH is where it needs to be in a pH-sensitive process).

### Testing topicals

Like all prescription products, topical dosages must be fully tested and meet specifications

prior to release. Some aspects of semi-solid analytical work are unique, such as viscosity, but to a large extent, most of the same methods that are used for traditional oral solid dosage analysis are applied. The difference is that topical dosage form analysis focuses on the structure of the emulsion or any heterogeneity instead of the particulate structure analyzed for capsules and tablets.

One method that is truly unique to topical dosage forms is in-vitro release testing (IVRT), which mimics how a topical formulation will penetrate and interact with human skin. It achieves this by placing a synthetic membrane or cadaver skin across an opening followed by application of the test product. Beneath the 'skin' or synthetic membrane is a solution that simulates the environment just under the skin and in IVRT testing samples of the solution are taken periodically to see how

much active drug has penetrated this membrane. This type of testing is generally done when equipment changes happen or during technology transfers. In some cases, the FDA will require the applicant to conduct IVRT testing on every batch due to concerns around batch-to-batch reproducibility.

Topical dosage form products will also need to be tested for bioburden to demonstrate that they do not harbour any microbial contaminants. Topicals often contain water as an ingredient, making them more susceptible to microbiological contamination than oral solid dosage forms. Bioburden and microbial testing needs will vary based on the drug product being formulated but must be exhaustive. Depending on the type of product, topicals will undergo the following tests:

- Bioburden testing to measure the population of viable microorganisms in a product



**The Ekato 150L Mixer Homogenizer is used for semi-solid manufacturing from 40 to 150L employing either high or low solid-liquid shear and comprises a jacketed main vessel and 75L side vessel under PLC temperature control. There is also a clean-in-place (CIP) system to ensure safe and highly-efficient cleaning of the equipment.**



**The Romaco Unipac 20100 Tube Filler is also used in semi-solid manufacturing, specifically to fill PVC, laminated and metal tubes with topical products in quantities ranging from 2-250g.**

- Microbial testing for objectionable species (there are some species that must be zero)
- Microbial enumeration of microorganisms in a product and comparison of that to release specifications (typically 100 CFU/mL)

Additional preservative efficacy testing and antimicrobial effectiveness testing (AET) are performed prior to launch/approval of a product to assess the effectiveness of antimicrobials preservatives added to the formulation. In any case of failure, speciation testing must be performed.

### Topical formulation manufacturing

The number of pharmaceutical companies with the right level of existing topicals manufacturing capacity and internal topical dosage expertise is very small compared to the number of oral

solid dosage-focused firms. Most often, it is not cost-effective for these companies to manufacture every product themselves. Particularly in the case of complex topical formulation development, scale-up and commercialization, it is common for this work to be outsourced to an expert contract development and manufacturing organization (CDMO).

Regardless of whether formulation and manufacturing are done in house or outsourced to a CDMO partner, achieving

a stable, clinically effective and cosmetically acceptable formulation is critical to success. Due to the highly specialized science of formulating and manufacturing topical products, when outsourcing many companies will look to work with a CDMO that can support the process from start to finish.

With formulation development and manufacturing capabilities at its Mirabel, Quebec, Canada site, and sterile ointment production capability at its Whippany,

New Jersey, US site, Cambrex offers a one-stop approach to topical formulation from process development, through to scale-up, transfer and commercialization. Across the company's drug product sites, high-performance semi-solid formulation support is available from 10kg to 900kg with complementary packaging options.

Cambrex is able to work with new products or complete technology transfer for existing products to bring safe and effective topicals to the market by combining state-of-the-art technologies, accessible capacity, and a quality-driven approach, thus safeguarding the integrity of the process for the life of the product.

### About the author

**Dr Ralph Landau** is Head of Development at Cambrex's Whippany, NJ site and has 30 years of pharmaceutical experience in both branded and generic businesses. With formal training in chemical engineering, he has spent the majority of his career leading operations and R&D/regulatory functions in a number of companies, including Merck & Co, Novartis, Fougere and Sandoz, and over the past decade has led several companies through compliance and profit growth initiatives.

**Further information:**  
**Dr Ralph Landau**  
**Head of Development**  
**Cambrex Whippany, NJ, USA**  
**Email: [ralph.landau@cambrex.com](mailto:ralph.landau@cambrex.com)**



# Eigenmann & Veronelli - Creating value for customers in chemical manufacture and distribution for more than 100 years

Eigenmann & Veronelli was established in 1910 and now offers distribution, manufacturing and logistics services to customers across 17 industry sectors. Here, company CEO Luca Mantovani describes how the business has developed over the past 110 years and outlines its vision for the future.

Established in 1910 by entrepreneurs Giovanni Eigenmann and Adolfo Veronelli, Eigenmann & Veronelli has been creating value for customers and suppliers in the distribution and production of fine chemicals, speciality chemicals and performance materials for more than a century. The company combines local market knowledge with international chemical innovation to meet the ever-evolving demands of the global life sciences, nutrition, polymers, and industrial chemical sectors with a direct presence in five countries across Southern and Eastern Europe, and sales in more than 30 countries around the world. Eigenmann & Veronelli offers a range of manufacturing, analytical and logistics services for customers across 17 industrial sectors, and is organized into four business units: Life Sciences; Nutrition; Polymers; and Industrial Chemicals.

## Sustainable innovation

"For more than 100 years, Eigenmann & Veronelli has supported both principals and end-customers, leveraging our extensive market knowledge and technical know-how to develop customized solutions that deliver value across the supply chain," says Luca Mantovani, the company's CEO. "This combination of long-standing experience and wide-ranging expertise makes Eigenmann & Veronelli a reliable partner to ensure the quality, safety and sustainability of its customers' products and materials. Building on this enduring foundation has enabled us to



**Luca Mantovani**

seize unprecedented opportunities for innovation, discover novel applications for existing products, introduce new products to the market and ensure long-term sustainability and a constant focus at the company on offering targeted solutions based on the individual needs of customers and suppliers. This has been the key factor in E&V's past, present and future success," Mantovani states.

## Successful history

"E&V has a successful history of business growth based on solid and sustainable company values and strong expertise. Our main mission of 'being the catalyst between supply and demand' has been the base for developing very solid relationships with primary speciality chemical companies that have been working for several decades in providing existing and innovative products for distribution in the territories where E&V operates. In addition, E&V has, over the years, developed manufacturing capabilities in order to provide contract manufacturing services to major companies as well as for developing its own products," Mantovani adds.

"Cosmetics is a very important sector within E&V and the most

important within the company's Life Science cluster. We distribute products from major international companies and also carry out manufacturing of some key products used in the cosmetics industry on a CMO basis. Business has been growing organically by adding new suppliers in order to complete our range of products as well as by expanding geographically. On the manufacturing side, we specialized in producing esters that were wholly of natural origin, these ingredients finding application in skin-care and make-up products," he says.

Eigenmann & Veronelli's business has overall a value of about €380 million and a CAGR of about 4-5% with distribution representing the largest part of the company's business. "We have both the ambition to continue growing organically as well as via selected acquisitions that fit our overall strategy," says Mantovani. "Over the past ten years we have added four new companies to the group and we intend to accelerate this process through further investment, with cosmetics as one of the main growth options for the future. On the geographic side, we aim to strengthen our position in the regions where we are already present and also develop sales of our products outside Europe."

## Investing in human resources

Mantovani says that one of the key success factors for E&V has always been investing in human resources with strong technological

and industry knowledge, which he says has helped the company to transfer innovative products from its principals to customers by providing the necessary expertise to its clients: "We believe that this is the right way to differentiate and satisfy all our 'stakeholders', principals and customers alike. In the cosmetics sector, we have both commercial as well as technical people, with an application lab that can also develop tailor-made formulations for different clients," he says, adding that cosmetic is one of the most innovative and fast-growing sectors within the life sciences industry, one that will benefit from major new developments such as health & wellness, sustainability, and increased connectivity via digitization.

"These trends will drive innovation and an appetite for further investment. E&V will pursue all this by continuing to develop relationships with primary industry leaders as well as by continuing to develop its CMO business.

"Building on our strong values, keeping alert to the main trends and staying agile in executing actions are themes that will keep us busy for the future in order to pursue our ambitious objectives of growth and making a contribution to sustainable progress in the cosmetics sector," Mantovani concludes.

**Further information:**  
**Luca Mantovani**  
**CEO**  
**Eigenmann & Veronelli**  
**E: [lmantovani@eigver.it](mailto:lmantovani@eigver.it)**



Your Peptide needs, from R&D to GMP Manufacturing,  
PolyPeptide provides **Global Support** for a **Quality Solution**



© Frédérique Clément © Shutterstock

## GLOBAL SUPPORT FOR A QUALITY SOLUTION

At PolyPeptide, going the extra mile with our customers is a priority. Agility, global presence, flexibility, ability to create fast custom-tailored solutions, and exceeding the highest requirements, are all key benefits that you could only expect from a world leader in peptide manufacturing.

Our client's success is our primary goal, with a proven track record in producing cost-effective proprietary and generic GMP grade peptides for the pharmaceutical and biotechnology industries.

Our long term relationships with our customers are based on transparency and an approach to partnership which ensures that we provide **global support** for a **quality solution!**



THE ULTIMATE PEPTIDE PARTNER

[www.polypeptide.com](http://www.polypeptide.com)

Sales contacts: **France** +33 388 790 879 - **Sweden** +46 40 366 200 - **USA** +1 310 782 3569

**BELGIUM - FRANCE - INDIA - SWEDEN - USA**

# Hi-tech cosmetics products and services give an individual look

George Henry, Associate Analyst at GlobalData, explains how digital technologies and personalization are meeting individual consumers' needs in the cosmetics sector

Personalized beauty is the design of products and experiences tailored to meet individual needs and creates a two-way relationship between brands and consumers. Personalization has become a core focus for the beauty industry, as digital lifestyles present consumers with greater options that align with individual needs and preferences. Manufacturers that create bespoke products gain 'granular' levels of customer information that most traditional brands would not have access to. This allows companies to gain unique insights from their consumer base and use this data to better optimize their product offering. From self-learning algorithms to data collection for hyper-specificity, personalized beauty has revolutionized the cosmetics industry; and will remain a core consumer trend going forward.

Personalized beauty has emerged to meet the demands of previously neglected consumer segments of the cosmetics market. It has gained momentum in the mass-market as consumers crave products tailored for specific needs; particularly as cosmetics are inherently individualistic. In turn, more brands are striving to reach consumers that have previously not been catered to by generic products produced for the mass-market.

Halal beauty is one instance of personalization



**George Henry, Associate Analyst at GlobalData.**

that has emerged in response to a specific need for ingredient-conscious Muslim consumers. Other examples include hair care for women with African-Caribbean hair, as well as skincare products for Asian men.

## 'Beauty tech'

The Internet has removed many previous inhibitors to traditional brand relationships as consumers are now able to communicate directly with manufacturers through platforms such as social media. Digital technologies are becoming vital to the consumer relationship -

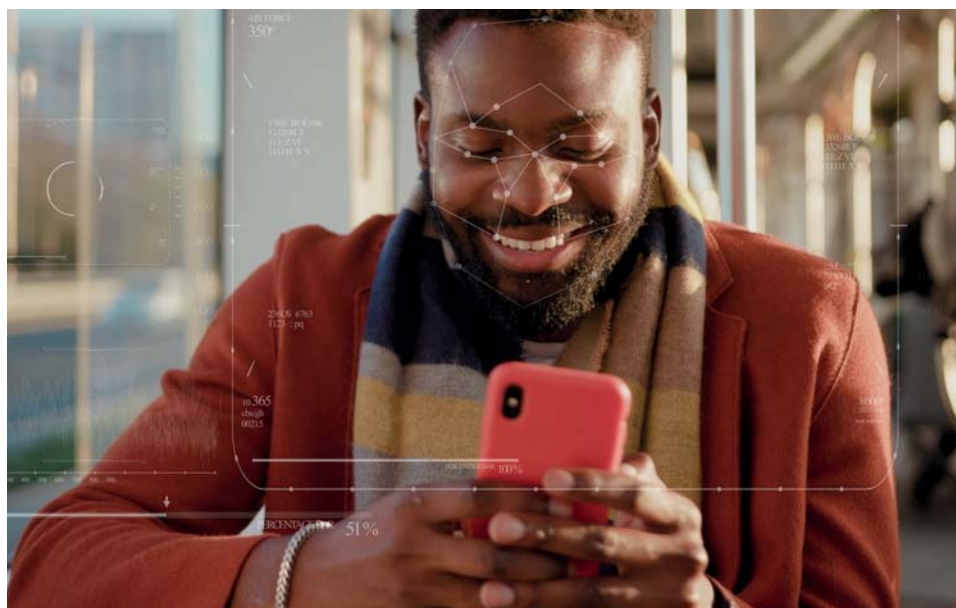
indicating the influence beauty technology continues to have. Direct to consumer (D2C) relationships will continue to grow as customers share their personal insights as standard. Such 'beauty tech' has led manufacturers to develop product experiences that cater to processes, rather than just the transactional retailing of mass-produced products. Major players are creating their own tech-enabled devices to better the individual steps in personal care routines.

For example, new technologies, such as genomics, enable unprecedented levels of analysis at a granular level. The integration of these sciences can be used in cosmetics to identify various individual skin needs, including sensitivities and allergies, and other important details that enable brands to optimize individual formulations. DNA-based skincare is another pioneering category of the beauty market, with market entrants already showcasing the potential that a deeper understanding of genetics can have on personalized beauty.

Technology helps manufacturers align with what customers deem to be important. Ethical consumerism includes the reduction of single-use plastic and is one such trend that can be confronted by brand investment in sustainable alternatives. One example is L'Oréal's investment in biotech start-up, Carbios, which develops plastic recycling technologies. L'Oréal's commitment to move to 100% recyclable or compostable packaging by 2025 is supported by the influence these new sciences have on beauty products of the future.

Emerging technologies such as Artificial Intelligence (AI), Augmented Reality (AR), and data analysis, empower brands to create ultra-personalized personal care solutions direct to consumers. L'Oréal Perso was unveiled in January 2020 as an AI-powered device that creates personalized skincare, foundation, and lip make-up on-demand. This is supported by omnichannel integration with its Modiface AR app and social media.

L'Oréal's Perso can also analyze trending images online to help users mix and match the lipstick colours of their favourite influencers. AI's ability to personalize formulas enables consumers to broaden their access and try out new trends at their convenience. Its functionality,



**Apps can make use of biometric facial recognition and 3D scanning to deliver granular levels of personalization.**

(Photo © Shutterstock.com / america\_stock)



**Halal beauty is one instance of personalization that has emerged in response to a specific need for ingredient-conscious Muslim consumers. Other examples include hair care for women with African-Caribbean hair, as well as skincare products for Asian men**

therefore, resonates with the 23% of global consumers that somewhat/completely agree that “beauty/grooming products in unusual colours appeal to me” as reported in GlobalData’s 2019 Q3 global consumer survey.

### Ambient commerce and experimental retail

Ambient commerce and experimental retail are two developments that increasingly present tailored product choices to consumers before they purchase them. This process is based upon an analysis of past spending patterns, detections of customer location, and stock levels of goods. With past spending data, brands can create strategies for repeat purchases, or disrupt the purchasing occasion for challenger products.



**A consumer uses an augmented reality concept to change the colour of her fingernails without the need for physical application.**



**Smart mirrors exemplify the move to digital lifestyles, providing users with updates on personal data and information.**

Sephora is one brand that utilizes ‘moment marketing’, seeking to identify the ideal moment to deliver real-time content to consumers. The use of Bluetooth beacon technology triggers in-app offers like discounts and personalized content when shoppers approach its stores. Furthermore, consumers can be tracked in-store so that targeted brand information can optimize their retail experience. Personalized content has the potential to improve conversion rates and present brands with opportunities to cater to the 65% of global consumers, more often than not, who are influenced by how well beauty and grooming products are tailored to individual needs and personality.

Beacon integration can personalize rewards programmes, allowing brands to empower

customers with the ability to find nearby stores, earn loyalty points, and redeem rewards. For the brand, the collection of customer data allows it to accurately market services to their target audience, and identify which locations are most popular amongst its customer demography. This, in turn, allows a company to further optimize its services accordingly.

### A new form of customer loyalty

As product personalization becomes popularized, brands are acknowledging the evolution of traditional transactional relationships that breed a new form of customer loyalty. With complex technologies like emotional AI now available in some commercial products, cosmetics brands must, at the very least, embrace basic digital tools to ensure consumer-centric personalization. With widespread Internet penetration, brands cannot afford to miss out on opportunities like analytics and the insights gained from data.

Increasing personalized beauty approaches will lead to a further proliferation of independent brands, empowered by the specificity that digital technology offers and the digital experience has become crucial to product appeal. Smaller brands today have improved routes to market access and are increasingly well-positioned to respond to demands from niche market segments. The rise of the digital consumer has encouraged market movement beyond mass-produced products – giving both manufacturers and customers greater opportunities for personalization.

### Further information

**E: [george.henry@globaldata.com](mailto:george.henry@globaldata.com)  
www.globaldata.com**



# Capturing the essence of Africa

Zeze Oriakhi-Sao, founding director of Malée Natural Science, explains how the company was founded to serve the African beauty products market with a brand that reflected the rich natural resources of the African Continent and how it has become a thriving business that continues to grow.

“Malée Natural Science was born out of circumstance,” says Zeze Oriakhi-Sao, Founding Director of Malée Natural Science. “I had just finished my master’s programme and moved to South Africa from the UK in the middle of the recession in 2009 and found myself in the centre of a hiring freeze. I saw that the market there lacked a local contender that expressed local culture, but also a brand that celebrated the rich natural resources that have been used for centuries by Africans and the beauty industry alike.

“During my time travelling within Africa, I also found that the appetite for such a product and brand existed, although no one knew where to look or how to access it,” she continues. “What was readily available in the markets as by-products of food lacked the aesthetic appeal, aromatherapy benefits and the scientific approach that would appeal to a more discerning consumer.”

Thus began the idea of Malée – based on the premise that it is possible to capture the essence of Africa in a bottle or jar, and produce a unique product made with



**Zeze Oriakhi-Sao, founding director of Malée Natural Science**

indigenous ingredients that capture the scents of the landscapes, celebrate its people and can be shared with all, regardless of their gender or age.

## Look to traditional ingredients

Oriakhi-Sao says a ‘huge’ part of Malée Natural Science’s ingredient selection involves looking back on traditional remedies, such as those used for healing, special occasions and traditional ceremonies: “Traditionally in Africa, the idea of

beauty and the use of natural oils, scents and natural colouring for adornment is an inherent part of the culture. To be able to celebrate and draw attention to this with Malée is an honour. For example, our logo is an Adinkrahene symbol from Ghana which means the keeper of secrets and Malée’s product packaging features ‘tribal’ markings that all have meanings,” she says, adding that the company’s scents are all expressions of moments and the landscapes unique to Africa: “For example, Verdure is inspired

by the atmosphere at 4am before a safari game drive – the moisture in the soil, the dewy leaves and the invigorating feeling one feels as the sun is about to begin to rise.”

She adds that as a pioneering luxury global African beauty brand, Malée Natural Science has been able to demonstrate that there is an appetite for a diverse range of products and voices from Africa within the global beauty market, adding that, locally, a sustainable approach is not only changing lives through job creation, but by pledging a percentage of its profits, Malée Natural Science is contributing to educating and mentoring students from disadvantaged communities while also providing the facilities and learning materials they need to reach their full potential. “With each sale, we want to help build a world where all people have the opportunity to achieve their dreams,” says Oriakhi-Sao.

## Scientific foundation

To achieve these aims, Malée Natural Science works with leading cosmetic chemists who



**The goal for us as a brand is to maximize the use of proven natural active ingredients that deliver positive results for skin health – like the rest of the world, formulation requirements vary country to country on the African continent – a challenge all brands face when looking at cross-border trading or markets**

not only look at preferences for indigenous ingredients but also ensure they are proven scientifically for their efficacy so that the claims the company makes are substantiated. “The goal for us as a brand is to maximize the use of proven natural active ingredients that deliver positive results for skin health – like the rest of the world, formulation requirements vary country to country on the African continent – a challenge all brands face when looking at cross-border trading or markets. Our focus is always on skin health and utilizing natural active ingredients, minimizing the use of filler ingredients and, as a result, we find our formulations meet most regulations. The consumer appetite is growing alongside the industry on the continent and ingredients, suppliers and brands alike are all working towards a larger reach and, as a result, this influences the quality and diversity of what is on offer,” Oriakhi-Sao says.

#### **A new frontier of opportunity**

“Undoubtedly, a worldwide global trade shift is happening and has already happened across the industries recognizing the African

consumer. Such industries are focusing on the potential of the African continent and its growing population amidst globalization. The cosmetics industry should follow suit to capture the marketplace in these growing economies and the African cosmetics market is poised as the new frontier of opportunity and growth for the cosmetics industry.

“Internally, African governments are investing heavily in industry, opening trade barriers between member African states with the African Continental Free trade agreement. Such infrastructure investments and regulatory protections, as well as reform, have been implemented – including as part of industrialisation agendas in some countries – with hopes of serving its growing populations and increasing their chances of success through job creation.”

Oriakhi-Sao says Malée Natural Science is, therefore, a new type of global and pan-African consumer-focused cosmetics brand that serves both local African consumer and diaspora needs while also entering into the global brand race, based on merit and consumer appeal: “Local brands operate without the need to weigh investment or resources with other regions, they are focused on creating a solution for the increased spending power in their countries and are catering to luxury tastes while staying true to their origins, tradition and heritage,” stating that common practice includes the use of traditional brand and product names with meanings that embody a brand’s ethos and that there is an emergence of products that cater to routines that mimic age-old traditions, such formulas being often inspired by traditional healer remedies and skin health but combining scientific knowledge and the use of sustainably sourced natural or organic indigenous ingredients and sustainable production practices. She expects that over the next decade, increased access to readily available capital, coupled with



growth in consumers’ disposable income, will result in consistent growth and more investment opportunities within the African beauty products market:

#### **Investing in and growing the industry**

“In recent years, I’ve seen interest mostly focused on our distribution channels,” she comments, “and I suspect that larger global cosmetics companies will explore acquisitions in order to diversify their portfolios. Historically, these global companies have maintained hold of a large percentage of the market share, however, the emergence of new players – such

as Malée Natural Science – into the market, will mean they may struggle to maintain this.

“Malée Natural Science is in its tenth year of business and we currently have a presence in nine countries, with a goal to continue establishing ourselves as a global player, so we are still quite young to be planning an exit strategy. The hope is, however, in future to be able to invest in the local ecosystem and help more people realize their ambitions, in turn growing the industry,” she concludes.

**Further information**  
**W: [www.maleeonline.com](http://www.maleeonline.com)**





# Building resilience with the digital twin

By Paige Marie Morse, Industry Director, Chemicals, Aspen Technology, Inc.

**This article explores how plant digital twin technology can help chemicals companies drive operational resilience, manage disruption in these challenges times and prepare for the ongoing volatility expected to continue into the next year.**

These are truly exceptional times as we all adapt to the unprecedented health, social and economic disruptions we are experiencing across the globe. Scroll back even a few months and it would have been all but impossible to anticipate the scale of this pandemic and its ongoing impact on all aspects of our lives.

In this unanticipated environment, many companies are finding that their agility is being tested to its limits — how effectively can they respond to huge shifts in demand, supply, working environment and economics? For most companies, these shocks have stretched beyond planning boundaries, and as they do, many are asking what more can be done to prepare for their effects.

Chemical companies are finding themselves right at the heart of this unforeseen storm. The need for plants to respond to vast changes in demand, supply and workforce caused by COVID-19 has left many operators re-evaluating how effectively they prepare for

and manage severe levels of disruption. Business resilience is being critically tested, and with uncertainty in the recovery and the possibility of further waves of the virus increasing, pressures remain high. The likelihood is that extreme volatility will continue into 2021 and beyond. And with chemical plants being designated as essential industries during the crisis, solutions that address these challenges need to be found quickly.

## From digital migration to digital twin

Digital technologies have proven to be a critical tool for many

businesses during this time. Several chemical companies have expanded their agility by applying their digital scheduling capabilities in unique ways. Alternative scenario analysis is a clear application, integrating variable regional supplies and disparate demand segments, but some companies have creatively applied supply chain solutions to implement social distancing on the production floor.

With the ability to uncover new insights, enhance visibility and provide extensive scenario analysis, digital technologies are critical for many companies during this time. But one tool that

could be particularly valuable in optimizing operations in the current environment is the digital twin, which can be used to develop operational excellence. Digital technologies provide added insight on operations and capabilities of production systems, enabling greater visibility on status and integration, as well as deep exploration of alternatives to aid operational decision-making.

This type of simulation is particularly valuable in the current economy, when boundaries are well beyond what common spreadsheets can handle. Simulations with broad flexibility on constraints and parameters



## About the author

**Paige Marie Morse**, Industry Director, Chemicals at Aspen Technology, Inc. enables digital transformation progress at chemical companies worldwide. She has significant experience with leading operating companies, including Shell, Dow, Sunoco and Clariant, covering R&D, marketing, commercial and strategy roles. She holds a BA in chemistry from Kenyon College and a PhD in chemistry from the University of Illinois.



**In this unanticipated environment, many companies are finding that their agility is being tested to its limits — how effectively can they respond to huge shifts in demand, supply, working environment and economics?**

that also include economic considerations are precisely what is needed to optimise operations in this fast-changing and challenging market.

Digital twins are most commonly thought of in terms of engineering simulations of process operations and many chemical companies built them at the time of construction. This plant digital twin can be focused on a single asset, across a plant, or system-wide to optimize operations and production more generally. These models can be deployed offline and online and calibrated to plant operating conditions through autonomous model-tuning. Plant digital twins are especially helpful in optimizing alternative production scenarios, such as the reduced production rates and alternative raw material environment that many companies are experiencing now. This makes them especially powerful in the current crisis as they enable the operator to run those different process scenarios.

#### Alternative uses

Digital twins can help train operators for these atypical operations and especially for start-ups, shutdowns, slowdowns and other unexpected events. Such training simulations are especially important to avoid potentially

dangerous situations that can lead to safety and environmental incidents. Chemical plant operators after all need to be sure that all of their staff know their roles during these difficult times and a digital twin can again be very helpful in that context.

Digital twins could be useful too in the event that the original plant needed to close down for a period due to the pandemic. In this scenario, the digital twin could potentially make use of mathematical optimization methods to work out what the best combination of supply chain decisions would be over a planning time horizon in order to maximize enterprise profitability overall.

Moreover, a digital twin can enable a chemicals operator to create a single environment to look at all of their complex interactions. They might, for example, be running batch processes. They might also be operating continuous process. In the best digital twin environments, they can look at all of this activity together in order to make the best decisions about how to run their operations in the atypical environment that we are currently in.

These models can also be employed to develop alternative asset uses, such as the repurposing of existing operations to make products for surging medical and hygiene applications, such as personal protective equipment and disinfectant products, during the current crisis. Operational resilience will be a key capability in determining how companies will emerge from this pandemic. Building digital capabilities now will help improve such resilience during this time and prepare for the ongoing volatility to come.

**Further information**  
**Kate Jones, Senior**  
**Marketing Communications**  
**Manager, Aspen Technology,**  
**Inc**  
**E: [Kate.Jones@aspentech.com](mailto:Kate.Jones@aspentech.com)**

# make an impact...



## ...with your advertising

We offer you a range of media options to boost your brand visibility including print advertising, website banners, weekly newsletters and bulletins. Join us and let us connect with you too.

#### Benefits

- Boost your brand visibility
- A truly global reach when you advertise with us
- **NEW!** Production or graphic design service available

**[info@ckhglobal.org](mailto:info@ckhglobal.org)**  
**[ckhglobal.org/advertise](http://ckhglobal.org/advertise)**



Subscribe  
now

# Azelis: innovative service provider on a global basis

Specialty chemicals and food ingredients distributor Azelis has been expanding its business geographically in recent years and has already concluded a number of significant new acquisitions and mandates this year. In addition, the company is enhancing its innovative service to customers through an extensive digitalization programme aimed at enabling customers to generate value and shorten their time to market.

Azelis is a leading distributor of specialty chemicals and food ingredients present in more than 50 countries across the globe with about 2,200 employees. The company says that through employing knowledgeable teams of industry, market and technical experts, each dedicated to a specific market within life sciences and industrial chemicals, it offers a lateral value chain of complementary products to about 40,000 customers, creating a turnover of €2.15 billion in 2019. In the US, Azelis operates under a number of renowned co-brands that cater to the various markets in the region.

## New distribution agreements

As part of its business expansion programme, in June this year Azelis established a new distribution agreement with Stepan Company, one of the largest surfactant manufacturers in the world, in which Azelis will take over distribution activities for all of Stepan Company surfactants in Scandinavia and thereby adding to Azelis' long-lasting distribution partnership with Stepan in other European countries. Stepan Company offers a broad range of products, including a full line of anionic, cationic, nonionic and amphoteric surfactants, as well as surfactant blends and speciality esters. The company also creates custom surfactants and formulated blends to meet unique customer demands for tailor-made solutions.

In another recent development,



PRODUCTS TRENDS FORMULATIONS

UNITED KINGDOM  
PERSONAL CARE

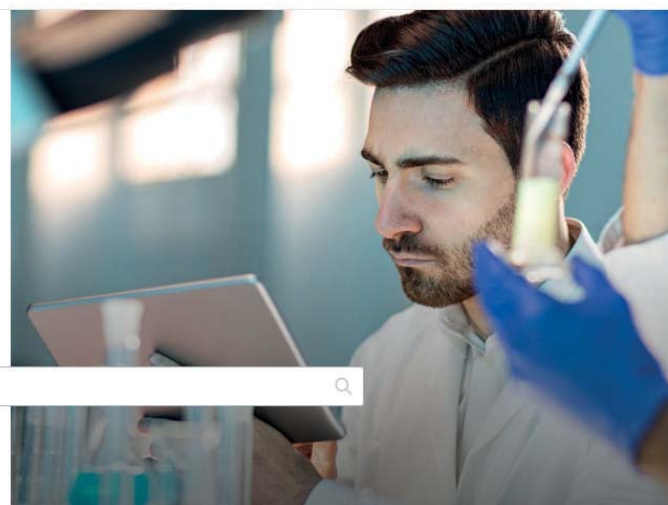
Search for ...

## We move markets forward

Azelis does much more than move goods. We move markets forward. Breaking new ground in our technical laboratories by combining ingredients with ideas and creating opportunities through innovation.

### Product search

Search for products, formulations or INCI



## Your local contact person

Helen Hill  
Regional Market Manager

+44 (0)1992 825555  
pctech@azelis.co.uk

## Azelis: moving markets forward by combining ingredients with ideas.

In May of this year, Azelis formed a partnership with OCSiAl, the world's largest single-wall carbon nanotube manufacturer for CASE and R&PA markets. This new agreement sees Azelis distribute OCSiAl's high-end TUBALL range of single-wall carbon nanotubes in France and the UK. These nanotubes are an advanced additive that improve the properties of base materials and have highly desirable properties such as superior conductivity,

high-temperature resistance, strength and flexibility, allowing customers to produce non-black finished products with antistatic properties.

In addition, in June, Megafarma, an Azelis company, strengthened its CASE presence in Mexico through an agreement with Celanese for the distribution of its emulsion polymers products in that country. Also in June, Roquette, a global leader in plant-based ingredients for food,

nutrition and health markets, and Azelis signed a distribution partnership for animal nutrition. The two companies already have an agreement in food and nutrition markets and this new partnership extends this to cover a number of countries in Northern and Eastern Europe.

## Brand promise: 'Innovation through formulation'

Last year, Azelis revealed its new brand promise and

## Meet Dr. Heli Kilpala and Matt Nancekivell of Azelis

**Dr. Heli Kilpala** has been Group Strategy & Digitalization Director at Azelis since November 2019. Prior to joining Azelis, she held the role of Digital Principal at DSM, where she was responsible for stimulating the digital mindset across the DSM IT organisation and business, increasing the number of digital initiatives, bringing in digital knowledge and expertise, and driving digital initiatives aligned with the company's strategy. Prior to this she worked at DSM Food Specialties, Deloitte Consulting and as an independent consultant. Dr Kilpala holds an MSc in Economics and Business Administration from Oulu University, Finland and a PhD in Civil & Environmental Engineering from Utah State University, USA.



**Matt Nancekivell** is Director Commercial Operations at Azelis. He has 15 years' experience in the specialty chemicals industry in New Zealand and Australia with roles in operations, supply chain management and technical sales for the personal care, homecare and industrial, and surface coatings sectors. He graduated from the University of Auckland with a Bachelor's Degree in Commerce (Strategy and Operations Management) and he also holds a Bachelor's Degree in Arts (History and Politics).



tagline: 'Innovation through formulation'. The company has been increasingly focusing on formulation support for its customers and wanted to formalize this strategy and its business practices to provide innovative solutions to meet stringent market requirements. To demonstrate its belief in innovation through formulation, Azelis has been investing heavily in its formulation laboratories and the innovative solutions that have come out of these laboratories have won awards from independent industry bodies: Azelis has won more than 20 innovation awards in the past five years alone.

"As a distributor, Azelis has specialized technical knowledge of a broad variety of products from many suppliers and provides medium and small size customers with technical advice and access to products and services that may otherwise not be available to them," says Heli Kilpala. "Formulation work performed in the company's labs is sometimes done at the request of customers and sometimes the company itself proactively comes up with a solution to meet a market requirement or trend, thus shortening customers' time to market and growing their business. Thus, since the

company was founded in 2001, Azelis has evolved from a leading distributor of specialty chemicals and food ingredients into an innovative service provider."

### 'Local for local' approach

The company stresses that a core element of its value proposition is its 'local for local' approach, a business model that enables local sales teams to sell to local customers. Azelis' formulation laboratories, located in all the markets it serves, are each

dedicated to a single market segment and this approach, the company says, together with its widely differentiated product portfolio, innovative services and increasingly integrated sustainability efforts, gives it several advantages over its competitors:

"Azelis has been successful in bringing its suppliers into new geographies or introducing them to new customers," says Heli Kilpala. "This all requires excellent market penetration,

customer intimacy, product and production process knowledge, and many other aspects. This is why we employ industries' best local experts and we pride ourselves on the quality of people we have. People are our biggest asset and they are the ones who are at the core of Azelis' success."

### Investing in digitalization

In pursuit of these goals, Azelis has been investing in digitalized systems in different regions for

The screenshot displays the Azelis Customer Portal interface. At the top, the Azelis logo is on the left, and navigation links for PRODUCTS, TRENDS, and FORMULATIONS are in the center. On the right, there are links for UNITED KINGDOM | EN and PERSONAL CARE, along with user and cart icons. A search bar is also present. Below the navigation, the breadcrumb 'Products > Silkpro' is shown. The main product title is 'SILKPRO' in large bold letters, followed by its chemical composition: 'Aqua, Hydrolyzed Silk, Butylene Glycol, Methylparaben, Propylparaben'. Under 'Product information', the INCI name, SKU (BP132274), and Supplier (Ikeda Corporation) are listed. A 'Download data' section offers links for TDS, SDS, and All certificates. On the right side of the product page, there is a 'Pack size' dropdown menu set to '20kg', an 'Order' button, a 'Request a quote' button, and a 'Request a sample' button at the bottom.

**The Azelis Customer Portal features comprehensive downloadable product information.**



some time. Two examples of such efforts include an on-line formulation project management channel aimed at optimizing customers' time to market in the Americas and a portal for customers in a selected number of EMEA countries that provides product and marketing information.

"In our industry, business is established through personal long-lasting partnerships based on knowledge-sharing and industry expertise. Taking our innovation capabilities into the digital space, which has been accelerated by the coronavirus crisis, will however never replace the importance of these personal relationships; digitalization is complementary to these personal relationships and will take our interactions with suppliers and customers to the next level."

Matthew Nancekivell says Azelis' platforms are there to

**As a distributor, Azelis has specialized technical knowledge of a broad variety of products from many suppliers and provides medium and small size customers with technical advice and access to products and services that may otherwise not be available to them**

service customers in the best possible way and enhance their experience of working with

the company, providing much more added value than just sales: "To further standardize, professionalize and boost our original and individual digitalization efforts, we kicked off the global digitalization programme in September 2019. We had several drivers to start this global journey: first of all, we see that B2B buyers are using online portals to find information on sellers, products and formulations. Buyers today want high-quality technical information without lead times and at Azelis we are developing new digital offerings that respond to this demand. We made a decision to start from customer experience but to focus on all our users.

"For our employees, we will offer new digital tools to work even more efficiently. For our suppliers, we will offer a connected platform to share data and insight. In a nutshell:

our vision is to be a connected enterprise that delivers shared value to our customers, suppliers, and our employees.

"Virtual collaboration, new content formats, and new types of events are key to inspiring our customers in the digital era, which has proven critical during circumstances such as the ongoing crisis. We expect virtual collaboration to become more of a norm in the more traditional chemical industry and for Azelis this is a truly exciting opportunity to learn from the needs of our internal and external stakeholders and be able to enhance our digital offerings globally. Digitalization is all about knowledge-sharing; at Azelis this knowledge has been tremendous already but we are making it available more quickly, more efficiently and in a more accessible way than ever before," he says.

### Generating value in the supply chain

"Having expert content on the digital platform will also enable us to stimulate our customers and help them in their new product idea creation process which means that our expert work shifts from problem-solving to co-creation of new products with customers, helping them to shorten their time to market. This is where we want to be as this will generate value for all partners in the chemical supply chain – not just ourselves, but more importantly for our customers, suppliers, to end consumers and the environment," Heli Kilpala concludes.

**Further information**  
**Dr. Heli Kilpala, Group**  
**Director of Strategy &**  
**Digitalization**  
**E: heli.kilpala@azelis.com**

**Matt Nancekivell, Director**  
**Commercial Operations**  
**E: matt.nancekivell@azelis.com**

### Formulation

#### Phase A

Raw Material	INCI	%w/w	Supplier	Description	Function	Certificates
Deionised Water	Aqua	75.10		①	Thickener	VEGAN
Genu pHresh™ DF Pectin Pectin	Pectin	2.0	CP Kelco	①	Thickener	COSMOS CERTIFIED
Keltrol® CG RD	Xanthan Gum	0.10	Sharon	①	Lorem Ipsum dolor	
Sharon™ Biomix Clear	Phenoxyethanol, Glycerine, Citrus Reticulata Fruit Extract, Citrus Aurantium Amara Fruit Extract, Citrus Sinensis Peel Extract, Ascorbic acid, Citric acid, Lactic acid, Aqua	0.70	Genomatica	①	Lorem Ipsum dolor	VEGAN NATRUE

#### Phase B

Raw Material	INCI	%w/w	Supplier	Description	Function	Certificates
Brontide™	1,3-Butylene Glycol	10.0	Biosol	①	Lorem Ipsum dolor	ISO 16128

#### Phase C

Raw Material	INCI	%w/w	Supplier	Description	Function	Certificates
PAE Complex Oil Control	Aloe Barbadensis Leaf Juice, Phytic Acid, Fucus Spiralis Extract, Tetraselmis Chui Extract	10.0	Agrana	①	Thickener	COSMOS CERTIFIED NATRUE ISO 16128 VEGAN
Rice PO4 Natural	Aqua	75.10		①	Lorem Ipsum dolor	NATRUE

Due to its ability to act as a moisturizer, the hemp oil prevents the skin from catching dryness, especially during the winters. Hemp seed oil contains healthy omega fats. Along with a plethora of our other healthy ingredients, you can see.

*The Azelis CustomerPortal also includes extensive information detailing how products have been formulated.*

# Let's drive forward to the future

By Dr Marcus Remmers, Chief Technology Officer, Royal DSM

From electric vehicles to bio-based materials and autonomous driving, the car industry is undergoing a dramatic transformation – and smart chemicals technology is leading the way...

**D**id you know that car manufacturer Henry Ford was fascinated by the soybean? During the Great Depression, he spent hour after hour in his laboratory trying to turn this bean into more affordable plastic to lower the price of his Model T car. By 1941, Ford had developed a handmade car with a plastic body, made completely from plant material. One reporter at the time described it as 'part salad, part automobile'.

Unfortunately, as is often the case when commercializing plant-based materials, the Ford Motor Company was never able to produce soybean-based plastics that could compete with petroleum-based equivalents on performance. Fair enough – we all know that it's not only sustainability that matters in the car industry. The durability, strength and heat resistance of the materials is equally important. But now, with technological advances unlocking higher and higher bio-based plastic performance, manufacturing industries should no longer view these bio-based materials with a suspicious eye – we might well be closer to achieving Ford's dream after all.

## A rapidly evolving industry

Around the world, the car industry is changing shape before our eyes. Emission reduction targets are speeding up the transition from traditional combustion engines to electric and hydrogen-powered vehicles. The need for greater circularity is adding pressure to find materials and manufacturing processes that allow for better recycling. On top of this, there is increased demand for connectivity to support trends such as autonomous driving. And, of course, vehicles still need to deliver



**By Dr Marcus Remmers, Chief Technology Officer, Royal DSM**

reliable performance.

Chemical companies are at the heart of this transformation – for example, DSM. This company uses its materials expertise to deliver several solutions to help OEMs meet these challenges – or even turn them into opportunities. Specifically, DSM's solutions deliver the low weight, durability and sustainability that manufacturers need, without compromising reliability, safety, or performance. These materials can help address three of the biggest automotive challenges: powering the car of the future, manufacturing the car of the future, and connecting the car of the future.

## Powering the car of the future

The world faces a series of urgent environmental challenges. Car emissions, in particular, are one of the biggest contributors to climate change. And, as vehicle production continues to increase, the impact of these emissions will only multiply. To turn the tide, the automotive industry needs to look for more sustainable alternatives – particularly when it comes to power.

One way to reduce the

and more of the latest models hitting the showrooms are hybrids, combining internal combustion engines with high-voltage electromotors and batteries. And 100% battery-powered vehicles are also continuing to grow in popularity.

While these high-performance, low-footprint vehicles bring many benefits, they also present challenges. Take electric vehicles powered by a hydrogen fuel cell. These vehicles refuel in the same time as conventional cars, go further on a single tankful than the maximum range of current lithium-ion technology, and emit H<sub>2</sub>O instead of CO<sub>2</sub>. All great advantages – but OEMs for these vehicles face the challenge of safely harnessing a highly explosive pressurized gas bottle.

To address challenges like this, DSM offers a range of solutions – for fully electrical vehicles with hydrogen fuel cells or lithium-ion batteries, for biofuel, and for hybrid technology. For instance, when it comes to hydrogen fuel cells, DSM applies its expertise in high-performance barrier and uni-directional tape materials to develop safe, effective, and ultra-lightweight hydrogen tanks from its engineering materials.

## Solar: a viable alternative energy source?

But with electric vehicles growing in popularity, how can we source all that electricity sustainably? As we all know, in many industries, the transition to solar energy is well underway. Solar-powered buildings, for instance, are becoming mainstream. But what about solar-powered cars? For a long time, people have been – and still are – sceptical of this technology's ability to fuel the cars of the future.

**Around the world, the car industry is changing shape before our eyes. Emission reduction targets are speeding up the transition from traditional combustion engines to electric and hydrogen-powered vehicles. The need for greater circularity is adding pressure to find materials and manufacturing processes that allow for better recycling**

environmental footprint of cars is to change from traditional combustion engines to (hybrid) electric- and hydrogen-powered vehicles. Today, this transition is already well underway. We've all seen that more

For DSM, this is a challenge that was embraced a long time ago. The company regularly supports scientists pushing boundaries in solar, such as the Delft University of Technology team in the Bridgestone World Solar Challenge. Traveling 3,000 km from Darwin to Adelaide with a solar-powered car, these students relied on DSM's solar expertise— as well as its light, strong engineering materials. And with success: the team has won seven times.

Of course, fueling the car of the future is a much bigger task – but DSM is also taking the next steps towards more commercial solutions. Specifically, the company partners with Lightyear, the manufacturer of Lightyear One. This fully electric car has a solar roof and hood – comprising five square meters of integrated solar cells within safety glass – and can travel up to 725 kilometres on a fully charged battery. The partnership now wants to scale up this unique solar-powered roof and accelerate the global adoption of electric vehicles. Developments like this demonstrate that, with the right materials and support, solar energy and alternative fuels can definitely drive the cars of the future.

### Manufacturing the car of the future

But it's not just automotive emissions that affect the environment. When it comes to manufacturing, the automotive industry has traditionally relied on scarce, fossil-based raw materials such as precious metals. Indeed, the automotive industry uses more lead than any other sector, yet experts forecast that lead reserves will run out by 2030. More renewable solutions are needed. And, with the pressing need for greater circularity, manufacturers must also look for new opportunities to repurpose, reuse, or recycle their materials.

One example of this is 'closed-loop recycling' of materials from end-of-life vehicles, which are then

used to manufacture new vehicle bodies and parts – an already common process. However, given the additional need to reduce weight (to reduce CO<sub>2</sub> emissions), car manufacturers will also need more lightweight materials, such as high-performance plastics. This offers an opportunity to introduce bio-based plastics, which are more recyclable than fossil-based equivalents.

DSM's history in materials science, world-class R&D facilities, and the company's global network of materials scientists give it the special opportunity to help its customers make this transition happen. For instance, DSM Engineering Materials has committed to developing and rolling out a complete portfolio of bio-based and/or recycled-

based alternatives by 2030. The alternative portfolio will contain at least 25% recycled or bio-based content, measured by weight in the final product.

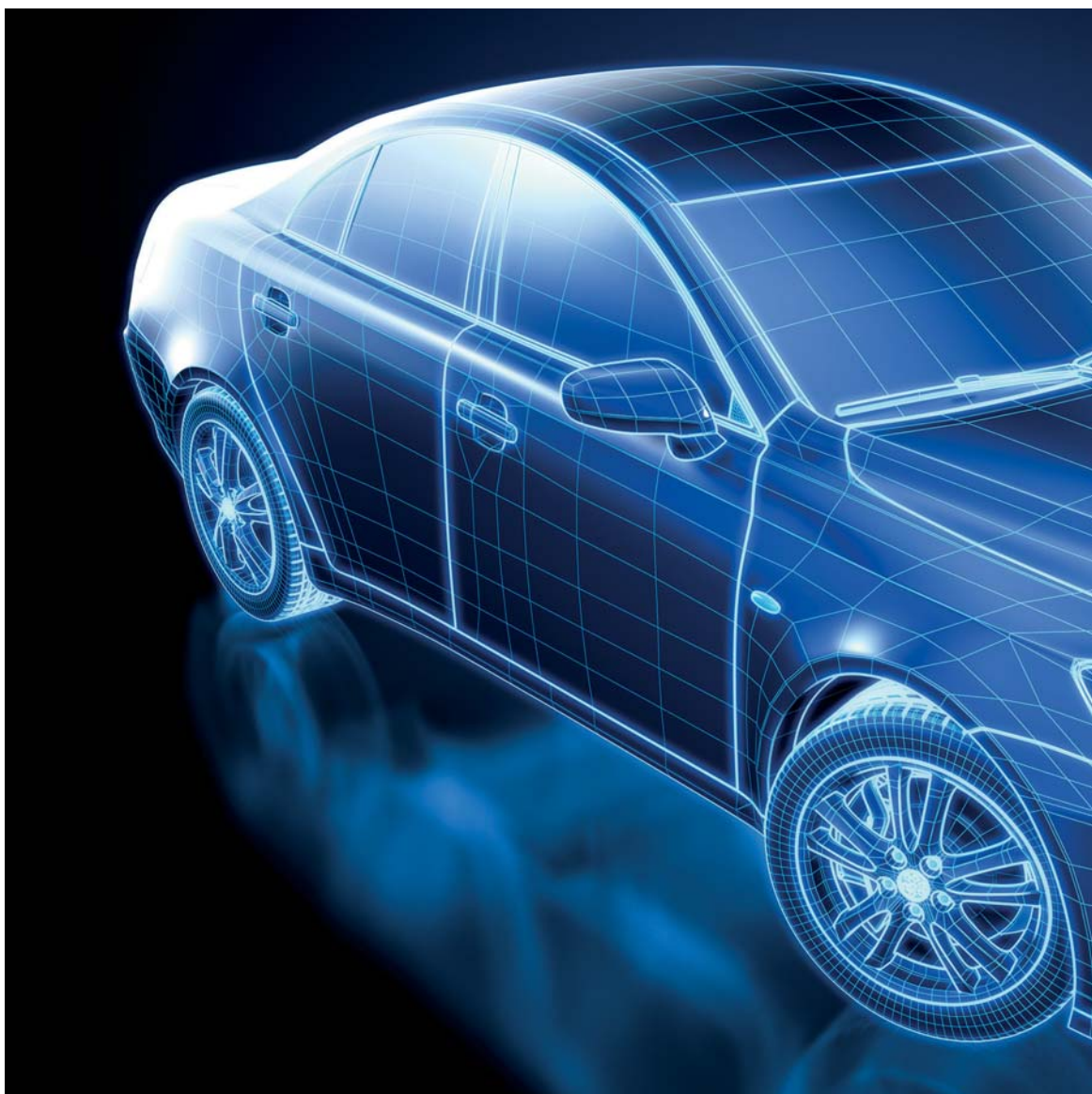
Importantly, all of the renewable or recycled-based products in this portfolio will deliver the same functional performance as their conventional counterparts, and will not require any special handling equipment or tooling. So, when it comes to the materials used in the car of the future, we might be close to achieving Ford's bio-based dream.

### Additive Manufacturing: rethinking automotive design

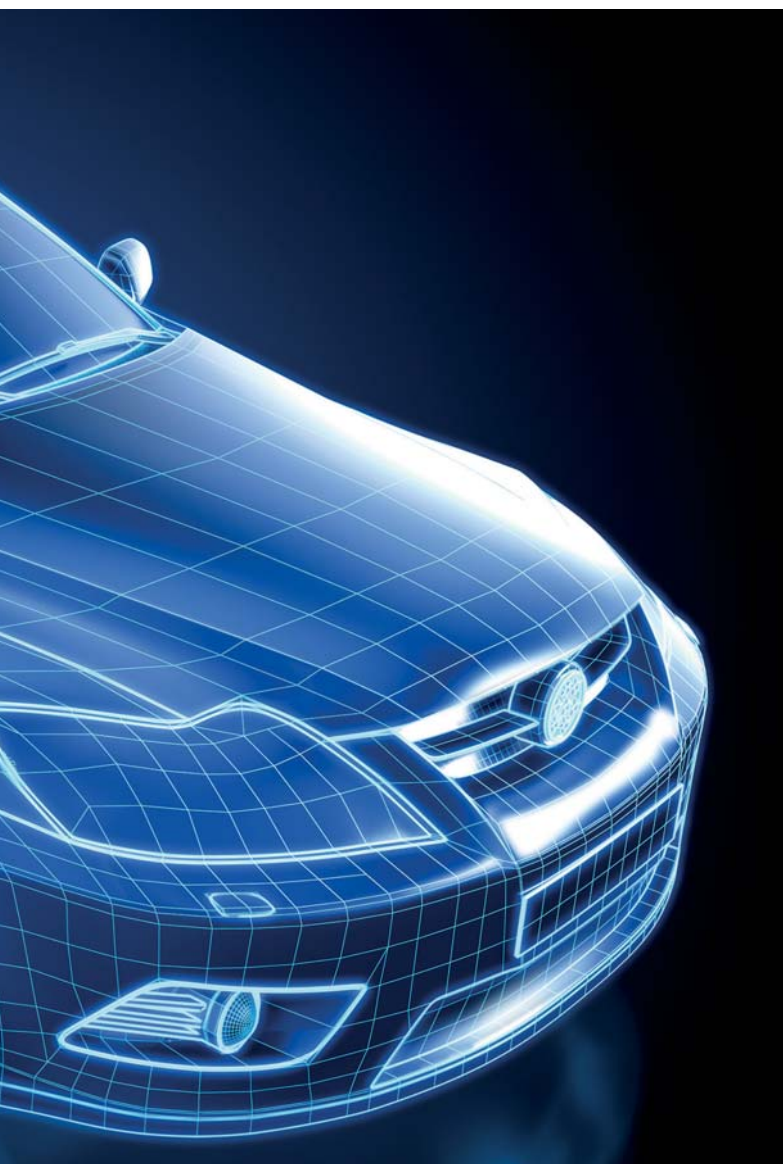
Besides the need for more renewable and recycled-based materials, car manufacturers are also facing the pressure of bringing

cars to market faster and at lower cost than ever. This means that design concepts and prototypes need to be produced faster, more efficiently, and cost-effectively.

The solution might just be Additive Manufacturing (AM), also known as 3D printing. The rate of progress in AM is little short of staggering: in just a few years, it has become a major disruptive technology set to turn industrial manufacturing upside down. No more expensive and time-consuming injection moulding to produce small series, spare parts, and tooling. Instead, additive manufacturing can now produce components that are indistinguishable from traditionally produced thermoplastics – in less time, with less waste, and at lower cost.







The practical implications of this are enormous. For instance, currently, car makers must hold significant stocks of all sorts of spare parts for a minimum of ten years. This is expensive and unwieldy. Major companies and their distributors have warehouse shelves stretching for countless miles holding components that may never be called for. With AM, those components could be produced only when they are needed – anywhere in the world.

But AM can also have major advantages for niche players. Take Briggs Automotive Company (BAC), a car manufacturer that builds limited-edition, personalized supercars. BAC was able to shorten production times and cut the cost of part production by more than 50% using 3D printing technology.

DSM collaborated with BAC to transform the manufacturing process of its Mono R model, resulting in lightweight, high-performance, custom-made parts.

But how well do DSM's AM materials perform? In fact, its printing materials are toughly tested in Formula 1 vehicles. AM allows teams to quickly test different design concepts, as multiple design variations can now be built at the same time, reducing product development cycles. On top of that, new computer-aided engineering technology helps DSM test materials in the lab. Predictive modeling, for example, can simulate parts' performance under stress even before printing. Indeed, DSM's collaboration with e-Xstream on predictive fatigue modeling for reinforced polyamide parts will

substantially reduce the need for material testing and design iterations.

AM could also become invaluable in personalizing cars. Mass customization is already here, with buyers choosing colour, engine size and type, interior trim, and 'infotainment' systems, but they still have to select these from a relatively limited set of options. With AM, customers can build truly unique cars at only moderate extra cost. For example, BMW's 'Mini Yours Customize' car lets Mini users personalize exterior indicator inlays, passenger-side interior trim, LED door sills, and door projectors, all with a mobile app. These parts are then produced at BMW's Additive Manufacturing Center in Germany.

### Making refinishes more efficient

But that's not all there is to manufacturing. Did you know that the most energy-intensive (and cost-intensive) process in car manufacturing is the painting of the car? The best car refinishes are efficient, sustainable, and durable. But this means that, traditionally, they consist of multiple layers, each with multiple properties and often based on a variety of resins.

Unless, of course, you open up DSM's scientific toolbox. Indeed, DSM's scientists have found a way to develop high-end car refinishes with excellent adhesion and hardness while enabling car manufacturers to reduce the spray booth cycle time from 30 to 15 minutes at 60°C, ready to polish after cooling down. In normal conditions, this represents a productivity increase of about 20%. In other words, with smart refinishes, additive manufacturing and bio-based materials, we're on the road to redesigning not just the car, but the entire automotive industry.

### Connecting the car of the future

Finally, when it comes to connecting the car of the future,

the move towards connectivity in the automotive world might just be as big as the transition to greener cars. We're seeing new standards for car usability, with autonomous driving being the most obvious. Meeting the extreme demands of these next-generation cars requires designers to re-think and reimagine what's possible, as we see two entirely different industries – automotive and electronics – converge.

You may have heard of 'thinovation' – the trend for making working parts in electronic devices such as mobile phones smaller, lighter, greener, and safer. The materials supplied by companies like DSM are used to create these components. Tomorrow, these same materials (and their descendants) will do a similar job in cars, as we discover smart new ways to integrate electronics into plastic materials. With knowledge and experience of both mobile phones and automotive applications, DSM is well placed to connect with partners worldwide to create something truly remarkable.

### Green cars for all

Above all, to enable these automotive industry transformations, OEMs will need suppliers that don't just understand materials, but also application challenges. DSM's approach is set to lead the way: dedicated R&D teams work closely with industry experts and engineers to look at the entire process of developing new parts and components – from design and material performance to production and compliance. With this kind of collaborative approach, parties across the automotive value chain can build a brighter future for the car industry – a future where mobility does not harm the world around us. More than ever, it's time to deliver on Ford's pioneering vision, and make green cars available for all!

### Further information

**E:** [www.linkedin.com/in/marcusremmers/](https://www.linkedin.com/in/marcusremmers/)

# Ozone and oxygen for sustainable odour and corrosion control

Paul Turgeon, CEO and Tonya Chandler, VP Sales & Marketing at Anue Water Technologies explain how sustainable oxygen and ozone help improve safety and decrease costly equipment damage in wastewater systems.

Wastewater systems have long been subject to issues with odour and corrosion, which is understandable given the nature of what they convey. The odour is the driving force behind implementing controls these systems. Corrosion, however, is the issue with the greatest potential for environmental harm and real systemic and economic damage. This damage can arise in the form of burst pipes and other equipment and system failures. Failures of this type require the repair and replacement of system materials and equipment, and they have the potential to expose the environment to unpredictable releases of hazardous wastes that are difficult, if not impossible, to contain or recover.

## Corrosion caused by hydrogen sulfide

A major contributor to odour and corrosion in industrial systems is hydrogen sulfide ( $H_2S$ ) and its associated compounds. Some industrial wastewater contains sulfur compounds, which provide the molecular basis for the generation of  $H_2S$ , which arises from the combination of anaerobic conditions and the presence of sulfites and sulfates in conjunction with colonies of microorganisms present on the inner walls of all collection systems, referred to as the slime layer. Sulfate-reducing bacteria (SRB) will use these compounds in the absence of free oxygen ( $O_2$ ) for their metabolism. These bacteria do not use the sulfur component, and it is available to react with water, specifically free protons ( $H^+$ ), which results in the generation



**$H_2S$  is a colourless gas that has a characteristic rotten egg odor, is highly toxic and is corrosive to certain metals. It is heavier than air, meaning it can accumulate in wells, manholes and other similar locations that do not have much ventilation.**

of  $H_2S$ .

Following its generation,  $H_2S$  can be released into the atmosphere and find its way to receptors through junctions of the atmosphere and collection system, at which point it is an odour concern.  $H_2S$  is a colourless gas that has a characteristic rotten egg odor, is highly toxic and is corrosive to certain metals. It is heavier than air, meaning it can accumulate in wells, manholes and other similar locations that do not have much ventilation. The effect it can have on humans, at varying concentrations relative to ambient air, is shown in Table 1.

$H_2S$  becomes a corrosion issue when it contacts moist concrete or steel, among other metals, in the presence of oxygen, even at very low gaseous concentrations. Conditions such as these are common in the headspace of some pipes and other areas where

the collection system has easy access to atmospheric oxygen. Bacteria in these areas convert the  $H_2S$  into sulfuric acid, which then begins a destructive reaction with the infrastructure.

Historically, control of odour and/or corrosion has been implemented through either vapour-phase techniques, where the headspace of a system is treated, or liquid-phase techniques, where treatments target the liquid flow. Vapour phase treatments like scrubbers do not provide corrosion control. Some of the liquid phase techniques offer corrosion control.

The most common method of inducing liquid-phase treatment, or directly treating the wastewater inside the collection system, has been by dosing chemicals into these systems. A constant and continuous dose of chemical is fed into the collection system from a large reservoir with a small pump, typically at a manhole or pump station. These chemicals are meant to react with the odour-causing compounds present in the wastewater or stop their formation and/or release from solution.

## Conventional control options

The conventional classes of reactions used to control  $H_2S$  are:

- **Oxidation** – Chemical oxidation of  $H_2S$  is accomplished through the use of an oxidant such as hydrogen peroxide or sodium hypochlorite (bleach).
- **Sulfide scavengers (iron salts)** – Chemicals that interact with  $H_2S$  and sequester, or scavenge, the sulfur into a relatively insoluble form, such as ferric chloride and ferrous chloride, can be used to remove

sulfur from the cycle entirely.

- **pH adjustment** – Because of the way that its ions dissociate in the aqueous phase, the release of  $H_2S$  from wastewater will not occur if the pH is at 9 or above.

## Alternate oxygen source/sulfate substitute

In an anaerobic environment, the microbiology in a collection system will use oxygen from a nitrate ( $NO_3$ ) group more readily than from a sulfate ( $SO_4$ ) group and, as a result, benign nitrogen is released rather than  $H_2S$ . Chemicals such as calcium or sodium nitrate are commercially available and can be used for this purpose. They can be expensive, however, and they feed and grow the SRB layer, potentially requiring a higher volume for treatment over time.

Upon cessation of treatment, the amount of  $H_2S$  can be even higher than before. Excess wet well build-up requiring increased clean-out cycles because of the addition of the waxes used to stabilize the nitrate molecules can be encountered downstream in the collection system. In addition, emerging federal and state regulations are beginning to include nitrate concentrations on discharge limitations.

Real-time, active monitoring of wastewater  $H_2S$  levels is seldom carried out, so enough chemical to control peak  $H_2S$  values is typically added on a constant basis. By treating for peak values with chemicals such as these, the likelihood is very high that excess nitrate will be present and actively added to the wastewater, requiring additional denitrification processes or fines, both of which can be very expensive.

Concentration (ppm)	Physiological effect
0.1 to 3	Odour threshold
3 to 10	Offensive odour
10 to 50	Headache Nausea Throat and eye irritation
50 to 100	Eye injury
100 to 300	Conjunctivitis Respiratory tract irritation Olfactory paralysis
300 to 500	Pulmonary oedema Imminent threat to life
500 to 1000	Strong nervous system stimulation Apnea
→ 1000	Immediate collapse with respiratory paralysis

**Table 1. H<sub>2</sub>S health effects at different concentrations.**

An issue with all chemicals is that to introduce them to a collection system, a bulk quantity must be stored nearby. To ensure that chemicals are always available for treatment, continued deliveries to the bulk storage tank must be made. To avoid adverse effects to the environment, engineered controls, such as secondary containment and leak monitoring, must be designed, implemented and maintained.

Ideally, a successful treatment of wastewater odour and corrosion would:

- End sulfide production
- Quickly eliminate sulfides that are present
- Bring about no additional hazard to life or the environment
- Do no harm to the collection system
- Create no additional challenges downstream

In addition, the treatment solution must be cost-effective. One answer is introducing ozone and oxygen into wastewater systems to control odour and corrosion.

Ozone has long been used in water treatment, dating back to at least the late 19th century, primarily for the disinfection and

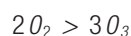
polishing of drinking water.<sup>4</sup> In Europe, ozone treatment of water is a common process. 50 years' environmental sustainability and relative safety versus chemical systems have established it as a favoured current and future technology. The controlled use of ozone as a treatment does not produce harmful byproducts that could contaminate or damage the environment or ecology. Typically, the only byproducts from its reaction are O<sub>2</sub> and inert oxides. In recent years, interest in its use to treat wastewater has led to the development of new and sustainable (green) technology for odour and corrosion control in wastewater collection systems.

Ozone is a naturally occurring form of atmospheric oxygen. Instead of two oxygen atoms it has three, represented by its chemical formula O<sub>3</sub>. This third oxygen atom makes it a highly reactive molecule and a strong oxidizing agent, the fourth highest overall after atomic fluorine, the hydroxyl radical and atomic oxygen. Ozone can be generated by exciting a flow of oxygen with sufficient electrical or optical energy. This will cause a certain amount of oxygen atoms to split

and recombine with other O<sub>2</sub> molecules (see below).



Under typical treatment conditions, using a relatively pure oxygen stream and a corona discharge chamber that uses a high-voltage electrical arc, this reaction can produce up to 9 to 12 percentage by weight (wt%) ozone,<sup>6</sup> although typically the output is in 1 to 9 wt% ozone.<sup>7</sup> The remainder of the stream is left as oxygen. The concentration is limited to this range because of the following reaction.



As ozone concentrations rise above this concentration, this destruction reaction becomes more frequent, returning greater quantities to O<sub>2</sub> and maintaining this equilibrium. This instability is also the reason ozone cannot be stored and must be generated immediately before application.

Because of its extreme instability and highly oxidizing nature, ozone is powerful and indiscriminate in terms of reactivity with other chemical species. Ozone has been shown as an effective treatment for the destruction of volatile organic compounds; removal of metals,

total suspended solids and organic carbon; and significantly reducing chemical oxygen demand.

In freshwater, the half-life of ozone is typically 10 to 20 minutes, but in wastewater, ozone has been documented as being entirely consumed within 8.6 seconds.<sup>8</sup> This is because of the extreme amount of potential reactants present in wastewater including H<sub>2</sub>S. The simple structure of H<sub>2</sub>S makes it an easy target for oxidation by ozone. Ozone's unique structure also tends to create free radicals, chemical species that have unbonded electrons making them highly reactive, especially in water. Not only is the benefit of ozone's direct reaction with different chemical species realized, but also as part of these reactions, additional free radicals, which can be even more reactive than ozone, can form. Additionally, radicals tend to create additional radicals as they react, in a free radical chain reaction.

These additional reactions are indirect effects of ozone.<sup>5</sup> With the source of ozone generation being ambient air, it is the ultimate in sustainable and green chemical treatment. The current technology for producing ozone has benefitted from more than 45 years of



ongoing development, resulting in cost-effective and robust operation. Using little more than an oxygen separator, a corona discharge chamber and some compressors and other electrical components, onsite generation of ozone is relatively simple and safe. This is in sharp contrast to most other treatments that are currently commercially available.

Because of the way ozone is produced, oxygen is necessarily going to be part of the treatment gas mixture when using ozone. This is beneficial because oxygen is also an oxidizing agent. Oxygen reacts more slowly than does ozone but is an excellent complement to it. Aside from its ability to assist in oxidation, its primary benefit is increasing the dissolved oxygen (DO) concentration of the wastewater, encouraging the growth of aerobic bacteria, which do not create compounds that are odorous, corrosive or otherwise harmful to collection systems. It also eliminates the ability of SRB to produce sulfides, either

by removing the SRB entirely or promoting the growth of aerobic species that will oxidize any sulfides before they are able to enter the wastewater stream.<sup>3</sup>

### Combined use of oxygen and ozone for treatment

In terms of a robust and green method of the treatment and prevention of odour and corrosion in collections systems, the combined forces of oxygen and ozone are at the top of the list. Oxygen is, of course, readily available, making up roughly 21 per cent of the atmosphere, and as has already been seen, is easily converted to ozone. The generation and infusion of these two gases into wastewater collection systems has proven to be a clean, safe and cost-effective treatment. The first method of action is the powerful destructive effects of ozone on  $H_2S$ , quickly converting it to sulfites and sulfates on contact. In addition, ozone's antimicrobial properties can help to reduce the presence of SRB and other microorganisms

present on pipe walls while oxygen is generated as a product of this reaction. This in turn adds more power to the oxygen portion of the treatment gas mixture, which provides secondary treatment by significantly increasing DO, and allows for more complete utilization of infused treatment gases.

Oxygen will also oxidize  $H_2S$ , but at a much slower rate than ozone does. Because of these indiscriminate and powerful oxidizing characteristics, concern is sometimes raised regarding the possibility of ozone attacking the wastewater infrastructure itself. This is unlikely to occur in application, especially in wastewater where liquid-phase infusion is implemented. This is due to the high ratio of liquid volume compared to pipe surface area per unit pipe length and the extreme availability of reactants in the liquid portion.

#### REFERENCES

1. American Society of Civil Engineers, "ASCE's Infrastructure Report Card," ASCE, 2009, <http://www.infrastructurereportcard.org/>.

2. A. Matthews et al, "Control of Hydrogen Sulfide Buildup in Force mains using Ozone and Oxygen," Proceedings of the Water Environment Federation, WEFTEC 2010: Session 101 to Session 112, pp. 7591-7611(21), 2010.
3. U.S. Environmental Protection Agency, "Odor and Corrosion Control in Sanitary Sewerage Systems and Treatment Plants," Design Manual, EPA/625/1-85/018, Cincinnati, OH, 1985.
4. Beltran, F.J., "Ozone Reaction Kinetics for Water and Wastewater Systems," Lewis Publishers, 2004.
5. Lenntech, "Water Disinfection Application Standards (For EU)," 1998, [www.lenntech.com](http://www.lenntech.com).
6. Drago, J.A. et al, "Municipal Wastewater Ozonation Practice in the United States: Past, Present and Future," Ozone: Science & Engineering, Volume 32, Issue 1, pp. 43-55, 2010.
7. Plasma Technics, Inc., "Plasma Block Product Line, Product Detail," 2011, [www.plasmatechnics.com](http://www.plasmatechnics.com).
8. Terry, P.A., "Application of Ozone and Oxygen to Reduce Chemical Oxygen Demand and Hydrogen Sulfide from a Recovered Paper Processing Plant," International Journal of Chemical Engineering, Volume 2010, Article ID 250235, 2010.

#### Further information

**T: +1 760 476-9090**

**E: [info@anuewater.com](mailto:info@anuewater.com)**

**Chemicals Knowledge Hub TV**

Connecting industry across the globe

AGROCHEMICALS

CS

Medical icons: syringe, ambulance, doctor, handshake, heart rate.

**CKHTV NEW! The one-stop-shop for industry interviews and insights. This is your platform to showcase your products, services and expertise to the industry. This unique video content platform is the best place to be seen and see what's hot in the chemicals industry! If you want to find out more get on touch!**

## PARENTERALS CDMO

---

# WE VALUE YOUR PRODUCT

Sterile Manufacturing  
Delivery Systems  
Parenteral Technologies

**GRIFOLS**

Contact us at [partnership@grifols.com](mailto:partnership@grifols.com) | [www.partnership.grifols.com](http://www.partnership.grifols.com)

# CPhI festival of pharma®

**5 - 16 October 2020**  
**Are. You. Ready?**



**20,000+**  
Pharmaceutical  
Professionals



**700+**  
International  
Exhibitors



**100+**  
Expert Speakers



**10 Days**  
Of Educational  
Content

## **Pharma's Most Anticipated (Virtual) Event of the Year!**

Forget what you already know about online events and remember these dates! CPhI's Festival of Pharma will land from 5-16 October 2020. Where? Your home office, of course.

Signalling a bold new age in pharma exhibitions, the festival is a virtual extravaganza, created to fill the gap left by in-person events and delivers the global pharma industry to you, in the comfort of your own home.

Join 20,000+ attendees for 2 weeks of unparalleled networking, sourcing and educational opportunities aided by an enhanced matchmaking system, a virtual pharma marketplace, and a world-class line up of industry expert speakers.

**[www.festivalofpharma.com](http://www.festivalofpharma.com)**

For more information contact:  
[salesoperations@informa.com](mailto:salesoperations@informa.com)





# Outsourcing as a key to success

Contract manufacturers and co-packers release capacity so that the customer can concentrate on his core competences – for example research and development or marketing and sales, says Mark Riemer of SternMaid GmbH & Co. KG.

The first step towards cooperation with a contract manufacturer is often taken when firms realise that through specific outsourcing they can reduce the workload on their own company. Such service providers open up access to technologies and skills outside the company's own production capabilities. Other reasons for outsourcing include cost-saving, rapid growth or a search for better quality, and also the additional know-how acquired through cooperation with specialist partners.

## Numerous advantages

Sometimes it is easier to approach a specialist service provider such as SternMaid, a company with a core business in blending, processing and filling products in powder form. First of all, outsourcing is an interesting option for firms that intend to expand but do not want to make additional investments. For after all, plant of one's own binds capital, space and personnel. Large companies, on the other hand, often want to restructure their production and outsource just part of it. For well-known brand manufacturers a second supplier strategy is becoming more and more important in order to safeguard their own ability to deliver large orders or for integrating a new product into their range. In many cases, whole product lines such as private labels are produced and packaged by contract manufacturers.

## The 'all-round carefree' package

The demand for more transparency in the supply chain has also contributed to a stronger focus on the role of toll production. Contract manufacturers have to keep the entire process chain in mind. The right choice and combination of



**Filling of cardboard cans. Such cans are increasingly being used in the food industry as more sustainable replacements for aluminium ones.**

process parameters is essential, depending on requirements. One example: A food manufacturer extrudes cereals and stores flours and sugar as single components in a silo, but the other raw materials are often added as a mixture and the manufacturer is looking for someone to produce this mixture. The service provider must first ask for a specification of the individual ingredients. In this context, regulatory criteria such as allergens and non-GMO status have to be taken into account to the same extent as the physical parameters of the product including bulk density, flow properties, particle distribution and the moisture content of the raw materials used.

SternMaid can offer the whole service chain from one source. The spectrum ranges from blending and processing to a complete service package that includes the purchase of raw materials, co-packing, quality control, warehousing and delivery and even product development can be offered through the development unit of SternMaid's sister company SternLife. Customers can either make use of the whole package or choose individual modules to meet their particular needs. Many customers also welcome the company's delivery service. It

enables goods to be dispatched straight from the contract manufacturer to the final recipient, thus saving transport charges – an important argument in view of the increasing pressure of costs and efforts to reduce carbon emissions.

A good service provider picks his customers up just where they are. He accepts their market objectives and listens to what they want. Together with the customer, he develops a convincing product and packaging concept tailored precisely to the customer's needs. Because ultimately, the contract manufacturer and his customer are pursuing the same objective: to put a successful product on the market.

## Sustainably packaged protein powder

An attractive pack is an important criterion for the success of any product in the retail trade. The pack must be eye-catching, stand out from its competitors and be practical and inexpensive – and nevertheless safe. Optimisation from the ecological point of view, for instance suitability for recycling, is playing an increasingly important role, too. For example, since 2017, SternMaid has produced the vegan protein powder range of a company in Hamburg, Germany. Together, the

two firms have further optimised the production process, quality and packaging of the products.

There has also been close cooperation in the choice of packaging materials. The client wished to reduce the aluminium content of its products as far as possible. The spiral-wound composite cans for the protein powder are made of recycled cardboard and a new feature is the aluminium-free white interior lamination. In order to make the products more sustainable, a laminate consisting of PET film coated with silicon oxide and a carrier paper is used instead of aluminium. In this case, too, development work is continuing and SternMaid is now also able to replace the tin base of the cans with cardboard.

## More planning certainty

Product life cycles are becoming shorter all the time. On the one hand, products have to reach market maturity faster, and on the other hand market conditions change very quickly. That is yet another reason why more and more companies are resorting to contract manufacturing and classic co-packing. Companies have to think very carefully, nowadays, before investing in large plant and faster innovation cycles go hand in hand with shorter product lifetimes. There is a need for caution when introducing novel or niche products. Who knows whether the plant for a particular dry beverage base or food supplement will still be used to capacity in a few years' time? Outsourcing enables manufacturers to save costs and minimize risks.

**Further information**  
**Mark Riemer**  
**SternMaid GmbH & Co. KG**  
**W: [www.sternmaid.de](http://www.sternmaid.de)**

# Do you have something to say?

We are always interested in hearing your ideas for new articles in the magazine. If you have something interesting to say, get in touch with our Editorial team – we'd love to hear from you!

*Chemicals Knowledge* was founded to provide a rapid-publication service to the speciality chemicals industry. Covering pharmaceuticals and cosmetics to agrochemicals and polymers, and always with an eye on sustainability and corporate responsibility, this fast-growing, ever-evolving industry needed a one-stop site that provides up-to-date news and reviews from key opinion leaders and captains of industry.

Topics covered:

- Pharmaceuticals
- Cosmetics & Personal Care
- Agrochemicals
- Food & Flavours
- Materials Science
- Oilfield & Energies
- Water Treatment
- Contract Services
- Regulations & EHS&S
- Corporate Responsibility

As with all good innovations that are typical of our industry, *Chemicals Knowledge* was borne of seeing a way to “do it better”. Our digital model allows rapid publication on-line at [chemicalsknowledgehub.com](http://chemicalsknowledgehub.com), with

weekly emails to tens of thousands of colleagues across the globe. Top news and articles are subsequently included in our printed magazines, like the one you're reading now.

If you have something interesting to share with our readers, get in touch with our editorial team at [Editor@ckhglobal.org](mailto:Editor@ckhglobal.org) to tell them your ideas. Writing an article for us does more than share information with your

peers – it raises the profile of you and your company, and lets the world know about your in-depth knowledge and expertise.

We don't charge publication fees, but any articles published in the magazine must comply with our guidelines. Most importantly, your article must be of genuine interest to our readers, which means it needs to have a focus on science and technology, or professional business matters in the industry. Articles with an overly promotional tone will not be accepted.

## Steps to success...

If you are interested in sending us an article, first email [Editor@ckhglobal.org](mailto:Editor@ckhglobal.org) with a very short summary – just a few sentences is enough – to explain the premise of your offering. If the editorial team thinks that it is suitable for the magazine, they will send you our guidelines and invite you to submit a full article.

Your article will need to be between 800 and 1500 words in length, depending on the topic (you will need to check the guidelines sent to you for your word limit). Following submission, your article will be reviewed within 2 weeks. If your article is accepted, we reserve the right to edit it (e.g. to reduce the length if it is too long, or to change the tone if it is too promotional). If your article is edited, you will be given the opportunity to review the edited version before it is published. Our reviewers might also have questions for you, in which case you will need to answer them before the article is finalized.

Submission deadlines must be adhered to. As we partner with so many different international events, our publication calendar is largely driven by the dates of those events – our magazines need to be printed in time to reach them. Extensions might sometimes be permitted, but if you are unable to meet a deadline your space in the magazine might need to be given to a contributor-in-waiting, and your own article might need to wait for space in the next appropriate issue. Please keep an open dialogue with our editorial team if you expect any delays, so we can accommodate your situation as much as we can.



## Editorial calendar for the rest of 2020:

Issue	Focus
2020-4 Sept-Oct	<ul style="list-style-type: none"> <li>• Innovation in pharma</li> <li>• Natural cosmetics</li> <li>• Agrochemicals</li> <li>• Materials science</li> <li>• Water treatment</li> <li>• Oilfield &amp; Energies</li> <li>• Contract services</li> </ul>
2020-5 Nov-Dec	<ul style="list-style-type: none"> <li>• Pharmaceuticals</li> <li>• Oligonucleotide &amp; peptide therapeutics</li> <li>• Plastics &amp; polymers</li> <li>• Flavours &amp; fragrances</li> <li>• Innovation in cosmetics &amp; personal care</li> <li>• Regulatory issues</li> <li>• Women in Science</li> </ul>

## Precious Metals

Edelmetale  
Metale te cmuar  
Qiyemetli Metallar  
Metal preziatuak  
Dragoceni metali  
Metalls preciosos  
Bililhon nga Mga Metals  
Zitsulo Zamtengo Wapatali  
贵金属  
Metalli Preziosi  
Dragocjeni metali  
Drahé kovy  
Værdifulde metaller  
Kostbare metalen  
Altvaloraj Metaloj  
Väärismetallid  
Mahalagang Metals  
Jalometallit  
Métaux Précieux  
Edelmetalen  
Métais preciosos  
Edelmetalle  
Metali presye  
Karfe mai daraja  
Nā Metala kūpono  
Lub Neej Zoo Nkauj  
Nemesfémek  
Dýrmæt málm  
Alsdj ola di oké onu ahja  
Logam Berharga  
Metalli preziosi  
贵金属  
Metals Logam  
귀금속  
Metayên hêja  
nobilis metalli  
Därgmetäli  
Taurieji metalai  
Metaly sarobidy  
Logam Berharga  
Metalli prezzjuži  
Metara Raraemi  
Edelmetaller  
Drogocenne metale  
Métais preciosos  
Metale prețioase  
O Metotia Taua  
Meatailtean luachmhor  
Metali ea Bohlokoa  
Metals anokosha  
Drahé kovy  
Plemenite kovine  
Birta Qaaliga ah  
Metales preciosos  
Logam lumayan  
Vyuma vya Thamani  
Ädelmetaller  
Değerli Metaller  
Qimmatbaho metallar  
Kim loại quý  
Metelau Gwerthfawr  
lintsimbi ezixabisekileyo



It doesn't matter what you know,  
until you know what matters.

# Expertise

Once precious metals catalysts reach their end of life, the final equation to be solved is their retained precious metal content. To do so, it is crucial to obtain accurate weights, truly representative samples and the highest quality of laboratory assay. This takes highly-skilled people, precisely calibrated equipment, and time-tested methodologies, but most of all ... the **Expertise** to get it done right. Trust your precious metals to the team with over 75 years invested in just this type of Expertise ... the Sabin Metal Group of companies.







JM

## Homogeneous ester hydrogenation for faster, greener processes

Homogeneous ester hydrogenation is an emerging technology for a challenging yet important transformation. At JM, we are committed to providing greener alternatives for your reactions. Our ester hydrogenation catalysts provide alternatives to the use of hydrides while enabling our customers to achieve highly chemoselective reductions at low catalyst loadings. With a wide substrate scope, our new ester hydrogenation catalysts provide higher reaction rates under milder conditions, allowing you to achieve more efficient and cost-effective processes.

**Johnson Matthey**  
Inspiring science, enhancing life

To find out more or request a sample,  
visit [matthey.com/pharmaceutical-catalysts](https://matthey.com/pharmaceutical-catalysts)