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DRUG DELIVERY & ENVIRONMENTAL SUSTAINABILITY

This edition is one in the ONdrugDelivery series of publications from Frederick Furness Publishing. Each issue focuses on a specific topic within the field of drug delivery, and is supported by industry leaders in that field.

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SUSTAINABILITY AND DRUG DELIVERY DEVICES

In this article, Rob Veasey, Senior Sector Manager, Medical and Scientific, at DCA Design International, explores the environmental challenges facing the drug delivery device industry – and the opportunities they bring.

We are witnessing a global boom in the use of drug delivery systems. Valued at approximately US$500 billion (£382 billion) in 2016, this market is forecast to reach nearly $900 billion by 2025.[1] An increase in demand for self-administration and home healthcare devices has helped fuel this expansion, meaning that today's drug delivery devices are not only much more widespread, they have become easier to use, safer and more effective. They form an essential part of our healthcare infrastructure, enabling the delivery of countless therapies that save lives and improve patient outcomes on a vast scale.

As they have been targeted at wider audiences, more drug delivery systems have been designed to be disposable. This market trend has been driven primarily by the desire to improve safety and usability. Disposable devices typically require fewer operating steps than reusable ones and, because they have a finite life, they are less susceptible to wear and contamination. A good example is the evolution of dry powder inhalers (DPIs). These began in the 1970s and 1980s as relatively simple reusable devices, such as the Spinhaler® and Diskhaler® (GlaxoSmithKline, UK), in which users fitted replaceable capsules or blister packs containing the drug product. They are now predominantly disposable products, in which the primary pack is sealed for life.

Drug delivery devices have also evolved to become more mechanically sophisticated. For DPIs, the requirement to automatically manage drug primary packaging and the addition of safety features such as dose counters has driven this trend. A similar story is found with injection devices, where one of the latest generation of spring-powered disposable insulin pen injectors has 17 components. In contrast, when first developed in the late '80s and early '90s, disposable pen injectors typically had fewer than 10 parts.

Alongside the increase in device complexity, designers are now also able to select from an ever-growing pallet of polymers. This has enabled improvements in performance and reliability, but the mix of materials now found in many devices adds to the already significant challenges for recyclability.

> "The mix of materials now found in many devices adds to the already significant challenges for recyclability."

THE NEED FOR CHANGE

As scientific evidence of the environmental challenges we face becomes clearer, the necessity to reduce the environmental impact of products we use daily has become more pressing. We all share this responsibility, but governmental bodies have taken measures to drive adoption of more sustainable practices. Under the 2015 Paris Agreement, the United Nations (UN) is aiming to keep the global temperature rise to below 2°C above pre-industrial levels. Nationally determined contributions will lay out how each country aims to reduce emissions and adapt to the impacts of climate change.

The UK's current target is a reduction in greenhouse gas emissions of at least 80% by 2050, relative to 1990 levels.[2] As countries develop and publish their individual strategies, the impact of their commitments will become evident. It can be expected that changes will be needed to the way that most products are manufactured, distributed, used and recycled.

The contribution of our industry to environmental damage is also beginning to receive greater attention. Within the last couple of years, reports have emerged describing the global warming effects of pressurised metered dose inhalers (pMDIs). For example, it has been estimated that the propellants used within these devices contribute a staggering 4% of the total carbon footprint of the NHS in the UK.[3]

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Figure 1: Single-use plastics play a vital role in healthcare.

"Greener" alternatives are being developed, with at least two major players – AstraZeneca and Chiesi – recently announcing a commitment to develop pMDIs with near-zero global warming potential. This is one example of the steps our industry is taking, but further substantial actions will be needed and we must all start to plan for and develop more sustainable drug delivery systems.

A further concern that has recently received publicity is the dramatic increase in plastic waste entering and damaging marine environments. In response, the European Union (EU) has taken action to ban an array of single-use items, put in place new targets to encourage recycling of plastic products and mandated the use of more recycled polymers.[4]

Due to the vital role that single-use plastics perform in healthcare (Figure 1) and the difficulties in reusing many types of medical devices, this EU legislation does not apply to the medical industry. The performance and inherent safety of polymers, coupled with their cost effectiveness, makes them ideal for medical applications. This is unlikely to change in the short term but, in the context of increased legislation and efforts within other sectors, it seems almost certain that our reliance on single-use plastics in healthcare will start to come under greater scrutiny.

THE CIRCULAR ECONOMY

The environmental challenges we face are complex and multifaceted, meaning there is unlikely to be a simple "one-size-fits-all" solution. So what factors should we be thinking about and what opportunities might these bring?

At the heart of sustainable thinking is the concept of the circular economy (Figure 2). This idea involves the gradual decoupling of economic activity from consumption of finite resources and seeks to remove waste from systems. The aim is to build long-term resilience, generate new economic opportunities and provide environmental and societal benefits.

One important aspect of this model is the distinction drawn between biological and technical cycles. The ultimate aim is that consumption happens only within biological cycles, where biologically derived materials can be returned to the system through processes like composting. In contrast, technical cycles should aim to recover and restore products, components, materials and chemicals through strategies like reuse, repair or recycling.

"Whilst a fully circular economy will be hard to achieve, by searching out opportunities to minimise waste throughout the lifecycle of products, we can take steps towards this goal."

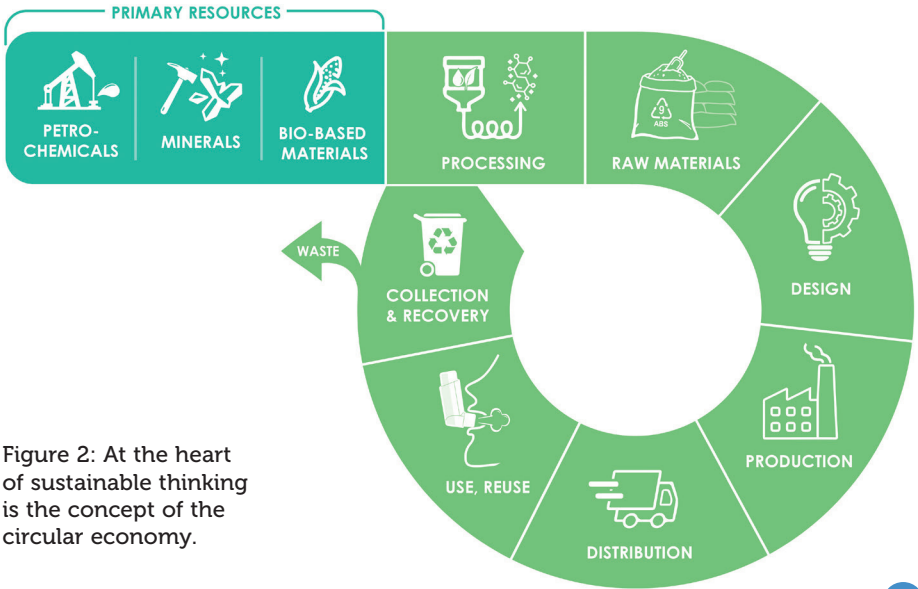

Figure 2: At the heart of sustainable thinking is the concept of the circular economy.

Whilst a fully circular economy will be hard to achieve, by searching out opportunities to minimise waste throughout the lifecycle of products, we can take steps towards this goal.

MEASURING SUSTAINABILITY

When you set out to improve a system, it is essential to define the metrics by which the improvement will be assessed. Without doing so, it is impossible to know if or when progress has been made. The first step in defining sustainability targets is therefore to decide what to measure and how to compare performance. In the context of the circular model, three key parameters are important:

- The energy consumed in the manufacture, distribution and use of a product
- The amount of material that is derived from renewable or recycled content
- The amount of material that can be recovered for reuse at end of life.

In some instances, factors influencing the choices made in relation to these parameters may be conflicting, or they may conflict with other design requirements. It is therefore essential that we develop objective ways in which conflicts can be understood and resolved to achieve the best environmental profile for a product. This understanding is typically gained through lifecycle analysis (LCA), following methods defined within the ISO 14000 standards.

Owing to the huge array of factors involved in manufacture and distribution of products, LCAs are complex and time

consuming to compile. This makes them an impractical tool to inform design decisions in real time and, as a result, they are often used to analyse designs and production systems retrospectively.

To achieve the maximum value from an LCA, a detailed analysis of existing product solutions is best suited to inform the development of new ones. This identifies where the biggest opportunities for improvement exist, enabling effort to be directed where it will be most effective. This can sometimes be in unexpected places – for example, in the case of a device that requires cold-chain distribution, significantly more energy may be consumed in transporting and storing the product than manufacturing it. In this instance, improving the secondary packaging to increase packing density may be the most effective way to improve its environmental profile.

Whilst LCA remains the "gold standard" means for assessing the environmental impact of a product, the design industry needs other tools to help assess and inform design decisions rapidly during development. Such tools do not need to be fully comprehensive but they should allow engineers to make informed decisions about options that might have an impact on the environment.

Some promising early options, such as Eco-Indicator 99[5], have been developed, but to remain relevant and useful it is essential that these continue to be maintained and improved. Given the increasing focus on sustainable development, it seems inevitable that new tools will become available in the coming years.

DEVELOPING MORE SUSTAINABLE DEVICES

If we restrict our analysis to mechanical drug delivery devices, two issues that are commonly encountered in relation to sustainable development are materials selection and product lifetime. Neither of these issues are straightforward, since environmental design decisions are never taken in a vacuum. Instead, these factors must be weighed alongside many other requirements that safety-critical products such as drug delivery devices must achieve.

SUSTAINABLE MATERIALS

Most drug delivery devices are made predominantly from plastics, so careful selection of these materials is important when targeting more sustainable solutions. Following the principles of the circular economy, we can break this down into three aspects for consideration:

Renewable And Recycled Polymers

Devices are typically manufactured from "medical grade" polymers. These can be traced back to their raw material batches and come with guarantees that the formulation will not change. Recycled polymers are not currently available with medical grade certification and so the most sustainable alternatives in the medium term are likely to be biopolymers.

Derived from biological rather than petrochemical sources, a small range of biopolymers is starting to emerge. Unfortunately, in the short term, device developers are likely to be faced with a lack of choice for medical grade biopolymers. They also carry a price premium compared with conventional polymers, and some grades need to be separated from standard recycling streams.

Because of the relatively small size of the medical sector in comparison with the wider polymer market, it is unlikely that our industry will drive the development of new sustainable materials. Instead, we should seek to be fast followers of other industries, such as food packaging, that use greater quantities of polymer and for whom both regulators and customers are demanding rapid adoption of greener solutions.

End-of-Life Solutions That Enable Better Recovery And Recycling

Recycling the polymer materials contained in drug delivery devices is challenging, leading to problems in establishing the infrastructure to do so safely and effectively. Firstly, they usually contain some residual drug product (and may also be contaminated with biological materials). Secondly, because each component is optimised for its particular function, they typically contain a mix of polymer types as well as materials such as glass, aluminium and rubber. Thirdly, they are often designed to be inherently difficult to disassemble in order to deter tampering or counterfeiting.

As a result, it is difficult and expensive to reprocess devices by any means other than incineration for energy recovery. Chemical recycling, in which polymers are broken down into more basic chemicals that can be reprocessed to create new high-performance polymers, may be one option in the future, but is not yet a widely established technology. To improve the recyclability of drug delivery devices, many of these issues will need to be addressed at a design level, so must become a requirement at the outset of new development programmes.

Lower Embodied Energy

Not all polymers are created equal, having subtly different environmental profiles. Generally, more complex polymers require higher energy usage during their manufacture. For this reason, simple polyolefins, such as high-density polyethylene (HDPE) and polypropylene (PP), are usually considered more sustainable than alternatives such as acrylonitrile butadiene styrene (ABS), polycarbonate (PC) or polyoxymethylene (POM). Clever design and materials selection can optimise part count and the use of polymers, ensuring that more complex and highly refined materials are only used where they are absolutely necessary.

EXTENDING DEVICE LIFE

Given the challenges in sourcing more sustainable materials, extending product life may be the most effective path to improving the environmental profile of drug delivery devices in the near term (Figure 3). The longer a device can be used, the lower the environmental impact is likely to be in terms of material usage, waste and energy expenditure when assessed over a fixed period of therapy.

In this context, it is evident that reusable drug delivery devices are likely to have better environmental profiles than disposable ones. At the beginning of this article, I outlined that recent trends have been in the opposite direction, so what can be done to reverse this?

Reusable Devices That Are Easier, Safer And More Convenient To Use

A primary concern with reusable drug delivery devices has often been usability. Patient groups regularly contain large numbers of individuals with reduced manual dexterity or vision impairments. These patients can struggle to correctly replace a primary pack or reset the operating mechanism. To address this, we should continue to make reusable devices easier to use, for example ensuring that the mechanism resets automatically when the old primary pack is removed or when a new one is fitted.

Figure 3: Extending product life may be the most effective path to improving the environmental profile of drug delivery devices in the near term.

> "By good design, there is no reason why more sustainable drug delivery devices cannot also be more cost effective and better for patients."

Reusable Devices That Are More Appealing

In the past, there have often been no real advantages to selecting a reusable device over a disposable one. Indeed, as described above, there have been some legitimate concerns in relation to usability; yet this should not be the case. With reusable devices, cost is typically offset against a usable life of years rather than days or weeks, so there is an opportunity to specify better materials to achieve improved performance and to include more automated features.

One interesting development that may help to tip the balance in favour of reusable devices is the advent of connected drug delivery systems. For many applications, the cost of electronic monitoring and control functionality is currently seen as a barrier to embedding this technology within disposable devices – making reusable solutions much more attractive. Connected systems may also help to balance some of the usability downsides of reusable devices – for example, by providing warnings of potential use errors.

For some applications, it may remain impractical to offer fully reusable drug delivery devices. In these circumstances, an alternative solution may be to develop disposable products that have greater dose capacity, so that their use life is prolonged. This approach may, of course, bring challenges with drug stability and device affordability but it is a trend that is already well established in some consumer markets and we are likely to see further developments of this sort within drug delivery in the future.

CLOSING THOUGHTS

The environmental challenges we face are complex, but they also bring opportunities. By good design, there is no reason why more sustainable drug delivery devices cannot also be more cost effective and better for patients. But given the relatively long development cycles required for drug delivery devices, new environmental legislation may emerge that imposes targets that some businesses find difficult to achieve in the time frame demanded. We are currently witnessing this in the automotive industry, where companies that have proactively developed sustainable product ranges are now in a much stronger position than those that left it late.

In many ways, our industry is well equipped to deal with environmental challenges. We are systematic in our approach, data driven and highly analytical in our methods. Drug delivery devices are not subject to the whims of fashion; a device's performance and effectiveness must be comprehensively demonstrated before it enters the market, meaning that we tend not to embrace short-term thinking.

To effect change, we will all need to adopt a more sustainable mindset, in which we question the environmental impact of our decisions in the same way that we currently think about patient safety and therapeutic efficacy.

ABOUT THE COMPANY

Founded in 1960, DCA is one of the world's leading product design and development consultancies. Its multidisciplinary service offering includes systems engineering, mechanical engineering, industrial design, insight and strategy, UX/UI, human factors, electronics, software and prototyping.

With a range of global pharmaceutical, biotech and device companies amongst its long-standing clients, DCA has deep experience in the field of drug delivery devices. Work undertaken in this area includes design, development, analysis and industrialisation support for injection devices, inhalers, wearables, intra-nasal devices and applicators, including smart and connected devices. DCA has won many major industry awards and contributed to over 1,000 granted patents in the last 10 years. The company's development service is certified to ISO9001 and ISO13485.

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ABOUT THE AUTHOR

Rob Veasey leads projects within DCA's medical device sector. He has 30 years' experience in engineering, design and management roles with leading manufacturing and consultancy businesses and has worked exclusively on the development of drug delivery devices for over 20 years. His experience encompasses both mechanical and electromechanical devices, including work in the fields of injection, body-worn devices, metered dose and dry powder inhalers, intra-nasal sprays and topical applicators. A particular area of expertise is the development of pen injectors, in which Mr Veasey led DCA's team for the SoloStar®, Lyxumia®, AllStar® and AllStar® Pro device programmes with Sanofi.

Kindeva
DRUG DELIVERY

NEXT-GENERATION PRESSURISED METERED DOSE INHALERS: A HOLISTIC, PATIENT-CENTRED APPROACH TO SUSTAINABILITY

In this article, Mike Needham, Global Respiratory Product Development Manager, Phil Cocks, Product Design and Optimisation Lead, and Louise Righton, Global Strategic Marketing Leader, all of Kindeva Drug Delivery, discuss how sustainability should be a central theme of future innovation in inhalation drug delivery but must be balanced with the needs of the patient.

Kindeva Drug Delivery has a legacy of advancing the environmental sustainability of inhaled medicines. Formerly 3M Drug Delivery Systems, Kindeva was a founding member of the International Pharmaceutical Aerosol Consortium (IPAC), which was established to represent the industry in navigating the Montreal Protocol in the late 1980s.

Kindeva, a pioneer in hydrofluoroalkane (HFA)-based formulations for pressurised metered dose inhalers (pMDIs), has developed the world's first chlorofluorocarbon (CFC)-free pMDI (launched in 1995) and the first CFC-free nasal pMDI (launched in 2012). These innovations were milestone accomplishments that delivered step-change improvements in the environmental impact of inhaled drugs. There is more work that needs to be done across the pharmaceutical industry, and Kindeva remains at the forefront of environmental progress.

Today, there is renewed energy around the sustainability of inhaled therapies. At its core, this scrutiny is positive and will propel the industry forward. However, much of the debate is narrowly focused on propellants and the comparative global warming potential (GWP) of different devices. As a result, advocacy too often provides blanket recommendations that amount to "device switching" – the notion that propellant-free devices, such as dry powder inhalers (DPIs) and soft mist inhalers (SMIs), are categorically superior to pMDIs, regardless of patient considerations.

Kindeva believes that all inhaler types have a role to play in the management of lung disease and no specific device should be singled out for replacement. It does not support blanket switching based on carbon footprint alone. Kindeva believes in a holistic approach to advancing sustainability in the pharmaceutical industry that offers a longer-term view of environmental and patient impact. This approach involves empowering patient and physician choice to optimise overall disease management, innovation of novel propellants for pMDIs to reduce their carbon impact, and full life-cycle analysis and sustainable improvement of devices. Kindeva's view is that we must simultaneously acknowledge the role of pMDIs as a critical option for patients and seek to alleviate the environmental impact of all inhalation therapies.

> "There does not need to be a trade-off between patient needs and sustainability; these twin goals can be complementary."

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PATIENT-CENTRIC DECISIONS LEADING TO OPTIMISED DISEASE MANAGEMENT

As with any drug delivery development, an innovation that promotes sustainability must consider the needs of the patient. There does not need to be a trade-off between patient needs and sustainability; these twin goals can be complementary. Well-managed, stable patients have lower carbon footprints and less detrimental effects on the environment. They are less likely to be hospitalised and less likely to experience progression of their diseases, impacting their lifetime use of medication and devices. Therefore, a sustainability strategy that depends wholly on broad advocacy for device switching based solely on the relative GWP of different devices is unlikely to satisfy diverse patient needs and may be counterproductive to sustainability goals.

There is no systematic evidence showing that DPIs are categorically more effective than pMDIs.[1] Matching the patient with the right inhaler is a complex decision, which must be judged by the clinician. Guidelines from the Global Initiative for Asthma (GINA) and the Global Initiative for Chronic Obstructive Lung Disease (GOLD), as well as current research, emphasise this. If we limit the choice of devices for patients and practitioners, we risk reducing the quality of care. Recent studies demonstrate that pMDIs are clinically equivalent or even significantly more effective than DPIs, indicating that pMDIs are a crucial option for physicians.[2] In short, there's no "one size fits all" inhaler; treatment must be tailored from the plethora of options available and patients should be engaged in the decision.

An essential element of optimised disease management is the training and correct usage of devices.[3] If patients are using their devices incorrectly, the medication will not work as intended. Incorrect usage can be particularly problematic for patients who are prescribed multiple DPIs because it can be challenging to train patients to use various DPI devices – some incorporating reservoirs of powder, others requiring single-use loading with a capsule, for example.

Asthma and chronic obstructive pulmonary disease (COPD) patients with stable disease should have continuity of inhaler device.[4] Suddenly asking the patient to switch from a device that is working for carbon-led reasons, not medical reasons, can have negative consequences. Patients can lose confidence in their medicine; they can lose satisfaction with their treatment; they can even lose trust in their doctor. Learning to handle a new device when the old one was working can lead to exacerbations and even hospitalisations.

Figure 1: The Kindeva Intelligent Control Inhaler.

Novel pMDI device design can also support the overall management of lung disease. The baseline rate of correct use of inhalers is low, with the literature suggesting that up to 94% of DPI users and 74% of pMDI users make mistakes.[5] Beyond correct use, overall adherence to inhaled medicines is low, with 60% of COPD patients and up to 70% of asthma patients non-adherent to their prescribed therapy.[6,7,8]

Kindeva's Intelligent Control Inhaler (Figure 1), which is currently under development and not yet available for commercial sale, may provide a solution to both the correct usage and the adherence challenge. Designed for easy and intuitive use, the Intelligent Control Inhaler provides flow governance designed to optimise inhalation technique, and real-time feedback to aid in proper inhaler technique. It also provides reminders and scoring to promote adherence. The industry should continue to invest in innovation that will transform the way patients engage with their medicine. These solutions will systematically improve the management of respiratory diseases and ultimately lead to lower-cost, more sustainable treatment over the patient's lifetime.

> "Any alternative propellant must be safe for patients to use from a toxicology perspective and must be safe to manufacture."

INNOVATION OF NOVEL PROPELLANTS FOR pMDIS

There is a clear drive towards the use of alternative propellants in pMDIs aligned to the desire to reduce their environmental impact. We need to remember that the use of hydrofluorocarbons (HFCs) in pMDIs represents less than 0.05% of all greenhouse gas emissions. These emissions are a tiny part of the global sustainability challenge. Nevertheless, given the outsized importance of the pMDI as the mainstay treatment for asthma and COPD control, it is sensible to address environmental concerns related to propellants.

It is possible to make a significant change in the carbon footprint of the pMDI. By switching propellant from HFA227 or HFA134a to a lower GWP propellant, such as HFA152a, a considerable reduction in overall device carbon footprint can be achieved (Figure 2). History tells us, however,

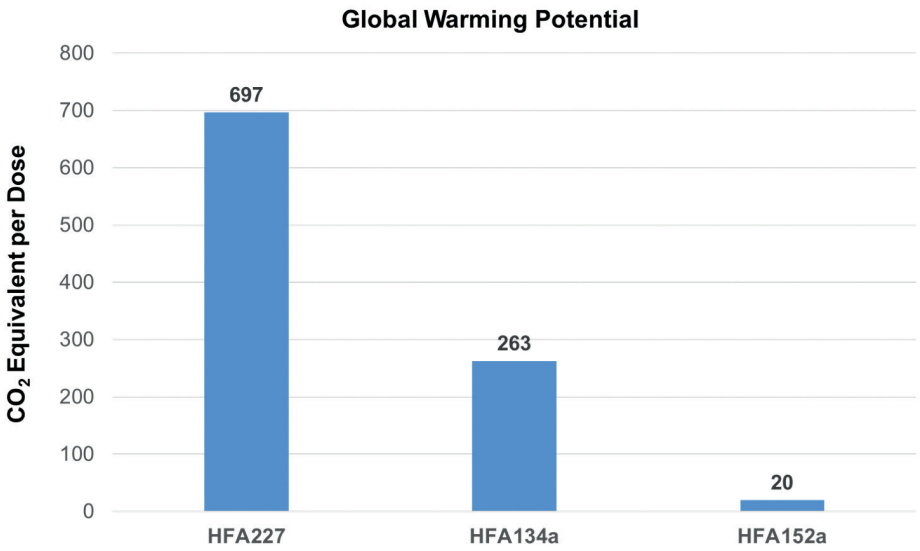

Figure 2: Global warming potential for different propellants.[9]

that it is not entirely straightforward to switch propellants. Kindeva learned this first hand during the transition from CFCs to HFAs following the establishment of the 1987 Montreal Protocol. When considering any alternative, we must think seriously about many factors.

Safety is the primary concern. Any alternative propellant must be safe for patients to use from a toxicology perspective and must be safe to manufacture. The flammability of volatile propellant raises some technological challenges with HFA152a, which must be overcome. Formulation is another concern. A viable propellant must have suitable physical and chemical properties to fully enable solution and suspension pMDI formulations to meet the rigorous pharmaceutical performance and stability standards set for today's inhalation products.

Finally, the cost and quality of any alternative propellant must be acceptable from a supply chain perspective. GMP supplies must be established and made available at an appropriate scale and at an acceptable cost to meet future commercial needs. HFA152a does, however, initially appear to be a highly suitable pMDI propellant candidate. Given the amount of research and investment in this area, commercial manufacturing capabilities are likely to be available soon but a wide range of products in patients' hands is still some years away.

Kindeva has also completed several solubility studies on HFA152a. Pharmaceutical product performance has also been successfully demonstrated on a range of formulations using a typical container-closure system. Following the completion of various flammability and Dangerous Substances and Explosive Atmospheres Regulations (DSEAR) assessments, Kindeva has had small-scale, non-GMP manufacturing equipment installed, giving it the capability to manufacture cold-fill HFA152a safely. This equipment is adequate for most early-stage development projects and enables the company to perform small-scale feasibility assessments and short-term stability studies on future HFA152a opportunities.

There are other developments in novel propellants with negligible carbon impacts that are perhaps even more future-proofed than HFA152a. For example, HFO1234ze is a commercially available propellant that has both technical and consumer applications. With very low GWP, HFO1234ze could offer a sustainability improvement for inhaled medicines.

HOLISTIC DEVICE LIFECYCLE OPTIMISATION

Propellants are only one part of the story. We need a shared understanding of each product's lifecycle and its total environmental impact to expand the discussion from a single focus on propellants and GWP. A holistic approach to sustainability will consider other raw materials used in the drug product or device, how they are sourced, how easily they are recycled, and where they go after the patient has finished using them.

The current carbon-led switching discussion is based on only one element of the environmental issue: global warming. While climate change absolutely should drive policy when it comes to consumption of fluorinated gases, we must not overlook other environmental impacts such as human toxicity, fossil depletion and marine water

quality degradation caused by pollution leading to algae growth and damaging aquatic life. The excessive use of single-use plastics and the resultant burden on landfills are also key considerations in making inhalation therapy more sustainable. While a DPI has the lowest GWP, it is the least environmentally friendly option with respect to eight other impacts.[9] We need to look holistically at sustainability and broaden the avenues that we go down to come up with solutions.

At the forefront of sustainability thinking at Kindeva is a reduction in the parts count of plastic devices. For example, the company is developing a new metal-free dose counter with far fewer parts than has been available previously. This endeavour shows that there does not need to be a trade-off between performance and sustainability. Kindeva believes this new dose counter delivers benefits throughout the value chain – simplicity of assembly, compatibility with a broad range of actuators and valve types, robust reset of dose counting – but also represents a marked sustainability improvement by reducing plastic use. Our industry must recognise that these improvements are possible through the regular cycles of innovation and to continue to challenge ourselves on sustainability.

At one end of the product's lifecycle is the question of sourcing and manufacturing: what materials go into the product? At the other end of the lifecycle is the question of waste management: what happens at the end of patient use? Pharma companies and device makers can and should be influential in promoting the reusability and recyclability of devices. For example, Kindeva is developing new refillable devices that can help lessen the environmental impact of its inhalers. The Intelligent Control Inhaler is designed with a reusable top element with a reduced number of disposable parts. While the significance of propellants cannot be downplayed, the industry must also recognise the vital sustainability implications of materials selection, part counts, manufacturing methods, waste management and recycling.

CONCLUSION

Sustainability should be a central theme of future innovation in inhalation drug delivery but this must be balanced with the needs of the patient. Sustainability strategies that hinge solely on device switching for carbon reduction do not generally serve the patient's best interests. Patients deserve a thoughtful approach to treatment that is designed to optimally treat their conditions. Robust sustainability strategies require a holistic, end-to-end view of the product design, lifecycle and patient impact. By effectively optimising disease management and preserving patient options, innovating low GWP propellants, and sustainably designing devices and components, pMDIs will continue to play a key role in lung disease management.

> "Robust sustainability strategies require a holistic, end-to-end view of the product design, lifecycle and patient impact."

ABOUT THE COMPANY

Kindeva Drug Delivery is a contract development and manufacturing organisation offering its partners integrated, end-to-end capabilities spanning formulation, product development, scale-up manufacturing and commercial manufacturing. Its full-service innovation offering covers: inhalation (pMDIs, DPIs, connectivity, nasal delivery); transdermal delivery (drug-in-adhesive systems and gel patches); and intradermal delivery (microneedles based on solid and hollow microstructures). Kindeva Drug Delivery has locations in the US and the UK and employs over 900 people. It was formed in 2020 when 3M's Drug Delivery Systems business was acquired by Altaris Capital Partners for US$650 million (£503 million) and renamed Kindeva.

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H&T PRESSPART

CUTTING THE CARBON IMPACT: CREATING A MORE SUSTAINABLE pMDI COMPONENT SUPPLY CHAIN

In this article, Wim Kehoe, Global Key Account Manager, and Ameet Sule, Director of Inhalation Product Technology Centre, both of H&T Presspart, discuss the company's approach to sustainability, and the developments that are helping to reduce the carbon footprint of pMDIs.

INTRODUCTION

Sustainability has presented itself as a key talking point[1] within the pharmaceutical industry over the last few years, with intense scrutiny regarding the contribution that pharmaceutical companies make towards a sustainable health sector. An ageing and growing world population and improved healthcare systems are driving demand for an industry that is increasingly aware of the need to pursue sustainable development, whilst delivering a wider range of pharmaceutical products.[2] H&T Presspart is currently implementing process and product innovation to drive sustainability within the respiratory drug delivery market, whilst continuing with long-term commitments to manufacture responsibly for its global customer base.

Chiesi (Parma, Italy) was the first company to publicly announce its plans to bring a solution to market to address the carbon footprint of pressurised metered dose inhalers (pMDIs), with its development of a carbon minimal pMDI device by the end of 2025.[3] AstraZeneca (Cambridge, UK) unveiled an investment programme of up to US$1 billion (£773 million) at the start of 2020 to achieve zero carbon emissions, including the development of the next generation of respiratory inhalers with near-zero global warming potential (GWP) propellants.[4] Dubbed "Ambition Zero Carbon", the strategy outlines plans to eliminate carbon emissions by 2025 and to be carbon negative across the entire value chain by 2030, bringing forward decarbonisation plans by more than a decade.[4] Other pharmaceutical companies producing pMDIs are likely to follow by announcing their own commitment to developing a carbon minimal pMDI.

> "H&T Presspart is currently implementing process and product innovation to drive sustainability within the respiratory drug delivery market, whilst continuing with long-term commitments to manufacture responsibly for its global customer base."

Controversies surrounding the green credentials of pMDIs are at the forefront of conversations and, with over 85% of the world's pMDIs featuring an H&T Presspart component, there is an increasing responsibility to acknowledge the significant impact manufacturing these components has on the environment.

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H&T PRESSPART'S APPROACH TO SUSTAINABILITY

Sustainability has been an important element of H&T Presspart's strategy for many years. Manufacturing pMDIs with aluminium has a high carbon footprint output, driven by the energy required to produce these components. In 2010, H&T Presspart began a programme that aimed to actively drive down carbon emissions at its sites in Blackburn, UK and Marsberg, Germany. Implementing key performance indicator (KPI) measures alongside sustainability initiatives ensured focus remained after initial success was achieved. H&T Presspart's sustainability team is dedicated to driving sustainability efforts forward with initiatives being regularly reviewed. As global leaders for supplying critical components to the industry, H&T Presspart acknowledges the company's responsibility in contributing to a more sustainable healthcare sector for current and future generations.

Sustainable Supply Chain

The appetite for change is large, with environmental issues becoming the focus of business activity. Creating a forward-looking, sustainable supply chain is at the heart of H&T Presspart's strategy for a greener manufacturing future. The company's sustainability vision and strategy will be launched at the end of 2020 and will facilitate a much stronger approach to sustainability within the supply chain.

Figure 1: H&T Presspart's new MDI can wash plant.

Figure 2: Plasma MDI can manufacturing facility.

As part of this strategy, H&T Presspart will launch a sustainability survey for its suppliers to monitor their own efforts towards creating a greener supply chain. KPIs will be defined for suppliers to focus on key areas such as carbon footprint, emissions, recycling and energy efficiency, with suppliers expected to reduce their impact on the environment.

H&T Presspart supports customers with sustainability topics by sharing carbon metrics and energy consumption data to help customers understand the company's environmental maturity and impact as a supplier. In addition, employing energy efficient practices to permit attractive pricing to be passed onto the customer, whilst adapting to industry trends and completing customer audits, is a proactive approach taken by H&T Presspart when continuing to drive sustainability activities to the forefront of operations.

Substantial changes within the supply chain have already been made. H&T Presspart's manufacturing sites in the UK and Spain will be using 100% renewable energy sources by the end of 2020. Currently, 40% of all substrates used by H&T Presspart are from a recycled source and all scrap metal created during the manufacturing process is recycled.

Sustainable Device Manufacturing

H&T Presspart has a long-term commitment to focus on all aspects of the manufacturing process to improve sustainability. A number of key multimillion-pound investments have been undertaken in order to reduce carbon footprint and environmental impact across all H&T Presspart manufacturing sites.

pMDI Can Wash Plant Investment

In 2016, H&T Presspart's Blackburn site replaced pMDI canister wash plant equipment with multimillion-pound state-of-the-art wash plants (Figure 1). The old equipment used a hydrocarbon-based solution to remove oil, which was then washed off with water. This not only generated a large amount of CO_2 emissions, but used thousands of litres of water during the process. The new wash plants mitigated the need for water, so reduced water usage by over 100,000 m^3 a year, equivalent to 40 Olympic swimming pools. This led to a 95% reduction compared with previous years (Figure 2).

Over 250,000 L of hydrocarbon were removed each year from H&T Presspart's washing process as a result of the new plants recycling the solvent-based washing solution;

this is equivalent to 620 tonnes of CO_2 per annum. Eliminating the safe disposal of the hydrocarbon waste also resulted in a saving of 300 tonnes of CO_2 per annum.

In just three years, these initiatives helped H&T Presspart reduce its carbon footprint by over 60%. Redefining H&T Presspart's sustainability vision and strategy by the end of 2020 will help us to set even more ambitious targets for the future.

Sustainable Surface Treatment for pMDI Cans

Sustainability issues regarding coating pMDI cans with materials such as fluorinated ethylene propylene (FEP) are well known to the industry. The energy-intensive coating process, due to the cleaning and baking step that is needed, requires effective actions to protect the environment, which is why H&T Presspart installed a biofilter system.

H&T Presspart's unique plasma process – manufactured under licence from Portal Medical (Cambridge, UK) – for treating the internal surfaces of pMDI canisters was developed as a more sustainable option than coated cans (Figure 3).

The plasma surface treatment process treats the internal surface of the pMDI canister wall with a low-energy fluorocarbon polymerised nanolayer. The result is a surface barrier between the canister wall and API, which enhances drug stability in formulations, where interactions with the aluminium substrate of the canister wall can lead to product degradation and reduced shelf life. This helps to ensure the patient receives a consistent dose through the life of the pMDI.

There are significant sustainability benefits of using the plasma process over coating for pMDI cans – the first being a reduction in the raw material needed for the pMDI canisters. Coated cans need to be thick walled due to undergoing a pre- and post-heating process during manufacture. A thin-walled can is unsuitable for coating as the can becomes too soft to stand the crimping pressure when the valve is attached to the canister.

The use of thinner aluminium on plasma pMDI canisters results in a 30% reduction in the carbon footprint of the aluminium strip production. There is also a reduction in energy consumption from the presses when manufacturing thin-walled pMDI cans compared with thick-walled ones. A further benefit of manufacturing thin-walled cans is a reduction in noise pollution for our employees and the surrounding environment.

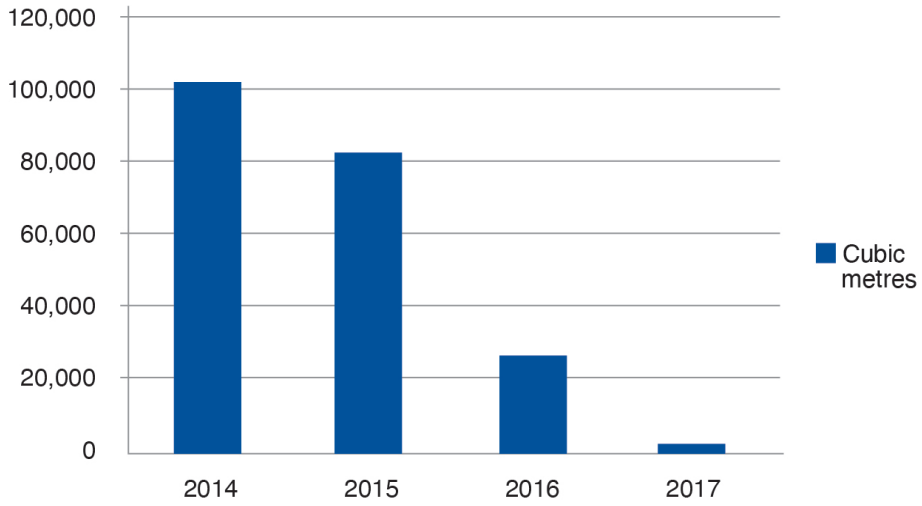

Figure 3: Water usage at H&T Presspart Blackburn, UK.

> "The major sustainable benefit of plasma-treated cans over coated cans is the reduction in energy consumption during the manufacturing process."

The major sustainable benefit of plasma-treated cans over coated cans is the reduction in energy consumption during the manufacturing process. The burn-off cleaning process and the baking of the coating onto the pMDI cans is very energy intensive. By switching to plasma, there is a reduction in energy consumption of 4,100 kWh per million cans, which is a reduction of nearly 50%. To put that into perspective, the energy reduced is the equivalent to running a washing machine over 1,700 times. Furthermore, plasma eliminates the use of solvents, leading to a further reduction in energy and water consumption as biofilters would no longer be needed. The plasma process uses standard industrial gases, so it is a future-proof technology, as the gases are REACH compliant.

Biofilter for Coated Cans

Emissions from manufacturing processes can affect the environment and public health, as well as cause global warming, and are an important area that drug delivery device manufacturers can make improvements in towards a more sustainable future.

To help reduce emissions produced during the manufacture of pMDI-coated cans, a multimillion-pound investment in a biofilter was introduced at H&T Presspart Marsberg, Germany. The can coating process produces vaporised solvent. Within the biofilter, these vapours are removed from the air flow by showers and subsequently cleansed by natural microorganisms. This process is constantly monitored online, ensuring H&T Presspart Marsberg meets all relevant EU environmental regulations.

Product Innovation and Patient Adherence

From an environmental point of view, pMDIs have been accused of being less sustainable compared with other devices, such as dry powder inhalers (DPIs), as a result of the propellant which acts as a drug carrier within the formulation. Previously, pMDI devices used chlorofluorocarbon (CFC) propellants which contributed to ozone depletion in the upper atmosphere until they were banned in 1996. As a result, the pharmaceutical industry switched to hydrofluoroalkane (HFA) which was believed to be a more environmentally friendly propellant. However, due to their higher GWP, these HFAs also contribute to increasing carbon emissions, which has led to the evaluation of propellants HFA 152a and HFP1234ze for medical use. This could potentially reduce the pMDI carbon footprint by 90% when compared with HFA-134a.[5]

GWP is high with pMDIs, however there are several other mechanisms, alongside a new propellant, which can be used to reduce the impact. This includes the use of biodegradable plastics and recyclable aluminium, dose-counter technology and the introduction of digital health to improve patient adherence.

Figure 4: Dose counter range.

"Product innovation such as H&T Presspart's eMDI smart inhaler and a range of dose counters and end of life indication systems, would allow patients to determine the amount of medication in doses remaining within their pMDI device."

In a study conducted in 2005[6], 70% of patients overestimated the number of remaining doses when shaking their inhaler device to determine the quantity of drug remaining. Nearly 20% underestimated the number of doses remaining and, as a result, were discarding their pMDI prematurely, adding to landfill waste and increasing demand for pMDIs with manufacturers.

Product innovation such as H&T Presspart's eMDI smart inhaler and a range of dose counters (a licensed design from Kindeva) and end-of-life indication systems, would allow patients to determine the amount of medication in doses remaining within their pMDI device. Reducing the number of inhalers that are prematurely disposed of will consequently reduce the carbon footprint of the pMDI market whilst improving patient adherence (Figure 4).

CONCLUSION

After 65 years, the pMDI remains one of the best portable devices for delivering drugs to the lungs. The patient's need for these devices still exists, with a number of big pharma companies working on the next-generation pMDI. With add-on technologies to provide safe and efficacious drug delivery, the longevity of pMDI devices remains certain.

Pharma companies and medical device manufacturers must continue to work together to reduce the carbon footprint of pMDIs. To achieve this, collaboration throughout the supply chain, from raw material suppliers to patients and drug manufacturers recycling devices, is required. This partnership will be significant if the industry is to be successful in creating a greener and more sustainable future for the next generation.

Both process and product innovation will need to be capitalised in order to make a considerable difference. Investments in new sustainable manufacturing techniques, such as H&T Presspart's wash plants, will help drive sustainability within the industry.

The introduction of new propellants, such as HFA 152a or HFO1234ze, will see the carbon footprint of a pMDI reduced by 90% which will be a big step towards sustainable business in the market. It is also important that the industry proactively addresses patient waste through product innovation such as dose counters, end-of-life solutions, smart inhalers (connected health) and the use of biodegradable plastics, as well as the introduction of an effective recycling system for pMDIs.

ABOUT THE COMPANY

H&T Presspart specialises in industrialising drug delivery devices and components. The products that the company offers its pharmaceutical clients include medical devices, metered dose inhaler components and a comprehensive range of dose-counting technologies. The company has 50 years' experience and a worldwide reputation for competence, quality and innovation in the pharmaceutical sector. H&T Presspart's Inhalation Product Technology Centre supports its customers' new inhalation product developments and strategic initiatives. H&T Presspart, part of the Heitkamp and Thumann Group, has three European manufacturing sites, in Germany, Spain and the UK, with sales offices in China, India, Singapore, South America and the US.

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Wim Kehoe, Global Key Account Manager at H&T Presspart, manages a number of large, strategic key accounts. Mr Kehoe joined H&T Presspart in April 2017 as Sales Manager, Europe. In January 2019, he assumed the role of Global Key Account Manager. He has over 10 years of experience in various sales management and business development roles within the pharmaceutical industry, with a focus on respiratory diseases during the past four years.

Ameet Sule, Director, Inhalation Product Technology Centre, H&T Presspart, is a pharmaceutical professional, having worked in the industry for more than 20 years, specialising in the development of inhalation products and devices. Mr Sule works closely with H&T Presspart's customers around the globe, understanding and mitigating the front-end development challenges of new and generic products for inhalation drug delivery.

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NANOTECHNOLOGY: A PATHWAY FOR SUSTAINABLE INNOVATION IN DRUG DEVELOPMENT

Here, Andrea Cusack, Chief Executive Officer, leon, discusses how, by using bottom-up nanotechnology techniques, efficiencies can be found both in the development of new chemical entities and in the repurposing of existing drugs, and how these efficiencies translate into reduced energy requirements and therefore more sustainable industry practices.

It seems that, across industries, every effort to go green requires some sort of compromise be made, whether that be on price, performance, stability or any number of other factors. For example, at the time of writing, electric cars are more expensive to buy than those with a conventional combustion engine, and they can't go anywhere near as far. Of course, we all recognise that very soon such compromises will become less pronounced, as the drive towards a more sustainable world gathers pace, and consequently green alternatives and solutions improve in performance.

However, there are already some areas in the pharma supply chain where going green need not cost the earth in terms of performance. In this article, we will explore how bottom-up nanotechnology can deliver oral and injectable APIs with enhanced bioavailability, increased solubility and improved stability, sustainably.

We will also take a look at the sustainability challenges that the current "gold standard" approach faces and demonstrate how bottom-up approaches to nanotechnology require a considerably lower equipment footprint, leading to a significant reduction in energy consumption. All of which is achievable without any compromise on performance, timescale or cost.

SHIFTING TO LOW-CARBON STRATEGIES

From the ice caps to the rainforests, there is no shortage of ready evidence reminding us that today's global economy can have a very direct impact on the world around us. In recent years, growing awareness of the extent of this impact has triggered an environmental awakening in consumers and businesses alike. Campaigns have been launched and corporate priorities adjusted in order to align behaviours and models with a more sustainable future.

For the pharmaceutical industry, where the ultimate goal is to improve health outcomes, an increasing emphasis is being placed on adapting existing approaches and

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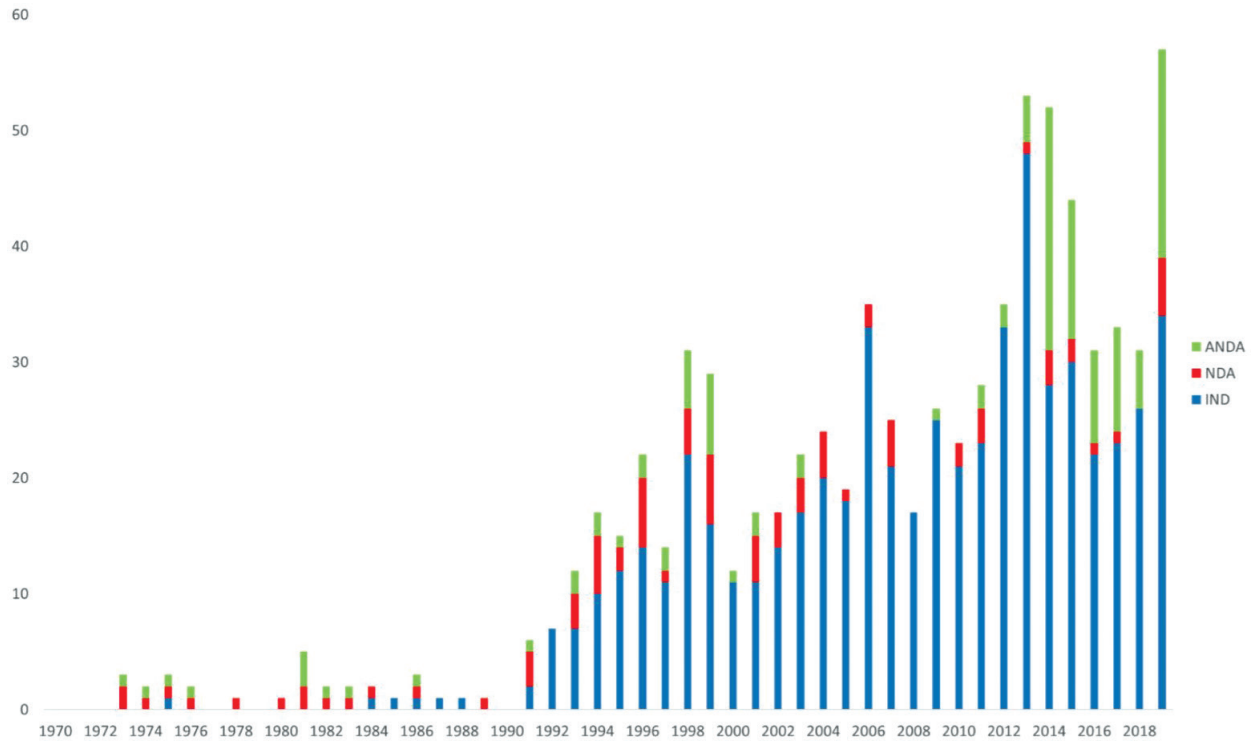

Figure 1: Human drug product submissions to FDA containing nanomaterials between 1970 and 2019.

adopting new ones that give consideration to the ongoing welfare of our planet. These efforts to support sustainability and limit environmental impact are being felt across the entire supply chain. Major pharmaceutical companies have publicly committed to achieve carbon reduction goals and, in some cases, even carbon neutrality as part of ambitious corporate social responsibility programmes.

It is a difficult yet important challenge, but one that the industry can meet by embedding sustainable thinking across all operations, from IT and finance through to R&D and manufacturing. Indeed, drug development, the cornerstone of activity among pharmaceutical companies, is another business area that will need to be carried out with growing consideration for aspects such as energy consumption, materials wastage and the potential for causing pollution.

THE RESURGENT ROLE OF NANOTECHNOLOGY

Drug development, for a significant number of pharmaceutical companies in today's market, is an area increasingly focused on the benefits of nanotechnology, whether for new chemical entities (NCEs) or in the repurposing of existing APIs. Since 1970, the Center for Drug Evaluation and Research (CDER) within the US FDA has received more than 600 submissions of human drug products containing nanomaterials. Furthermore, as shown by Figure 1, half of all of those were submitted within the last ten years, reflecting the acceleration in nanotechnology's growth since the turn of the millennium.[1]

One of the main reasons that nanotechnology has attracted ever greater levels of attention is its strengths in addressing the issues of solubility and stability. Oral administration methods continue to offer high levels of convenience to patients and generally support high levels of compliance. As such, oral remains the preferred administration method for drug formulations, accounting for 62% of all FDA-approved pharmaceutical products.[2] Drugs administered in this way achieve the required level of bioavailability by demonstrating sufficient levels of aqueous solubility to be dissolved in the gastro-intestinal tract.

But while this quality is highly prized, for many it remains just out of reach. An estimated 80% of APIs currently under development suffer from poor aqueous solubility, with high lipophilicity ("grease balls") or high hydrophobicity ("brick dust") commonly cited as reasons for abandoning formulations that may otherwise show promise in addressing unmet medical needs.

While a degree of lipophilicity is required to penetrate the membrane, high levels mean that the molecule may remain inside the membrane rather than passing through. Molecules must also be in solution and in a neutral state for diffusion across the cell membrane to be successful. Whilst nanotechnology cannot change the intrinsic properties of a molecule, it can provide a novel route to overcoming the solubility challenge. At the scale of nano, molecules possess a superior surface area to volume ratio and, therefore, solubility characteristics and dissolution rates are improved.

Further to its benefits in oral administration methods, nanotechnology's strengths are also being exploited for parenteral administration driven by a combination of NCE development, mRNA

"Whilst nanotechnology cannot change the intrinsic properties of a molecule, it can provide a novel route to overcoming the solubility challenge. At the scale of nano, molecules possess a superior surface area to volume ratio and, therefore, solubility characteristics and dissolution rates are improved."

and repurposing for covid-19 solutions. Over the last decade, its use has evolved from simple solutions to facilitating the development of more complex offerings in terms of both solubility and stability.

A DECADE OF PROGRESS AND INNOVATION

These qualities mean nanotechnology has become an area of great importance to pharmaceutical companies and their drug development programmes. Indeed, the potential to improve the chance of success in the development of NCEs addresses one of the key areas of risk in the inherently high-risk, high-cost R&D lifecycle. Although pharmaceutical companies typically employ techniques to enhance bioavailability at a later stage in development, its introduction earlier in the process can also bring greater efficiency overall. Importantly, any savings in time, resources and cost also translate into reduced levels of energy consumption.

Clearly, NCEs are far from the only area where nanotechnology can bring benefits. It is also opening new avenues for existing APIs, enabling them to be re-evaluated to explore the possibility of how, at nanoscale, they can address new disease areas or improve delivery. For example, this is of significant interest in the area of generics, where so-called supergenerics are the product of successful efforts to reap new rewards from drugs whose credentials in terms of safety and efficacy are already well established.

In a similar vein, by addressing shortcomings in the area of oral bioavailability, nanotechnology is enabling new life to be breathed into drug candidates that have either been deemed to have failed previously or whose development may have been placed on hold.

A NEW SENSE OF PURPOSE

Repurposing drugs in this way has been brought into sharp focus this year with the outbreak of covid-19. The novel coronavirus has had a devastating effect on populations across the world, and the pharmaceutical industry has urgently accelerated efforts to bring treatments to market. Given the timeframes involved in developing entirely new treatments, repurposing has taken centre stage, providing a model for rapidly reviewing existing drugs with a view to addressing the symptoms caused by covid-19.

Researchers from the University of Cambridge (Cambridge, UK) were among those in the scientific community to advocate investigating the use of known antivirals to mitigate the effects of covid-19 alongside exploratory work to develop a vaccine, suggesting a co-ordinated global approach to examining the spectrum of licensed drugs.[3] An example of this in action is remdesivir (Gilead Sciences, Foster City, CA, US), an antiviral initially targeted at hepatitis C and used to treat Ebola, which has now been given emergency use authorisation by the FDA for all hospitalised coronavirus patients, after having been indicated for only severe cases initially.

Repurposing, then, presents a significant opportunity for both patients and pharmaceutical companies looking to innovate at speed and reduced cost, and nanotechnology has significant potential in

"The technology used by leon, for example, enables small molecules, peptides and hormones, including large molecules and high-potency oral and parenteral drugs, to be processed very cost-effectively, without the efforts associated with mechanical intervention."

supporting this approach. However, there is no single, agreed pathway to nano success. There is a broad range of approaches under the wider nanotechnology umbrella, principally separated into top-down and bottom-up methods and carrier technologies, each of which has implications, not only for characterisation and regulatory requirements, but also for cost and energy consumption.

INTENSIVE EFFORTS REQUIRE INTENSIVE ENERGIES

Wet milling or media milling, for example, which are common top-down techniques, employ abrasion to physically erode the API down to nano scale. In such environments, in order to produce molecules that meet the desired tolerances, several operation cycles may need to be completed, each of which may last for several days, resulting in the need for large amounts of energy to be consumed in the process. It is estimated that particle-size reduction accounts for as little as 2% of the energy consumed during the milling process, with the remainder spent on deformation of particles, inter-particulate and particle-machine friction, heat, sound and vibration.[4]

Another example in the top-down category is high-pressure homogenisation. As the name indicates, this is an energy intensive process, where in the course of milling, the drug particles are exposed to a power density of up to 1013 W/m^3 – a level comparable to power densities observed in nuclear power stations.[4]

Needless to say, the energy requirements, and therefore environmental impact, involved in such approaches is relatively high when compared with bottom-up continuous precipitation methods, which are characterised by higher levels of efficiency. The technology used by leon, for example, enables small molecules, peptides and hormones, including large molecules and high-potency oral and parenteral drugs, to be processed very cost-effectively, without the efforts associated with mechanical intervention. The drug is dissolved in a solvent and then combined with an antisolvent to precipitate stable crystalline or amorphous nanoparticles of uniform size down to 10 nm.

This precipitation method can also be simply and quickly scaled-up from the bench to larger scale, since the nanoparticle production process is identical in the development phase and in commercial production. While it is slightly larger in scale, the footprint of the equipment can be easily integrated into the production facilities of any CMO. This efficient pathway not only means less API is required for screening and validation, it means that decisions about likely success can be made with greater confidence earlier in the process, and the journey to GMP production can be achieved faster, at lower risk and cost and, again, consuming less energy in the process.

The cost-effectiveness of this highly efficient technique is really exposed at the point of scaling to commercial production. While wet milling requires an investment of approximately €20–30 million (£18.4–27.7 million), GMP commercial production equipment based on leon's technology represents an outlay of less than €1.5 million (£1.4 million).

A SINGLE-SOURCE, SUSTAINABLE SOLUTION IS AVAILABLE TO GO, NOW

Underlying this economic argument for creating nanoformulations using bottom-up precipitation techniques is an important environmental argument. From the scalable manufacturing process to the potential for rapidly repurposing existing APIs, efficiency is embedded into the model. Indeed, in the case of leon, this quality is amplified by the company's strong network of alliance partners, which streamlines multi-stakeholder engagement into a unified offering.

All of this means that, along with time and cost, energy consumption and carbon impact are inherently kept to a minimum. It may even extend all the way to the patient, who receives the convenience of orally administered drugs with greater bioavailability at a lower dose, which limits the waste and other complications associated with higher or more frequent dosing and can lead to better compliance outcomes.

Taken together, this shows how, for a pharmaceutical industry with a growing awareness of its responsibilities to the environment, nanotechnology can offer a sustainable pathway for the patient, the patent holder and the planet.

ABOUT THE COMPANY

leon delivers novel, validated and optimised pharmaceutical nanotechnology solutions that create value for clients and provide better outcomes for their patients. It enhances APIs to deliver greater bioavailability, increased solubility and improved stability, revitalising forgotten formulations, and breathing new life into generics. leon's proprietary technology platforms offer access to the next generation of SMART nanoparticles and nano-formulated drugs, adding value at every stage of the supply chain, from partners and payers to caregivers and patients.

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ABOUT THE AUTHOR

Andrea Cusack is a high performing, energetic leader, who has over 25 years' experience in the life science sector. Having acquired a novel blend of technical and commercial expertise in global healthcare organisations across the pharma, consumer health, medical device, biotech and life sciences sectors, Mrs Cusack is uniquely positioned to lead leon and its clients into the next stage of development.

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SUSTAINABLE PHARMACEUTICALS CAN OUTPERFORM THROUGH NATURALLY DERIVED INGREDIENTS AND DEEP EXPERTISE

In this article, Rina Chokshi, Global Commercial Marketing Leader, Pharma Solutions at DuPont Nutrition & Biosciences, discusses the benefits of naturally derived, sustainable ingredients and their benefits to the environment and pharmaceutical industry.

As industries around the world look to become better stewards of a sustainable future, pharmaceuticals are ripe with opportunities to embrace sustainability. In addition to ways to reduce their carbon footprint and enable sustainable practices within their organisations, drug formulators can also rely on excipient suppliers to provide naturally derived, plant-based ingredients with impressive sustainability stories. But only through deep manufacturing expertise can those materials be harnessed to optimise performance. After all, an abundance of quality, sustainable ingredients means nothing if those ingredients cannot be converted into safe and effective drugs that promote patient compliance.

> "Using plant-based ingredients is no longer just a matter of social consciousness – in many instances, these natural substances outperform their less sustainable counterparts, and thus are in greater demand."

Using plant-based ingredients is no longer just a matter of social consciousness – in many instances, these natural substances outperform their less sustainable counterparts, and thus are in greater demand. In the capsule market alone, demand for plant-based solutions has grown twice as much as that for their animal-based analogues. Over 375 million people around the world identify as vegetarian, and even more consumers possess a desire to better the planet through their dietary choices.[1] As the global population trends towards more sustainable and non-animal options, ingredients like gelatine have become undesirable.

Pharmaceutical and dietary supplement manufacturers have several viable ingredients at their disposal to help promote holistic sustainability, including those derived from seaweed, which can be used in gummies, soft capsules and other delivery formats; pectin, a natural hydrocolloid present in citrus fruit peels that provides gelation, viscosity, texture and protein stability in a range of pharma and dietary supplement applications; and cellulose, which is responsibly sourced from wood pulp to improve compression, flow and act as a filler in tableting applications.

Sustainability plays a part at every stage in the lifecycle of these ingredients, and, by implementing them into their portfolios, pharmaceutical manufacturers can position themselves to thrive in a more sustainability-focused market.

PERFORMANCE STARTS AT THE SOURCE

For years, formulators have used gelatine, an almost tasteless substance made by boiling down animal byproducts, to produce pharmaceuticals and dietary supplements in a variety of formats – from hard and soft gel capsules to the increasingly popular gummy format. It produces a familiar mouthfeel that resembles the gelatine-based foods consumers may have grown up eating – such as gummy candy, jellies and marshmallows – and allows manufacturers to encase bitter-tasting ingredients in capsule form. However, its inclusion in products can be a turn-off to a growing population of vegans and vegetarians, not to mention the many generations of people who follow halal or kosher diets.

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"In soft capsules, carrageenan has superior thermal stability to gelatine, allowing the capsules to maintain their integrity throughout processing, transportation and ultimately, on the shelf."

Formulators have access to several high-performing vegetarian alternatives to create safe, sustainable drug products and dietary supplements. Carrageenan, for example, is sustainably sourced from red seaweed and can replace gelatine in the production of soft gel capsules and gummies. With centuries of safe use as a food product behind it, carrageenan can help to overcome many of the most daunting sensory challenges in formulating vegetarian pharmaceuticals.

In soft capsules, carrageenan has superior thermal stability to gelatine, allowing the capsules to maintain their integrity throughout processing, transportation and, ultimately, on the shelf. Soft capsules made from carrageenan do not melt or stick together within the bottle, staying true to form throughout their lifecycle. Soft capsules with carrageenan can be developed into various shapes, colours and sizes depending on a manufacturer's brand strategies. And, as an added benefit, these ingredients incorporate easily into existing gelatine manufacturing operations, which means only minimum capital investment is required to switch from animal-based to plant-based soft capsules.

As previously mentioned, gummies are growing in popularity as a delivery format to combat pill fatigue. Carrageenan can reduce stickiness to the teeth while chewing and create an overall pleasant mouthfeel – building a compliant consumer base is all but impossible without checking both of these boxes. Plus, with carrageenan maintaining structural integrity under high temperatures, it can deliver a pure, superior quality gummy product, time after time.

Seaweed-based alginates can be used as a gelatine substitute to coat capsules, both hard and soft, as well as tablets. The naturally derived alginate helps to reduce unpleasant flavours and odours and improve the consumer experience, while protecting APIs against the stomach's acidic environment, where they are often prematurely digested. Alginates have even gained popularity as an API to combat acid reflux as either a premier raft formation in liquid products or in the form of alginic acid for chewable products.

In addition to mouthfeel, gelatine gives products a familiar sheen that appeals to end-users. Pectin is a plant-based stand-in derived from the discarded peels of oranges and other citrus fruits that can match or exceed the sheen of gelatine to ensure patient compliance.

Wood pulp-based cellulose has a long track record of safe use as a naturally derived polymer in food. Cellulose has become increasingly popular in the pharmaceutical space for addressing a wide range of applications, from tablet coatings, granulation and controlled release to drug layering, vegetarian hard-shell capsules and amorphous drug stabilisation.

NOT JUST "WHAT" BUT "HOW"

These naturally derived ingredients certainly perform, but they also leave a positive sustainability impact before even reaching the drug formulation – embodying the environmental, and even social, aspects of sustainability.

For instance, the red seaweed used to source carrageenan is a naturally occurring ocean plant that is sustainably cultivated on small family farms, primarily off the coast of Southeast Asia and East Africa. Due to the low cost of production, farming carrageenan is a viable solution for small family seaweed farmers around the world. Additionally, the process of farming carrageenan bolsters the surrounding environment rather than depleting it – it requires no arable farmland, needs no pesticides or special fertilisers and helps protect coral reefs and fish populations. Seaweed farmers benefit by not only making a living, but also securing a better quality of life for themselves and for their children. They can send their children to better schools, gain access to better technology – including mobile phones and electricity – improve sanitation and develop specialised knowledge in coastal marine ecology that increases their income.

Alginates are derived from brown seaweed, which grows in colder waters and is often harvested sustainably by large trawler boats. Compared with the practice of logging, which takes an exacting toll on forests, removing most if not all trees in a designated area, alginate harvesting takes only a very limited portion of seaweed per harvest. In fact, depending on how hilly the seabed is, a harvest vessel might catch as little as a quarter of the seaweed. This means that much of the seaweed in a harvesting field is left untouched; only the adult plants are captured by the trawl, leaving young seaweed plants behind to grow rapidly in the newly accessible sunlight. This still allows fish and marine organisms to find sanctuary, even in fields that have been recently harvested. In line with current regulations, four to five years must pass between harvests, ensuring the re-establishment of seaweed beds before the next harvest can take place.

Pectin is made from the discarded rinds of citrus fruits, such as oranges and lemons. These byproducts typically end up in animal feed with a suboptimal nutritional profile for the intended livestock, or go straight to the landfill. Pectin demonstrates a circular economy and a simple way that manufacturers can utilise the earth's natural products to deliver high-quality drugs and dietary supplements. In addition to reducing environmental waste, pectin products can support at least four of the United Nations Sustainable Development Goals: good health and wellbeing, responsible consumption and production, climate action and life on land.[2] By choosing to use pectin instead of gelatine, manufacturers contribute to a more sustainable world by repurposing waste in a safe and effective way.

Cellulosics are sourced from wood pulp, a process that depends largely on stringent sustainability initiatives to minimise environmental impact and protect our precious woodlands. A reputable supplier of the wood pulp must have established sustainability initiatives, as well as strong environmental and health and safety policies to actively improve their impact on the environment and the communities

"Pectin demonstrates a circular economy and a simple way that manufacturers can utilise the earth's natural products to deliver high-quality drugs and dietary supplements."

they serve. Also, they must be able to provide third party certifications for forestry practices and wood-sourcing chain of custody practices.

GREAT INGREDIENTS DEMAND GREATER EXPERIENCE

Nature's finest ingredients are far from uniform in their consistencies, bringing a high variability to the table that can make manufacturing difficult. Quality ingredients mean nothing if they are not manufactured and applied by a team of knowledgeable experts. And the most sustainable sourcing leads nowhere if consumers do not like the end product. To take full advantage of plant-based ingredients, formulators should partner with an ingredient supplier with a solid track record in traditional pharmaceutical application development, technical service and quality manufacturing that meets worldwide regulations and can handle inconsistent natural ingredients. In other words, a partner who can help formulators deliver the right product to meet present-day market challenges and capitalise on future opportunities.

But, how can an excipient supplier live up to those standards and earn the trust of pharmaceutical manufacturers in the arena of sustainable ingredients? A successful strategy to achieve this goal hinges on securing critical ingredients in support of various product lines. This involves ongoing evaluation of raw material suppliers to ensure quality, safety and regulatory standards. Without this solid framework in place, bringing safe and sustainable pharma ingredients in-house will remain nothing but a good intention, and the raw materials so carefully cultivated from nature will never meet their full potential.

> "Sustainable business practices in the pharmaceutical space must come from responsible ingredient manufacturers, whose deep expertise can lead to indispensable ingredients that outperform traditional ones."

PROMOTING A GREENER WORLD

Sustainable business practices in the pharmaceutical space must come from responsible ingredient manufacturers, whose deep expertise can lead to indispensable ingredients that outperform traditional ones. Only then can formulators take full advantage of plant-based ingredients to impact our oceans, farms and landfills in a positive way.

By utilising plant-based products instead of gelatine or chemically manufactured polymers, the pharmaceutical industry can reduce its dependence on ingredients produced through carbon-heavy factory farming, or products that might be unsustainably manufactured, as well as satisfying the requirements of a growing population of vegan and vegetarian consumers. And when you consider the socially promotive nature of carrageenan farming, the thoughtful process of alginate harvesting, the ingenious repurposing of pectin production and the careful creation of cellulose, it only compounds our need as an industry to fully embrace these sources. We have much to gain by making the most of these versatile ingredients, creating a sustainable world without giving up performance or profit.

ABOUT THE COMPANY

DuPont (NYSE: DD) is a global company with technology-based materials, ingredients and solutions that help transform industries and everyday life. DuPont's employees apply diverse science and expertise to help customers advance their best ideas and deliver essential innovations in key markets including electronics, transportation, construction, water, health and wellness, food and worker safety.

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Rina Chokshi is Global Commercial Marketing Leader for the Pharmaceutical Solution Business of DuPont Nutrition & Biosciences. In this role, Ms Chokshi is responsible for developing and implementing global and regional strategies that align regional growth and business targets. Ms Chokshi and her team actively focus on identifying market trends, customer needs, growth opportunities, brand positioning and creating value through differentiated product and service offerings.

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ON drugDELIVERY

2020/21 EDITORIAL CALENDAR

Publication Month	Issue Topic	Materials Deadline
October 2020	Prefilled Syringes & Injection Devices	PASSED
November 2020	Pulmonary & Nasal Drug Delivery	Oct 8, 2020
December 2020	Connecting Drug Delivery	Nov 5, 2020
January 2021	Skin Drug Delivery: Dermal, Transdermal & Microneedles	Dec 3, 2020
January/ February 2021	Prefilled Syringes & Injection Devices	Dec 17, 2020
February 2021	Novel Oral Delivery Systems	Jan 7, 2021
March 2021	Ophthalmic Drug Delivery	Feb 4, 2021
March/ April 2021	Drug Delivery & Environmental Sustainability	Feb 18, 2021
April 2021	Pulmonary & Nasal Drug Delivery	Mar 4, 2021
May 2021	Delivering Injectables: Devices & Formulations	Apr 1, 2021
June 2021	Connecting Drug Delivery	May 6, 2021
July 2021	Novel Oral Delivery Systems	Jun 3, 2021
August 2021	Industrialising Drug Delivery	Jul 1, 2021
September 2021	Wearable Injectors	Aug 5, 2021
September/ October 2021	Drug Delivery & Environmental Sustainability	Aug 19, 2021
October 2021	Prefilled Syringes & Injection Devices	Sep 9, 2021
November 2021	Pulmonary & Nasal Drug Delivery	Oct 7, 2021
December 2021	Connecting Drug Delivery	Nov 5, 2021

LEADING PHARMACEUTICAL DEVELOPMENT IN A SUSTAINABLE WAY – SKYEPHARMA'S EXAMPLE

In this article, Aline Moulin, PhD, Pharmaceutical Development Director, and Laurent Rigaudeau, PharmD, Business Development and Marketing Director, both of Skyepharma, discuss how the company fulfils its sustainable development policy through its technologies and processes.

At Skyepharma, sustainable development is not just a buzzword, but a way of working that is perfectly integrated all along the value chain as early as the business development policy and deeply anchored into the corporate culture.

SKYEPHARMA ANCHORS SUSTAINABLE DEVELOPMENT IN ITS CORPORATE CULTURE

At Skyepharma it was chosen not to entrust the lead of the sustainable development policy to the HR/HSE department, as is the case in most industrial groups, but instead to entrust this leadership to a transversal working group made up of employees who have volunteered.

A sustainable development committee was set up under the impetus of the site's management and a call for volunteers was a great success; more than 15 volunteers responded to the call to devote one day each month to work on projects related to the sustainable development of the site. Their mission: to make concrete project proposals to the site's management committee in connection with the sustainable development of the site, and to carry them out. Two or three people are dedicated to each project, with specific timelines, reporting and associated budget (Figure 1).

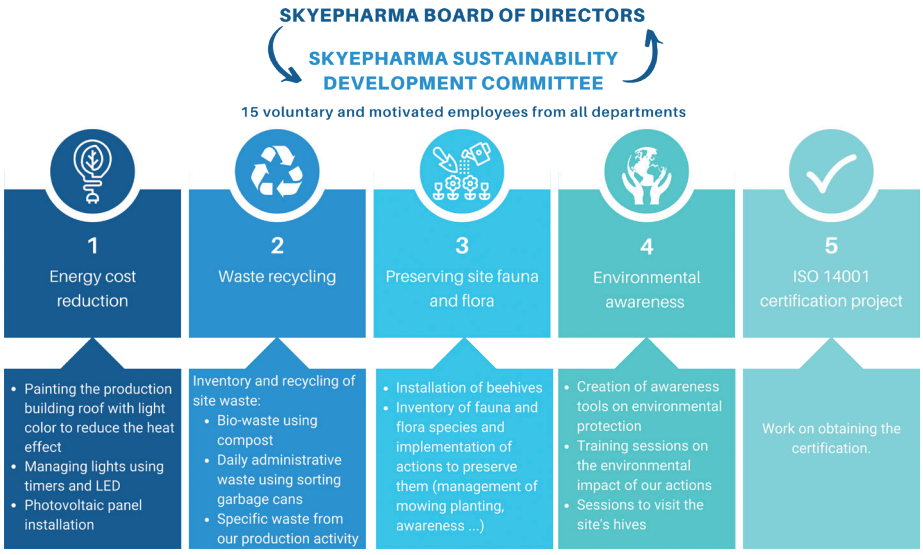

Figure 1: Skyepharma's sustainability development committee.

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Figure 2: Particle size before the use of Microfluidizer technology: 100 µm.

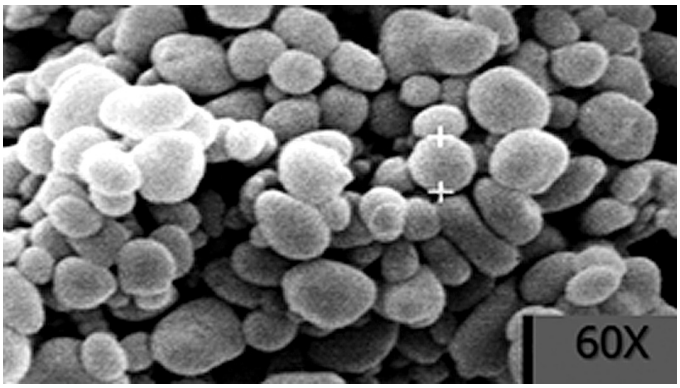

Figure 3: Particle size obtained with Microfluidizer technology: 500 nm.

All these projects are evaluated following full compliance with GMP regulations, in particular pest control. Of course, these action projects have an economic impact with substantial savings, and also a direct impact on the quality of life in the workplace and on the attractiveness of the company to new employees, who in general, not only the younger ones, are increasingly sensitive to sustainable development. This proactive policy enables the company to attract and retain the best talent to serve its clients and their projects.

SKYEPHARMA MAKES ITS OPERATIONS AND PRODUCTS MORE SUSTAINABLE

Supply Chain Policy

Skyepharma is able to use eco-friendly packaging made from sugarcane. This sustainable packaging can be handled by the company's automatic bottle line without any additional fees for same format. These bottles are fully recyclable.

Early Stage Formulation Development: From the Improvement of the API Bioavailability to the Use of Specific Drug Delivery System Technologies

The design of sustainable pharmaceuticals starts at the formulation design stage. This can go through two main steps: the improvement of the bioavailability of the active ingredient by specific techniques and the use of adapted technologies allowing a targeted release. Indeed, by allowing the use of lower, better administered doses (at the right time, in the right place), and by promoting better compliance by the patient, drug delivery systems are an excellent means to move towards more sustainable drugs by reducing drug intake.

Technology	Examples Of Technical Challenge Met	Track Record
GEOMATRIX®	• Once- or twice-daily dosing • Rapid onset followed by sustained duration • Several drugs released at different times / rates in single dose form • Absorption of drugs in lower GI tract	• Nine products on the market • Approximately three early-stage development projects per year
GEOCLOCK®	• Minimisation of side-effects at certain times of day • Drug effect at predetermined time after administration • Delivery to colon where absorption is high, or for local effect	• One product on the market • Approximately two early-stage development projects per year
SOCTEC®	• Delivery to narrow absorption window or local action in stomach	• Several clinical phase projects

Table 1: Skyepharma's technologies for modified-release applications.

Skyepharma has developed different technologies that help its clients target these two challenges.

The first is the use of Microfluidizer® technology to improve the bioavailability of the active ingredients. This technology consists of a dynamic high-pressure process where two liquid streams, solution or suspension, pass through micro-channels towards an impingement area through which the fluids flow and interact. The obtained liquid solution, or suspension, is then sprayed on a neutral support to remove the solvents and produce a dried particulate system, ready for compression. Microfluidization, followed by a drying step, can be used to improve solubility, and thus bioavailability, of poorly soluble APIs.[1]

Indeed, in most cases, new drugs that are currently being developed have poor water solubility (BCS II and IV compounds). Such limited aqueous solubility is one of the major hurdles in the development of oral-dosage forms, thus leading to high dosage strength and use of high quantity of expensive and hard to synthesise material. Figures 2 and 3 show an example of results obtained with Microfluidizer® technology: micrometre to sub-micrometre particle size with narrow size distribution.

The second type of technologies developed to help to the design of more sustainable drugs are complex oral dosage forms grouped under the names of Geomatrix®, Geoclock® and Soctec®. These have been described in previous literature[2] and are able to meet a wide range of challenges, as summarised in Table 1.

Quality by Design Approach in Development Strategy

A critical stage of development, during which a sustainable approach takes on its full meaning, is the scale up and industrialisation stage. To rise to this

challenge, Skyepharma has developed a systematic Quality by Design approach that allows it to obtain very good results in terms of reducing the risks associated with scale up, reducing costs and development time, and also reducing the quantities of materials and waste generated and the energy consumed.

Skyepharma's general methodology is a four-step process (Figure 4):

- Global risk assessment on the whole process, using FMEA as a tool, determining which is the most critical process step
- Fault tree analysis to determine the potential critical process parameters having an impact on the critical quality attributes
- Determination and quantification of the influence of each of the CPP previously identifies on the CQA, thanks to a Design of Experiment approach
- Determination of the process design space.

In previous development projects, one of the critical stages Skypharma has studied is the compression stage. A key tool used to perform such studies on the compression step is STYL'One Evolution (Medelpharm, Beynost, France) compression simulator, which allows for design of experiments (DOE) to be performed at laboratory scale, while having excellent correlations with industrial equipment.[3]

The comparison of material quantities and time required to perform the operations on an industrial press, and on the compression simulator, are shown for a typical size batch in Table 2. It can be seen that the time needed for the operations is divided by seven and the quantities of raw materials and waste is divided by more than 220. The energy required is divided by 10.

Taking the example of an 11 assay DOE, 70–95% savings in terms of raw material, associated waste, time and energy are obtained.

Of course, this has an impact on commercial performance – it enables more rapid and less costly developments compared with market standards – and also

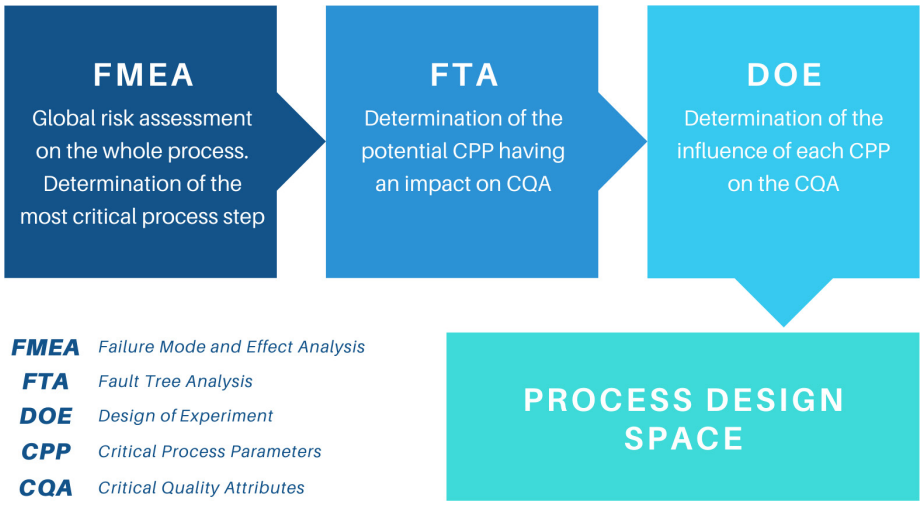

Figure 4: Quality by Design methodology.

"Sustainable production is the last, but not least, step of the development cycle of sustainable drug products."

on performance in terms of environmental impact and sustainable development.

Industrial Operation Policy

Sustainable production is the last, but not least, step of the development cycle of sustainable drug products. This requires the implementation of a continuous improvement plan in terms of energy savings, waste and effluent management, but also, above all, a state of mind that must be deeply rooted in the corporate culture.

ABOUT THE COMPANY

Skyepharma is an expert CDMO which specialises in formulating, developing and

STEP	BATCH SIZE (kg)		TIME (h)	
	Industrial Press	Simulator	Industrial Press	Simulator
Tool assembly	-	-	5	0.5
Setting of comp parameters	1	0.05	1	0.5
Production of trial batch	33	0.1	2	1
Disassembly and cleaning	-	-	20	2
Total	34	0.15	28	4
TOTAL SAVING	33		3 x shifts	

Table 2: Time and materials saving using compression simulator.

producing complex oral dosage forms, with complex and tailor-made modified-release profiles. The Skyepharma site offers a full range of services, from early stage development to industrial manufacturing and packaging. The scientific expert team, supported by patented technologies, has a solid track-record of successful development, reformulation and transfer projects. The FDA-approved GMP site in France serves worldwide customers with a recognised high level of service.

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ABOUT THE AUTHORS

Aline Moulin, PhD, graduated from the National Graduate Chemistry School of Montpellier (France) and received her MSc in Biomolecular Chemistry from the University of Montpellier in 2004. She then achieved her PhD at the Institut des Biomolécules Max Mousseron in Montpellier. She was appointed Medicinal Chemistry Research Scientist in 2007 at Sanofi Research Center (Vitry sur Seine, France). She joined Flamel Technologies (now Avadel Pharmaceuticals, Venissieux, France) R&D team in 2009 to work on the design, development and industrialisation of drug delivery systems. In 2018, Dr Moulin joined Skyepharma as Senior Project Manager and was appointed Pharmaceutical Development Director in 2020.

Laurent Rigaudeau, PharmD, graduated from the Paris Descartes University (Paris, France) and received his MSc In Production and Pharmaceutical Control from INP Toulouse in 2001. He joined Famar Group (Athens, Greece) in 2004 as Production Manager and then worked in various positions in pharmaceutical operations. Dr Rigaudeau then joined the Business Development Management Team at Famar Group in 2015, and was then appointed Business Unit Head and Site Director at Famar L'Aigle (France) pharmaceutical production site in 2019. He joined Skyepharma as Business Development and Marketing Director in June 2020.

RETHINKING DRUG DELIVERY DEVICES FOR SUSTAINABILITY AND INNOVATION

In this article, Sergio Malorni, Senior Consultant, and George Bostock, Senior Consultant Engineer, both at Cambridge Design Partnership, discuss the issue of designing for sustainability, including going beyond "Reduce, Reuse, Recycle" to "Rethink" and looking to adjacent and consumer industries for inspiration on innovations the drug delivery industry can adopt with a view to reducing its environmental impact.

The drug delivery industry is putting ever increasing efforts into the pursuit of both measuring and reducing its impact on the environment. While a large portion of this effort has been focused on improving operational efficiency in drug, device, product packaging and distribution areas, attention is now starting to turn towards their product development processes, using "design for sustainability" methodologies, as seen recently with AstraZeneca's[1] product environmental stewardship and Novo Nordisk's Circular for Zero[2] initiatives.

> "Zooming out from the product and exploring the broader therapy eco-system with Systems Thinking can help find impactful opportunities to improve the sustainability of the drug delivery device."

Efforts vary in ambition, such as having greener propellant ingredients in pressurised metered dose inhalers[3] or sophisticated take-back schemes that enable closed loop recycling. But most of the efforts have tended to be directed towards a focus on material substitution and reduction. This approach is perfectly valid and often justified by its associated cost savings.

However, these incremental steps tend to be too limited in scope to push forward the significant changes needed to shift the needle towards the greater sustainability goals that the industry is likely to be asked, if not required, to meet in the future. In this article, we will share a variety of additional "design for sustainability" approaches that our engineers and designers at CDP have applied to drug delivery device development projects. These have not only resulted in significant improvements in sustainability and reduction in cost – but also are a means of driving product and service innovation.

SYSTEM-LEVEL INNOVATION FOR SUSTAINABILITY

As a rule of thumb, the first port of call when considering how to make a drug delivery device more environmentally sustainable is to apply the first R in the "Reduce, Reuse, Recycle" mantra, specifically looking towards material content reduction. Whilst rules of thumb are useful, they may lead you to bark up the wrong tree. For example, the main environmental culprits of a delivery device design may be its energy-intensive production process and high part count requiring transport-intensive sourcing. In this case, exploring less intensive production methods through shape or material changes, reduced part count and simplified sourcing may yield much higher sustainability gains than simple material reduction.

Lifecycle assessment (LCA) can help identify a design's "hotspots" through a systematic cradle-to-grave calculation of several environmental impact metrics, such as greenhouse gases (GHG), water usage and waste tonnage. If appropriately done in line with the ISO 14000 series of standards, and with the right assumptions and boundaries, LCAs can guide a product development team to focus on the real design changes that count for sustainability.

However, despite this cradle-to-grave viewpoint, this approach still may not be holistic enough to find more significant opportunities. The analysis can sometimes be too focused on the drug delivery device and/or packaging. Zooming out from the product and exploring the broader therapy eco-system with Systems Thinking can help find impactful opportunities to improve the

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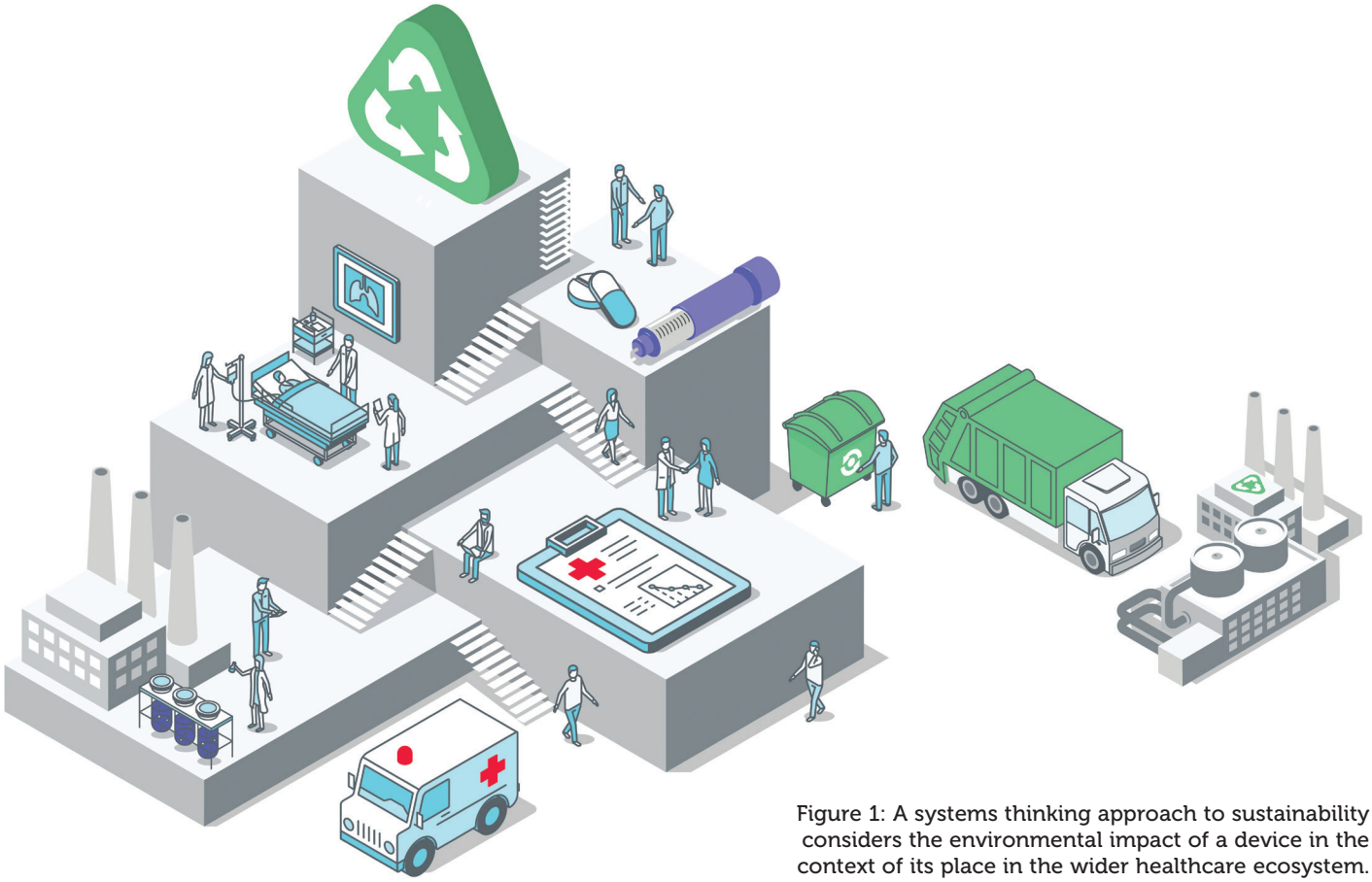

Figure 1: A systems thinking approach to sustainability considers the environmental impact of a device in the context of its place in the wider healthcare ecosystem.

sustainability of the drug delivery device. Essentially this approach asks, "how can we reimagine delivering the same benefit more sustainably?" – but at a higher level.

Systems thinking starts with mapping out the interrelationships between drug, delivery device, diagnostic system and a patient's visits and communications with their healthcare provider. It even includes other medical interventions that may result in low efficacy or poor adherence to medication. Although it might seem to be a significant endeavour, it can be scaled using simple approximations that will ultimately help to identify other potential routes of exploration. Data on care pathways is becoming richer and more transparent, and it can be complemented by primary research, mapping the ecosystem components and their relationships. Systems thinking tools and techniques such as functional modelling, "Rapid LCAs" and design sprints can then be used to help create unique configurations, evaluate trade-offs and sense-check their potential viability.

This type of systems thinking approach can drive strategies such as reducing the number of different devices through consolidation, replacing products with services and setting a focus around reducing the need for patients to visit clinical settings or stay in hospital. In short, it considers not just the device itself, but the device as part of the larger healthcare ecosystem (Figure 1).

Systems thinking can also help justify less intuitive approaches. For instance, connected devices are not typically viewed as green compared with unconnected versions. However, the environmental impacts of their disposable electronics and batteries might be counterbalanced by a reduction in patient journeys to clinics, avoidance of complications and earlier interventions, all of which come with environmental impacts. Diabetes is a good example, where poor disease management can lead to difficulties in later life that create additional hospital visits that come with significant GHG emissions impacts.[4]

Similarly, some single-use wearable injectors might appear less "green" than the intravenous infusion therapies they replace. However, the increased cradle-to-grave environmental footprint might be offset by the footprint savings from a reduced number of injection devices, reduced drug waste, improved adherence and, as seen with the aims of Neulasta® Onpro® injector,[5] to reduce hospital stays.

Essentially, systems thinking has the ability to manage the tension between the desire to reduce product material for the environment, versus the desire to create more complex products to deliver more patient-centric care. If performed credibly, LCA analyses could show that, on balance, more complex products could be better for the environment, by offsetting the preventable wider impacts of less effective treatments.

However, the more exciting scenarios are when systems thinking allows you to create new pathways, products and services in areas where few have ventured, fuelling innovation.

"The more exciting scenarios are when systems thinking allows you to create new pathways, products and services in areas where few have ventured, fuelling innovation."

SUSTAINABILITY-DRIVEN TECHNOLOGY INNOVATION

Following on from the higher system-level perspective, we can now zoom inwards to the device and packaging design to find further design for sustainability opportunities.

"Platform drug delivery device solutions can provide ample opportunity to illustrate the Rethink approach."

This focused approach starts with identifying sustainability-themed insights from the therapy journey that can drive product development. These can be gained concurrently during primary and secondary research to define the unmet needs of stakeholders. Do stakeholders and users care more about a perceived reduction in waste or GHG emissions? Will patients separate different recycling materials? Is there a demand for such materials in the material recovery market?

Armed with such insights, the second step is to understand the main environmental culprits of the device, packaging or service using an LCA analysis. With hotspots identified, one can increase the opportunities for innovation by looking beyond "Reduce, Reuse, Recycle" – to Rethink!

Platform drug delivery device solutions can provide ample opportunity to illustrate the Rethink approach. Take the case of a platform single-use electromechanical wearable injector. Applying a Reuse approach to improve sustainability, one can change the architecture to a part-reusable (electromechanical power unit) and part-disposable (pump mechanism and primary container) provided patients accept the extra steps, and if additional risks are avoided. However, one can go further with a Rethink strategy by exploring non-optimal generalised solutions that might be present in platform designs.

In this example, the non-optimal solution may be found in the core pumping technology. As these platforms may ask the pump to serve many injection volumes, viscosities, flowrates and accuracy requirements, certain implementations may not be optimal as the core technology is too general – and carry over design elements may not be required.

For therapies like insulin delivery, where flowrate is critical, sensors and electromechanical systems are the go-to solution. However, if flowrate accuracy isn't crucial, as is the case with a good-sized portion of the market for subcutaneous biologics injections, there is an opportunity for Rethink. Instead of motors, complex mechanisms and batteries, could we make use of expanding materials or hydrogels that push against a flexible drug container? Or perhaps old-fashioned mechanical clockwork escapements might be a solution? The Rethink strategy, underpinned by a drive for sustainability, provides a methodology for challenging conventional thinking.

INSPIRATION FROM ADJACENT MARKETS

Drawing inspiration from other markets and sectors can also move you towards more interesting approaches. As an example, the reprocessing of single-use surgical devices (SUDs) is notable; hospitals realise that it not only reduces total waste but also net cost. Surgical drills, electrophysiology catheters, endotracheal tubes and balloon angioplasty catheters are all examples of SUDs suitable for reprocessing. While much of this reprocessing is done by hospitals themselves, there is still a market to be found, with new companies being created to fill this need in a service sector estimated to reach nearly US$1.7 billion (£1.3 billion) by 2022.[6] Likewise, this impetus has been further facilitated with the EU MDR Article 17 that allows SUD reprocessing if it is also permitted under national law.

Therefore, we can draw inspiration for potentially reducing environmental impact in hospitals by surveying which drug delivery devices are ripe for reprocessing. This may require further product development, such as having more resilient components and developing in-process functional testing. However, if cost savings are possible and the LCA analysis indicates a net environmental benefit, this can open new markets for the drug delivery device sector.

"We should look at how consumer brands are evolving, with an increasing number of pledges to improve their sustainability position by leading companies, such as Nestle and Unilever, aiming to achieve net zero emissions within a decade."

INSPIRATION FROM CONSUMER MARKETS

Drug delivery device manufacturers are coming to realise that patients are also consumers. This influences expectations on the usability and aesthetics of devices, apps and packaging. It would also be reasonable to expect that green initiatives and expectations seen in the consumer sector could also cross over into the drug delivery sector.

We should look at how consumer brands are evolving, with an increasing number of pledges to improve their sustainability position by leading companies, such as Nestle (Vevey, Switzerland) and Unilever (London, UK), aiming to achieve net zero emissions within a decade. With a strong emphasis on packaging recycling, systemic challenges have been encountered in this area, with material recovery facilities not processing a good portion of what they receive from consumers' recycling bins due to, for example, poor economics or technical feasibility in sorting and separating materials such as paper from multi-layer beverage cartons.

As a result, significant industries have banded together to create their own materials recovery routes and recovery technologies on a local and global scale, such as TerraCycle (Trenton, NJ, US) for popular consumer packaging, or beverage carton manufacturers like Tetra Pak (Pully, Switzerland).[7] Major consumer brands have also invested in the development of unique recyclable materials, such as Pulpex paper bottles.[8] Likewise, there is the potential for the uptake of specialist recycling methods aimed at the consumer sector, such as chemical reprocessing involving the conversion of polymers back into their raw monomers or other chemical substances ready for repolymerisation.[9] Such methods, paired with a renewable energy source, could be an interesting future solution for the medical industry. Lastly, consumers are increasingly willing to take that extra step of separating materials and binning them according to recycling needs, for both domestic and speciality waste streams.

We, in the drug delivery industry, can take inspiration from these consumer sector trends. Yes, it may take some time for consumer container technologies to evolve into medical ones, or for pharma and device companies to band together to create specialist recycling waste streams. However, in the interim, devices and packaging can evolve to leverage consumer recycling infrastructure and patients' willingness to take the extra steps for sustainability.

SUMMARY

Design for sustainability for drug delivery devices can often be viewed as an "add-on process" to reduce their environmental impact, employing the conventional Reduce, Reuse, Recycle mantra. However, there are other powerful methods beyond this, such as Rethink – considering how to deliver the therapy benefit more sustainably through systems thinking. Coupled with inspiration from other markets in terms of recycling and reuse, design for sustainability is not simply an add-on process to drug delivery development projects, but also the source of innovation for the future.

ABOUT THE COMPANY

Cambridge Design Partnership (CDP) is an end-to-end innovation partner focused on helping clients grow. Some of the world's largest companies trust CDP to design and develop their most important innovations. Located in Cambridge (UK) and Raleigh, North Carolina (US), CDP specialises in the consumer, healthcare and industrial markets. Its multidisciplinary teams have the expert knowledge to identify opportunities and overcome challenges throughout the product development and manufacturing process.

ABOUT THE AUTHORS

Sergio Malorni is a Senior Consultant at Cambridge Design Partnership. He specialises in leading multidisciplinary development programmes for drug delivery devices from early-stage user and stakeholder research, strategy, concept creation, engineering and production transfer. Holding a Mechanical Engineering degree from McGill University in Montreal, Canada, and being a named inventor on numerous patents, his 30-year career includes development of a variety of mechanical and electromechanical devices including wearable injectors, prefilled syringes, pen injectors, dry powder inhalers, sublingual spray and patient-controlled analgesia pumps – many of which incorporated design for sustainability.

George Bostock is a Senior Consultant Engineer at Cambridge Design Partnership. During his time at CDP he has had experience across a wide range of projects, from consumer goods through to performance-critical drug delivery devices. He was a named Red Dot Design Award winner for CDP's First Response Monitor, a wearable connected medical device. Having previously worked in the aerospace industry as a systems-design and integration engineer, Mr Bostock has a keen interest in systems thinking, tools and techniques. He now co-leads CDP's sustainability cross-sector team, where he believes that the consideration of the wider system and product context is critical to ensuring long-term impactful solutions.

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SUSTAINABLE POLYMERS FOR HEALTHCARE HELP ADVANCE THE CIRCULAR ECONOMY

In this article, Alexander Fix, Business Development Leader, and Hans de Brouwer, PhD, Chief Scientist, both of SABIC, provide an update on activities undertaken by the company's Specialties business to address the need for sustainable materials in the pharma world.

Sustainable materials are receiving increased attention by customers across industries. While efforts are primarily focused on food packaging, the healthcare industry is also looking for more environmentally responsible solutions. This article looks at the activities SABIC's Specialties business is undertaking in order to address the use of sustainable materials in the pharmaceutical industry.

THE PLASTIC DILEMMA

As they have for many decades, plastics support innovation in the healthcare industry and can help improve medical treatment and outcomes for patients. At the same time, plastics have received criticism due to plastic waste being discarded in the environment. A 2018 article from McKinsey and Company reported that around 260 million tonnes of plastic waste are being created every year.[1] This quantity of plastic waste is equal to the mass of around 26,000 Eiffel Towers.[2]

Only 16% of plastic waste is collected for recycling.[1] Eight million metric tons of plastic escape into the oceans every year, as reported in National Geographic.[3] A study from McKinsey and the Ocean Conservancy shows that land-based plastic waste ending up in the oceans will reach up to 20 million metric tons by 2030 if necessary corrective actions are not taken.[4] Beverage bottles, caps and lids are among the top single-use items found on ocean shores.[5]

> "A study from McKinsey and the Ocean Conservancy shows that land-based plastic waste ending up in the oceans will reach up to 20 million metric tons by 2030 if necessary corrective actions are not taken."

Next to these waste problems, production, processing and incineration of plastics generate carbon dioxide (CO_2) contributing to increased climate change.

CHEMICAL UPCYCLING OF PLASTIC WASTE

How can polymer technology continue to drive innovation in the medical industry while helping to create meaningful uses for plastic waste and reduce CO_2 emissions?

One answer is chemically upcycled polybutylene terephthalate (PBT) resin that

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is synthesised from single-use polyethylene terephthalate (PET) bottles. This solution is created by reusing post-consumer plastic waste to produce a drop-in replacement for virgin PBT, which avoids the need to consume fossil-based feedstocks to produce more virgin resin. This approach can help support the reduction of CO_2 emissions, plastic waste, energy demand and water consumption, according to a Lifecycle Assessment study completed by SABIC in 2020.[6] The study featured a comparison with virgin PBT produced with the terephthalic acid process.

MAKING PBT MORE SUSTAINABLE

PBT is an engineering plastic that is often used in the healthcare industry. It processes more predictably than PET and, being a semi-crystalline resin, offers excellent chemical resistance. PBT is made from 1,4-butanediol and either terephthalic acid or dimethyl terephthalate building blocks. These monomers are derived from crude oil – a fossil-based, non-renewable resource – through several intermediate steps. At each step, purification takes place, resulting in a well-defined polymer product.

Efforts to replace both the diol monomer and the diacid monomer with alternatives that are more sustainable, such as bio-sourced components, typically lead to polymers with different processing behaviour and material performance. Even small structural changes to either monomer can have large effects on processing, crystallisation behaviour and material performance. The resulting polymer may be interesting on its own, but it is never a drop-in solution for an existing application.

> "SABIC is using its chemical upcycling technology to produce PBT from post-consumer PET. Rather than mixing molten recycled PET into a new plastic, SABIC uses PET as a feedstock in a chemical process that deconstructs the material down to its basic building blocks."

Figure 1: Approximately 67 0.5 L PET bottles go into each kilogram of virgin-quality LNP™ ELCRIN™ iQ engineering resin.

Performance changes can also occur when mechanically recycled plastics are mixed with new material. First, the composition of most mechanically recycled plastics from post-consumer sources shows greater variation compared with non-recycled plastics. Mechanically recycled plastic may also be a mixture of different types of plastic and contain traces of its first life: colourants, stabilisers, flame retardants and the like. Some of these components are unacceptable in healthcare-grade plastics. They can restrict colour options and affect food contact compliance and biocompatibility.

UPCYCLING PET TO HIGHER-VALUE PBT

To help address this challenge, SABIC is using its chemical upcycling technology to produce PBT from post-consumer PET. Rather than mixing molten recycled PET into a new plastic, SABIC uses PET as a feedstock in a chemical process that deconstructs the material down to its basic building blocks. These building blocks are then purified with similar rigor as chemicals coming from a fossil source, before being fed into the polymerisation process to prepare PBT resin. SABIC's process uses dissolved monomers and oligomers from PET and adds fossil-based 1,4-butanediol to produce LNP™ ELCRIN™ iQ resin (PBT).

This upcycling process converts commodity plastic waste into virgin-quality engineering resin (approximately 67 0.5 L PET bottles – see Figure 1 – go into each kilogram) at reduced CO_2 emission levels compared with the production of virgin resin. Not only does 60% of the material originate from the waste stream, but this resin's performance is equivalent to that of traditional PBT resin. In addition, PBT may be used for more-durable applications than PET, such as medical device housings. In this way, upcycling can extend the lifespan of PET beyond its original application in disposable water bottles.

As shown in Figure 2, the upcycled PBT reduces global warming impact by 29%, has 43% less cumulative energy demand and consumes 15% less water compared with virgin PBT. All these values contribute to an improved environmental footprint.[6]

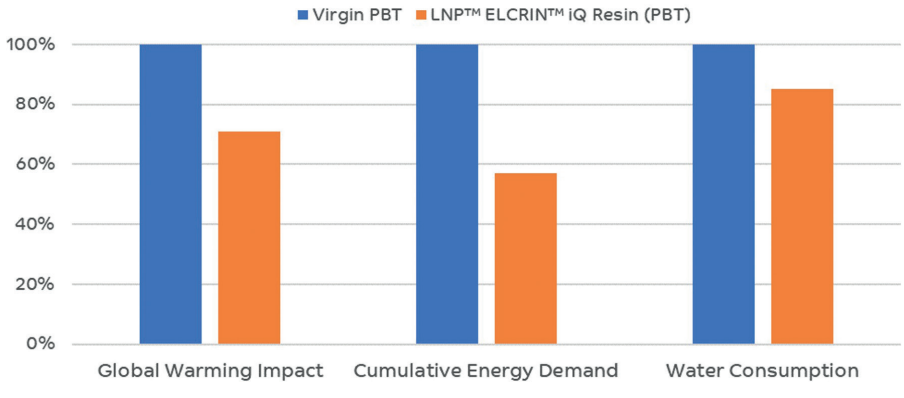

Figure 2: Comparison of resin cradle-to-gate footprint data.[6]

MATERIAL PROPERTIES FOR HEALTHCARE APPLICATIONS

The medical industry typically requires healthcare-grade materials to meet specific criteria, such as biocompatibility pre-assessment; management of change; plant and formulation lock; long-term supply guarantee; and production according to good manufacturing practices (GMPs). Further, each end application has its own set of material requirements.

Technical datasheets provide many of the important properties of a material: mechanical performance, electrical properties, rheological parameters and heat resistance, for instance. The properties of the upcycled PBT material are similar to those of a standard, unfilled PBT of comparable viscosity. Table 1 compares key properties of a representative grade for the upcycled PBT, LNP ELCRIN W1000JiQ resin, with those of a reference PBT material, SABIC's VALOX™ HX260HPR resin. This comparison reveals the strong similarities between the two materials. Even a parameter such as mould shrinkage, which is sensitive to small material differences, was identical (1.2%) in a side-by-side comparison on a tensile part specimen.

Environmental stress cracking resistance (ESCR) was tested using PDI's (NJ, US) Sani-Cloth® AF3 Germicidal Disposable Wipes, which include one of the strongest chemicals used on medical devices, as well as Banana Boat® Sunscreen lotion (Edgewell Personal Care, CT, US), which represents an aggressive skin contact situation. The tests featured tensile bars in continuous contact with these chemicals under 1% strain at room temperature for seven days. Table 2 shows that both materials performed very well against these harsh chemicals. A positive rating (+) in this table indicates over 90% retention of yield strength and 80–140% retention of elongation after exposure, indicating no significant change.

		LNP™ ELCRIN™ W1000JiQ resin	VALOX™ HX260HPR resin	Test Method
Tensile modulus	MPa	2450	2400	ISO 527
Stress at Yield	MPa	54	54	ISO 527
Stress at Break	MPa	25	28	ISO 527
Strain at Yield	%	3.3	3.5	ISO 527
Strain at Break	%	93	84	ISO 527
Impact Strength (23C)	kJ/m²	5	5	ISO 180/1A
Impact Strength (-30C)	kJ/m²	5	5	ISO 180/1A
Vicat softening temp.	°C	165	170	ISO 306, 50N
Heat deflection temp.	°C	122	123	ISO 75 0.45MPa
Heat deflection temp.	°C	52	54	ISO 75 1.8MPa
Mould shrinkage parallel	%	1.2	1.2	SABIC method

Table 1: Mechanical performance comparison.

Retention of:	LNP™ ELCRIN™ W1000JiQ resin		VALOX™ HX260HPR resin	
	Yield Strength	Elongation at break	Yield Strength	Elongation at break
PDI Sani-Cloth® AF3	+	+	+	+
Banana Boat® Sunscreen	+	+	+	+

Table 2: ESCR testing results.

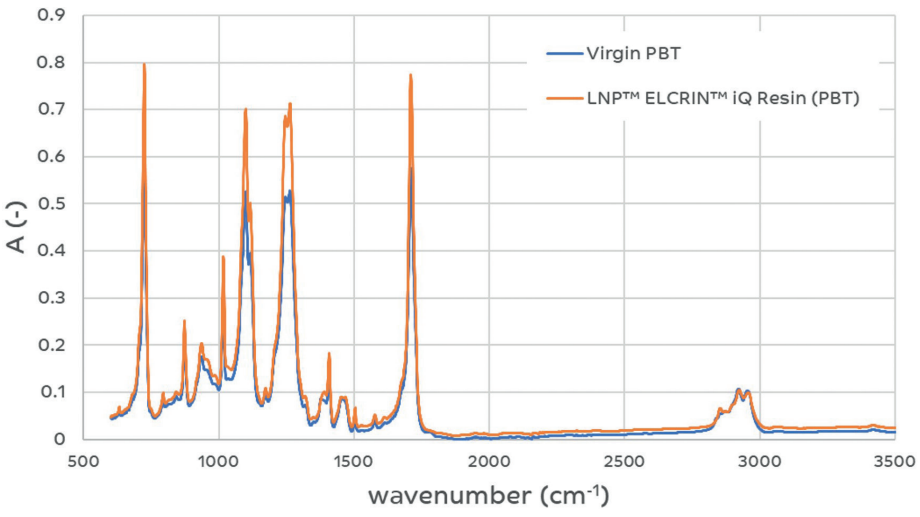

Figure 3: Infrared spectra of the two types of PBT indicate no structural differences. Peaks are the same in both samples.

ANALYSING TWO PBT MATERIALS

However, there is much more to a material than what is shown on a datasheet. Analytical techniques allow us to collect additional information, down to a material's molecular level. Infrared spectroscopy detects molecular vibrations and is often used for fingerprinting purposes: it can determine if materials are the same without interpreting and labelling every individual peak in the spectrum.

The infrared spectra overlay graph (Figure 3) shows matching fingerprints for the standard PBT and the upcycled PBT materials, indicating no significant difference between the two.

Other analytical techniques allow us to study extractables. These components can potentially migrate out of a material under extreme conditions. Extractables depend, not only on the type of polymer, but also on the quality of the raw materials used to build the molecules and the specifics of the chemical process. We studied both volatile and non-

volatile organic components and ran an elemental analysis with a focus on metals.

The elemental analysis was conducted using inductively coupled plasma mass spectrometry (ICP-MS) on an acidic liquid extract that had been in contact with the polymer material for three hours. This mimics a worst-case scenario as metal ions are typically extracted more actively under such conditions than in a pH-neutral aqueous environment. Of the 39 elements analysed, 34 were not detected above their individual quantification limits or the 0.010 ppm reporting limit.* Quantified elements, which are listed in Table 3, are low levels of common elements of no particular concern. In this particular data set, the levels of these elements in the upcycled PBT are lower than those in the virgin PBT.**

Volatile organic components (VOCs) were measured by analysing the gas emitted from a sample kept at 150°C for 45 minutes using gas chromatography with time-of-flight mass spectroscopy (GCMS). Under these extreme conditions, tetrahydrofuran (THF) was detected in both samples (Table 3). THF is a known by-product of PBT synthesis. In a polymerisation with terephthalic acid (virgin PBT), it is present at higher levels than in the chemically upcycled PBT, which is formed from transesterification, consistent with the literature.[7]

Further, ethanol was used to extract organic components from the samples at 70°C for 24 hours. The extracts were analysed for semi-volatiles with liquid chromatography coupled to a quadrupole mass spectrometer (LCMS), and for volatiles using GCMS. Quantification was executed using an internal standard. Both techniques revealed the presence of short cyclic polymer chains of PBT (Figure 4, Table 3).

These molecules are an integral part of the PBT molecular weight distribution. During the polymerisation process, all molecules pass through the stage of short chain oligomers. Molecules that happen to react with themselves form cyclic structures that stop growing due to the absence of a reactive chain end (either a carboxylic group or a hydroxyl group). As such, their presence is to be expected. The process to form LNP ELCRIN iQ resin results in fewer of these structures than the virgin PBT process in the current comparison. Neither sample showed any unidentified components. In a similar extract using hexane, lower levels of the same components were found.

DROP-IN SOLUTION FOR TRADITIONAL PBT

All snowflakes appear the same but none are identical. The same is true of plastics. It all depends on how deeply they are evaluated. This study was not restricted to a high-level comparison of macroscopic properties for upcycled and traditional PBT. It looked closely at the subtle differences between SABIC's sustainability driven PBT material and the oil-derived commodity product. Importantly, there were no significant differences between the two products: the same components were observed, and a quantitative comparison confirmed the cleanliness of the upcycled PBT product.

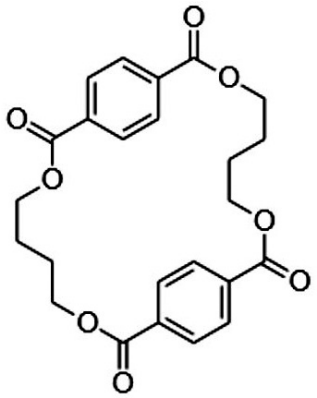

Figure 4: Structural formula of cyclic PBT dimer.

This analysis indicates that LNP ELCRIN W1000JiQ resin can be considered a more-sustainable, drop-in replacement for traditional PBT in many healthcare applications. This material also features formulation lock, US FDA food contact compliance and a stringent management of change process – and is produced according to GMPs.

Element	LNP™ ELCRIN™ W1000JiQ resin (ppm)	VALOX™ HX260HPR resin (ppm)	Method
Sodium (Na)	0.19	0.50	Elemental analysis, ICP-MS
Magnesium (Mg)	0.07	0.14	Elemental analysis, ICP-MS
Sulphur (S)	< 0.02	0.05	Elemental analysis, ICP-MS
Potassium (K)	0.07	0.25	Elemental analysis, ICP-MS
Calcium (Ca)	0.40	0.60	Elemental analysis, ICP-MS
THF	4.9	36.8	headspace, GCMS
cyclic PBT dimer	<0.1	12.0	ethanol extract, GCMS
cyclic PBT dimer	3.2	12.0	ethanol extract, LCMS
cyclic PBT trimer	0.7	2.2	ethanol extract, LCMS
cyclic PBT tetramer	<0.1	0.1	ethanol extract, LCMS

Table 3: Results from elemental analysis.

** Not detected above quantification or reporting limit: Li, Be, B, Al, P, Ti, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, Ge, As, Se, Sr, Zr, Nb, Mo, Ag , Cd, Sn, Sb, Cs, Ba, La, Ce, Hf, W, Hg, Tl, Pb*

*** Please note that even though the data in this document have been generated with the utmost care and most analyses have been executed in duplicate, the sample set is restricted to a single representative sample of LNP ELCRIN W1000JiQ PBT resin and VALOX HX260HPR PBT resin. It does not include statistical analyses of multiple lots, nor does it provide a complete picture of all available virgin PBT materials. Hence, a customer should always independently assess suitability of the material for the intended application.*

ABOUT THE COMPANY

SABIC is a global diversified chemicals company, headquartered in Riyadh, Saudi Arabia. SABIC manufactures on a global scale in the Americas, Europe, the Middle East and Asia Pacific, making distinctly different kinds of products: chemicals, commodity and high-performance plastics, agri-nutrients and metals.

SABIC supports its customers by identifying and developing opportunities

in key end-use applications such as construction, medical devices, packaging, agri-nutrients, electrical and electronics, transportation and clean energy. Production in 2019 was 72.6 million tonnes.

SABIC has more than 33,000 employees worldwide and operates in around 50 countries. Fostering innovation and a spirit of ingenuity, SABIC has 12,540 global patent filings, and has significant research resources with innovation hubs in five key geographies – US, Europe, the Middle East, South Asia and North Asia.

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Dr ir Hans de Brouwer is Chief Scientist Healthcare for SABIC's Specialties business, developing products to meet the future needs of the healthcare industry. He has 20 years of experience in a range of technical roles including the development of plastics for the healthcare, telecom, lighting and automotive markets and execution of continuous improvement projects in production and technology. Dr de Brouwer holds an engineering degree in chemical technology and a doctorate in polymer chemistry from Eindhoven University of Technology (the Netherlands) and is a certified Six Sigma Black Belt.

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THE PHARMACEUTICAL INDUSTRY'S ROLE IN THE GLOBAL ENVIRONMENTAL SUSTAINABILITY MOVEMENT

In this article, Alex Catino, Product Commercialisation Associate at Noble, discusses current trends in the pharmaceutical industry in relation to environmental sustainability in healthcare.

Environmental sustainability is a broad, expansive concept that can apply to everything from agriculture and manufacturing to building design. But how is it defined?

The United States Environmental Protection Agency (EPA) defines sustainability based on an overarching principle: "Everything that we need for our survival and well-being depends, either directly or indirectly, on our natural environment. To pursue sustainability is to create and maintain the conditions under which humans and nature can exist in productive harmony to support present and future generations."[1]

The creation of the EPA in 1970 is one of many inflection points that sparked the modern global environmental movement. In 1972, the United Nations (UN) held the first Conference on the Human Environment, which is widely considered one of the earliest global meetings to discuss the environment, conservation and sustainability.[2] In the early 1990s, "green brands" began to emerge, with companies using their environmental and sustainable business practices as selling points for consumers. By 2012, sustainability had cemented itself in the collective conscience of consumers and companies alike, with corporate social responsibility (CSR) and triple bottom line reports that measure financial, social and environmental performance emerging as standard responses to that consciousness.[3]

> "Within the healthcare sector, environmental sustainability involves using resources as efficiently as possible, without compromising the quality of patient care."

ENVIRONMENTAL SUSTAINABILITY IN HEALTHCARE

The WHO defines an environmentally sustainable health system as one that "improves, maintains or restores health, while minimising negative impacts on the environment and leveraging opportunities to restore and improve it, to the benefit of the health and well-being of current and future generations."[4] Most importantly, human health is inextricably linked to the health of the environment, according to the Australian Medical Association.[5]

Within the healthcare sector, environmental sustainability involves using resources as efficiently as possible, without

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"A major sustainability issue confronting the healthcare sector today is the number of hospitals that are ageing, meaning their technologies and systems are becoming outdated."

compromising the quality of patient care. Strategies that can foster environmental sustainability within this sector are promoting efficient management of resources and increasing sustainable procurement.

A major sustainability issue confronting the healthcare sector today is the number of hospitals that are ageing, meaning their technologies and systems are becoming outdated. Managing the renovation or replacement of these facilities in a sustainable way – using elements like green building design and construction, and incorporation of on-site renewable energy technology – can have a direct impact on the environment without impacting patient care.[4]

The healthcare sector is seeing increased pressure to make commitments and tangible progress that positively impact both the environment and society. The global shift towards achieving a sustainable future has made environmental stewardship an expected norm.

CURRENT TRENDS IN THE PHARMACEUTICAL INDUSTRY

An ageing world population and improved access to healthcare in emerging markets are driving increased demand within the pharmaceutical industry. Manufacturers today are responding to the demand by producing a wider variety of pharmaceutical products. However, the resulting changes to production can conflict with sustainability objectives.

A key challenge for the pharmaceutical industry is how to accommodate demanding production schedules and increased product variety while also keeping the environment and sustainability in mind. In a 2018 *Pharma Manufacturing* article on achieving sustainability in an evolving pharma sector, Tom Egan, Vice-President, Industry Services, PMMI, said: "Pharmaceutical manufacturers must implement packaging solutions that minimise the environmental impact of expanding product lines, build sustainability practices into the development of new delivery systems, seek utility savings in new automation strategies and leverage serialisation." For example, the article says, when it comes to accurate dosing, patients who achieve better results with oral, injectable or nasal sprays versus other formats provide a strong incentive for companies to offer those new delivery mechanisms.

A key challenge for the pharmaceutical industry is how to accommodate demanding production schedules and increased product variety while also keeping the environment and sustainability in mind."

These advancements in drug delivery add to the growing variety of products on the market. In addition, a shift towards smaller batch runs allows for more product diversity. However, more frequent changeovers on machinery are required to deliver this diversity of products, which in turn can have negative impacts on energy consumption at the manufacturing level.

CSR FOR ENVIRONMENTALLY SUSTAINABLE DRUG DELIVERY

Today, socially and environmentally responsible pharmaceutical companies are developing ways to produce their products more efficiently and sustainably. Companies have created self-imposed targets and initiatives to reduce the impact of their activities and products on the environment while keeping the patient and product efficacy top of mind (Figure 1).

APTAR IS A GLOBAL LEADER IN SUSTAINABILITY

One company making a difference in its commitment to creating a more sustainable future is AptarGroup, a global leader in drug delivery, consumer product dispensing and active packaging solutions. Earlier this year, Barron's included Aptar on its list of the "100 Most Sustainable Companies in America" for the second consecutive year, and Newsweek named it one of "America's Most Responsible Companies 2020".

A member company of the World Business Council for Sustainable Development, Aptar also recently joined the UN Global Compact – the world's largest citizenship initiative, which focuses on universal principles in the areas of human rights, labour, the environment and anti-corruption. "We are extremely proud of [our] commitment to reducing [Aptar's] impact on the planet while creating quality products," said Stephan Tanda, Aptar President and CEO.

Aptar Pharma, part of AptarGroup, is the company's provider of innovative drug delivery solutions to pharmaceutical, consumer healthcare and biotech customers worldwide. Its patented Freepod multi-dose, preservative-free nasal spray device with GlaxoSmithKline's Otrivin won the World Packaging Organisation's prestigious WorldStar Award in 2019 for its sustainability impact. The award annually recognises advancement and excellence in packaging design and technology.

Figure 1: A reusable, resettable Noble training autoinjector, built to replicate the form and function of the true drug delivery device upon which it is based.

Figure 2: Various Noble patient training devices, all of which are resettable for ongoing use and practice.

NOBLE'S COMMITMENT TO ENVIRONMENTAL SUSTAINABILITY INITIATIVES

Noble, an Aptar Pharma company, promotes healthy patient outcomes for people who self-administer their drug therapies through the development of robust training and onboarding solutions for the world's top pharma brands and biotech companies. The company shares Aptar's commitment to creating a more sustainable future.

A prime example of how Noble contributes to a sustainable environment is through resettable training devices (Figure 2). These reusable training devices allow patients to repeatedly practise the use of autoinjectors, prefilled syringes and nasal delivery devices to educate themselves on proper usage technique and to help them overcome their anxiety and fears – rather than using their single-use actual drug delivery devices filled with medication for practice, which requires disposal after a single use. In addition, pharma companies often achieve cost reductions and support their own sustainability initiatives by using Noble's resettable training devices.

There is an extraordinary, and often overlooked, downstream cost to the healthcare system when patients do not comply with their self-administered drug therapies – and noncompliance often begins because of a lack of upfront and ongoing training.

Not only does the patient suffer when they do not receive the proper dose of their medication, it also hurts the healthcare system by creating the need for additional goods and packaging, such as additional shipping and more sharps waste. When a patient uses a resettable training device, they are more likely to receive a proper dose when using the actual drug delivery device. Simply put, when a patient gets it right the first time, our footprint shrinks.

Noble is also an environmental steward when it comes to its packaging designs, balancing sustainability with an understanding that the patient and product efficacy are key factors in the design process (Figure 3). This commitment to sustainable packaging extends to Noble's travel kits (Figure 4), which are designed to protect temperature-sensitive medications.

All materials used within Noble's packaging are compliant with the Restriction of Hazardous Substances (RoHS) directive that originated in the European Union to restrict the use of specific materials that are hazardous to the environment, including lead, mercury, cadmium, hexavalent chromium, polybrominated biphenyls (PBB), polybrominated diphenyl ethers (PBDE), and four different phthalates (DEHP, BBP, BBP, DIBP).[6] Additionally, nearly all of the company's packaging is also free of harmful chemicals such as paint and electroplated plastic components.

Figure 3: A Noble patient training kit made with recyclable materials.

CONCLUSION

Due to pressing environmental needs, a focus on preserving the environment for future generations and a shift to more responsible consumption and production,

Working towards a more sustainable future.

At Noble, we feel it's our responsibility to help ensure a more sustainable future for our patients and customers, which is why we're proud to offer reusable training devices and recyclable packaging.

noble®
an Aptar pharma company

Noble Speaks Patient ™

Figure 4: A reusable Noble travel kit that is temperature controlled to keep medications at their optimal temperature while away from home.

companies have embraced more sustainable strategies. The link between sustainability, both environmental and social, has clear ties to human health, making advancement of these strategies a priority for healthcare and pharmaceutical industries alike (Figure 4).

ABOUT THE COMPANY

Noble is focused on fostering healthy patient outcomes for those who self-administer drug therapies through the development of robust training devices and onboarding solutions for the world's top pharma brands and biotech companies. Noble manufactures and commercialises training devices that mimic the exact feel, force and function of drug delivery devices such as autoinjectors, prefilled syringes and on-body, nasal and pulmonary devices in order to increase patient adherence and confidence and decrease usage errors. Noble is an Aptar Pharma company.

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PRODUCT SHOWCASE: ZwickRoell Luer Lock Testing System

REVISIONS TO ISO 80369

With a new series of ISO 80369 standards for Luer lock testing pending release, the industry will soon face changes to the design of these small-bore tubing connectors worldwide. The existing standards, ISO 594-1 and ISO 594-2, published in the 1980s, have become insufficient due to the rising risk of inadvertent misconnection by healthcare providers, which has resulted in patients suffering injury and even death.

To address the need for dimensionally unique connectors for different applications, an initiative was started by the European Committee for Standardization (CEN) in the late 1990s, which resulted in the first version of ISO 80369 in 2015.

Yet, this version of ISO 80369 makes complete compliance with device requirements difficult, most notably in the tolerance of the thread pitch, which is too tight for any supplier to measure. These issues were recognised and a new version of ISO 80369, sent for review in October 2019, is pending release after a typical approval process of 12 months. The ISO 80369 standard is valid for different application types, going by section (Table 1).

ISO 80369 Annex	Scope of Application
-1	General requirements
-2	Connectors for breathing systems and driving gases applications
-3	Connectors for enteral applications
-4	Connectors for urethral and urological applications
-5	Connectors for limb cuff inflation applications
-6	Connectors for neuraxial applications
-7	Connectors for intravascular or hypodermic applications
-20	Common test methods

Table 1: Scope of the relevant sections of ISO 80369 to Luer lock testing.

The general requirements for small-bore connectors for liquids and gases in healthcare applications are covered in Section 1. Sections 2-7 describe the detailed mechanical and leakage tests for the various applications. Section 20 and its annexes describe the common test methods used to evaluate performance requirements.

THE NEED FOR A RELIABLE TESTING SOLUTION TO ENSURE DATA INTEGRITY

Historically, assembly, mechanical test sequences and tests for leakage and pressure have been performed separately. This meant companies needed a separate testing solution for each set of tests, often having to source them from two different vendors. With multiple systems and users in play, obtaining reliable test results was a challenge.

Recently, manufacturers of connector systems, as well as pharmaceutical companies and their contract partners, have turned to ZwickRoell for a comprehensive testing system that minimises errors and improves data integrity and repeatability. ZwickRoell has developed a solution based on the single-column zwickiLine testing machine, which features a superimposed torsion drive to handle the assembly process

ENVIRONMENTAL PROTECTION, SUSTAINABILITY AND SOCIAL RESPONSIBILITY AT ZWICKROELL

Thinking and acting sustainably is of fundamental importance for a future-oriented company. ZwickRoell is committed to harmonising economic success, environmental protection and social responsibility for people in need.

Since 2014, all the company's production has been CO_2 neutral. In 2019, ZwickRoell offset more than five tons of CO_2 emissions. The company proudly supports underprivileged youth in India through its local training academy. In its annual ZwickRoell Runs the World charity challenge, employees and customers run together for a good cause. To date, this event has raised over €100,000 (£92,464) for charitable purposes.

ZwickRoell is also leading the way in terms of machines and processes. The company modernises its own machines, as well as those of other manufacturers, to extend their time in operation and achieve better ecological balance.

of the connectors. The solution also includes an integrated air pressure system with the capability to handle both positive and sub-atmospheric pressures.

The zwickiLine testing machine controls all process parameters, including the integrated air pressure system, allowing the system to perform the complete test method, from assembly to the mechanical and leakage test, required by ISO 80369 Annex 20 (Figure 1). This ultimately saves time and money in an area of healthcare that is critical to the safety of patients.

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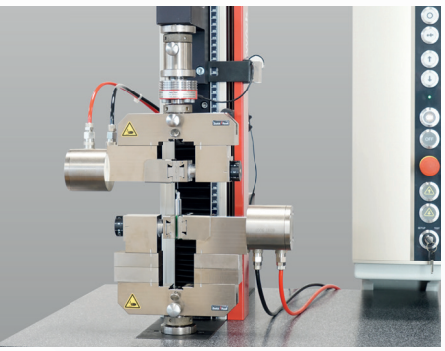
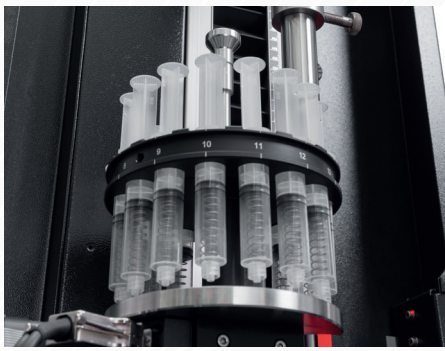
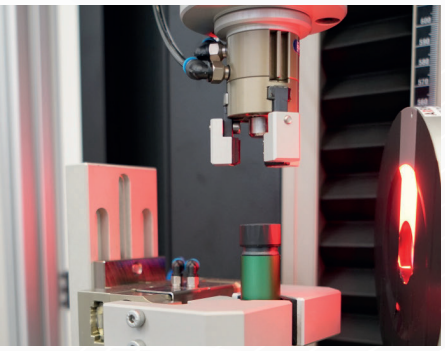
Figure 1: Luer lock testing in accordance with ISO 80369, as performed on a zwickiLine testing machine with testXpert testing software. The zwickiLine fulfills the requirements set out by the US FDA in 21 CFR Part 11.

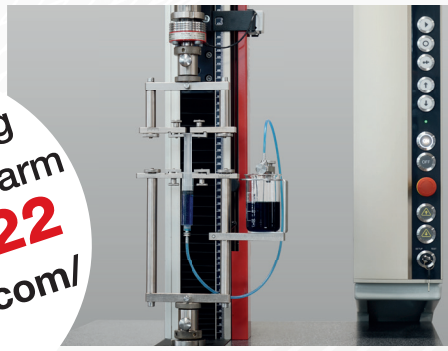
Testing systems

for the medical and pharmaceutical industry









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ZwickRoell

SMART GOALS AND CONTINUOUS IMPROVEMENT FOR A RESILIENT SUSTAINABILITY STRATEGY

In this article, Dirk Borghs, Chief Executive Officer of Datwyler Healthcare Solutions, considers the obligation of the pharmaceutical sector to implement environmentally responsible practices, and discusses the steps Datwyler is taking in its efforts for sustainability.

Forecasts on the effects of climate change have prompted all industries, including the pharmaceutical sector, to implement more environmentally responsible practices. In doing so, in 2015, some of the biggest names in the pharmaceutical industry, including Patheon, Biogen, Johnson & Johnson, Genentech and Novartis, joined the American Business Act on Climate Pledge.[1] Just last year, the European Commission outlined a strategic approach to pharmaceuticals in the environment[2] which entails expanding environmental monitoring, improving environmental risk assessment, supporting greener manufacturing methods, and reducing, as well as better managing, waste.

Now, even as the industry remains focused on the development and production of viable covid-19 vaccines and treatments, drug manufacturers can continue to support sustainability initiatives by working with suppliers aligned with their commitments to build more eco-conscious supply chains.

Already, many are doing just that by taking into consideration the sustainability initiatives of their suppliers before engaging in projects. Others are taking even larger steps. For example, in March 2020, Pfizer announced the completion of a US$1.25 billion (£970 million) ten-year sustainability bond[3] that will mature April 1, 2030 – the first ever sustainability bond for Pfizer, or any biopharmaceutical company. Proceeds from the bond will help support patient access to Pfizer's medicines as well as support the company's robust sustainability efforts[4] aimed at significant reductions in greenhouse gas emissions, waste and water use.

In the area of parenteral drug packaging, there are some key considerations to make when specifying solutions, such as plungers for prefilled syringes, and stoppers and caps for vials. How these system-critical elastomer components are manufactured makes up part of the sustainability story for every drug manufacturer.

SMART RESOURCE MANAGEMENT FOR A RESILIENT SUSTAINABILITY STRATEGY

In July 2020, Datwyler announced its long-term target for carbon neutrality after successfully reducing consumption of electricity, fuels and water per revenue unit for three consecutive years. Last year marked several key strides in resource

"In July 2020, Datwyler announced its long-term target for carbon neutrality after successfully reducing consumption of electricity, fuels and water per revenue unit for three consecutive years."

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Figure 1: A modern trigeneration unit at Datwyler's plant in Italy reduces the company's CO_2 emissions by 900 tonnes per year.

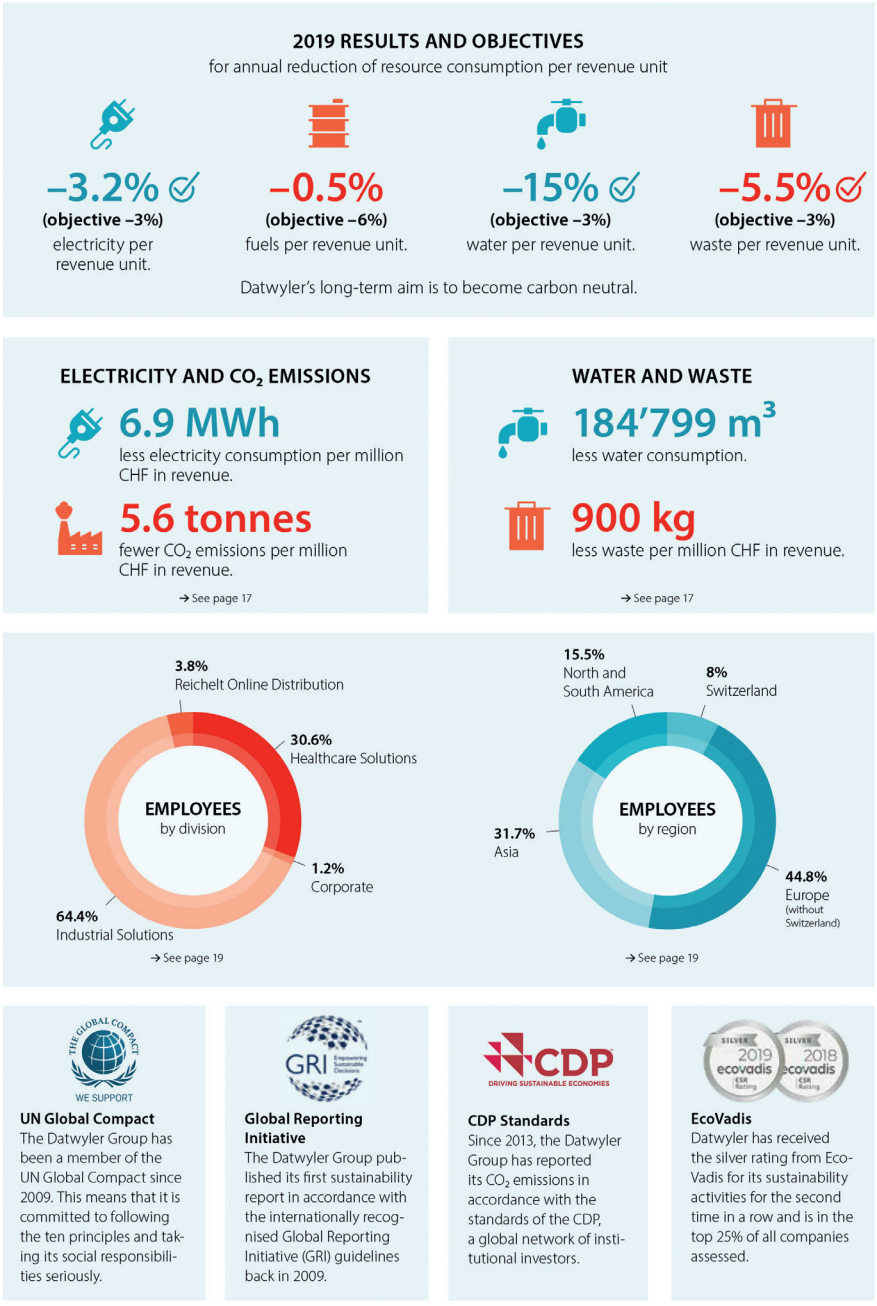

Figure 2: Datwyler's multifaceted approach to sustainability continuously reduces its carbon footprint.

management. The company reduced consumption per revenue unit for:

- electricity (-3.2%)
- fuels (-0.5%)
- water (-15.0%)
- waste volume (-5.5%).

Even though the company contends with the industry-wide challenges posed by covid-19, Datwyler is advancing its sustainability and climate strategy with the long-term goal of carbon neutrality. In Switzerland, Datwyler produces CO_2 neutrally by utilising a wood-fired heating plant for process energy and heating power, as well as using hydropower for electricity. As a result, every year the company saves 500,000 tonnes of fuel oil and 3,600 tonnes of CO_2. By implementing and operating a modern trigeneration unit at the Italian facility, Datwyler reduces the CO_2 emissions by some additional 900 tonnes per year (Figure 1).

These resource management changes help the company do its part in meeting the United Nations (UN) Sustainable Development Goals. The efforts also merited Datwyler with a top 25% ranking in the EcoVadis Corporate Social Responsibility (CSR) audit. As a company that continues to balance sustainability goals with the demands of designing and producing system-critical elastomer components for the primary packaging of parenteral drugs – meeting the highest standards for inertness, particle contamination prevention and compatibility with highly-sensitive large molecule formulations – Datwyler continuously improves the ways in which it can help pharmaceutical customers build a more resilient, environmentally conscious supply chain (Figure 2).

Compliance with Credible Sustainability Standards and Goal Setting Organisations

Demonstrating alignment with initiatives such as the UN Global Compact, a voluntary initiative based on CEO commitments to implement universal sustainability principles and take steps to support UN goals, or the Global Reporting Initiative (GRI), an independent international organisation that has pioneered sustainability for more than 20 years, reaffirms Datwyler's commitment and drives continuous improvement. As early as 2008, Datwyler published an annual sustainability report in accordance with the GRI guidelines. Since 2009, the Swiss-based healthcare supplier has been

"Over three consecutive years, Datwyler achieved reductions in resource consumption across key areas. Electricity consumption declined 6.9 MWh per million CHF in revenue and CO_2 emissions declined 5.6 tonnes per million CHF in revenue compared with the previous year."

a member of the UN Global Compact. The Carbon Disclosure Project is another example. The not-for-profit charity runs the global disclosure system for investors, companies, cities, states and regions to manage their environmental impacts. EcoVadis is one of the world's leading companies for CSR audits. It has assessed 60,000 companies from 155 countries, awarding performance ratings based on audits by sustainability experts. In addition to assigning rankings, EcoVadis offers industry profiles to improve performance.

Outside of sustainability-driven organisations, specific certifications from the International Organization for Standardization (ISO), including 14001, 50001 and OHSAS 18001, also provide important benchmarks. ISO 14001 is the international standard specifying requirements for an effective environmental management system. ISO 50001 is a company level certification requiring the use of an energy management system. This standard calls for the company to develop an energy policy, establish goals for energy efficiency, utilise data to meet said goals, measure policy effectiveness and make continuous improvements to the policy. These, and other standards and organisations, make for a robust guiding force for developing or reconfiguring sustainability goals.

Incremental Goal Setting to Reduce Utility Usage and Waste

Over three consecutive years, Datwyler has achieved reductions in resource consumption across key areas. Electricity consumption declined by 6.9 MWh per million CHF (£850,000) in revenue and CO_2 emissions declined 5.6 tonnes per million CHF in revenue compared with the previous year. Additionally, water consumption declined by 184,799 m^3 compared with the previous year and waste declined by 900 kg per million CHF compared with the previous year. To achieve this progress, Datwyler set challenging but achievable targets based on average annual reduction in the relative consumption of resources per revenue unit up to 2020: fuel -6%; electricity -3%; water -3%; and volume of waste -3%.

Evaluation of Chemical Compliance Management

Manufacturing 30 billion components a year requires 56,000 tonnes of raw materials, including polymers, fillers, aluminium, curing agents and antioxidants. As such, Datwyler must meet a variety of chemical law requirements at its production locations around the world, as well as additional industry and customer-specific rules. Chemicals legislation and the EU REACH (EU Regulation 1907/2006) governs the registration, assessment and approval of chemical substances within the EU, setting the standard for compliance. However, proactive advancements in chemical compliance management help to keep companies ahead of the curve on best practices for raw materials sourcing, usage, handling and disposal. Ensuring transparency on all substances makes seamless, open communication between customers and suppliers easier, especially if previously unproblematic substances must be re-evaluated (even if they continue to meet regulatory standards). In an instance where a particular material or ingredient is no longer desirable, implementing new solutions sooner rather than later could minimise product waste in the long run. Other important considerations for effective raw material management include the forwarding of waste rubber material for safe reuse, and efforts to curb packaging waste or switch to recyclable, or even reusable, packaging materials (Figure 3).

Figure 3: Proactive chemical compliance management can elevate best practices for raw materials sourcing.

Investment in Green Electricity to Support Carbon Neutrality

In addition to reducing overall energy and utility consumption, employing carbon-neutral electricity makes hitting major sustainability goals a stronger possibility for larger companies with global operations. In addition to the steps taken toward carbon neutrality at Datwyler's Switzerland and Italy plants, the company adheres to a plan to purchase carbon-neutral electricity at all its plants worldwide (Figure 4).

THERE IS NO TIME LIKE THE PRESENT TO PLAN A BETTER FUTURE

When it comes to driving sustainability in the pharmaceutical industry, the road ahead will be long. Last year, a study published in the Journal of Cleaner Production,[5] claimed that in 2015, the pharmaceutical industry generated 55% more greenhouse gas emissions than the automotive industry. The paper, "Carbon footprint of the global pharmaceutical industry and relative impact of its major players", asserted that the sector would need to reduce emissions by 58.6% from 2015 levels by 2025 to comply with reduction targets in the Paris Agreement.

However, from parenteral packaging component manufacturers to drug companies, the industry is in this together. Even in the most challenging times, setting and acting on goals for sustainable initiatives

Figure 4: Datwyler's Switzerland facility has achieved carbon neutrality with wood-fired heating and hydropower since 2012.

"When it comes to driving sustainability in the pharmaceutical industry, the road ahead will be long. Last year, a study published in the Journal of Cleaner Production,[5] claimed that in 2015, the pharmaceutical industry generated 55% more greenhouse gas emissions than the automotive industry."

is a promise to do even better for the patients that rely on both the medications produced and live in the world where they are made. By constructively working together, drug companies and suppliers can develop more resilient, long-term strategies that contribute to worldwide sustainability goals and help combat climate change – even amid a pandemic.

Datwyler is prepared to make its contribution as a socially and environmentally responsible company. There is only one planet Earth and we have to take good care of it if we want to secure it for our children and future generations. Datwyler proudly looks back on more than 100 years of value creation for the benefit of all its stakeholders. Sustainability is deeply rooted in its heritage and values and has always been part of the DNA of the company. A total of 11 years of membership in the UN Global Compact and 12 GRI sustainability reports proves its commitment. Despite the pandemic, Datwyler is continuing its efforts. An interdisciplinary project group is working on further advancing its sustainability and climate strategy with the long-term target of becoming carbon neutral. Specific milestones will be communicated with the next sustainability report in spring 2021. Adhering to the "People, Planet, Profit" concept, Datwyler aims to live up to its social responsibility, offer an attractive and agile work environment and attract the best international talent. Aware that resources are limited, the company wants to use them responsibly and contribute to achieving the UN Sustainable Development Goals. And above all, Datwyler wants to continue to create value for its customers, grow profitably and lay the foundation for its long-term success.

ABOUT THE COMPANY

Datwyler engineers high-quality, system-critical elastomer components for applications in healthcare, mobility, oil and gas, and food and beverage. With more than 20 operating companies, sales in over 100 countries and some 6,500 employees, Datwyler generates annual sales of more than CHF 1 billion (£850 million). Within the healthcare solutions business area, Datwyler designs, develops and manufactures solutions for injectable packaging and drug delivery systems to facilitate customers to create a safer medical environment of tomorrow. Looking back on more than 100 years of history, Datwyler is a reliable partner, now and in the future!

ABOUT THE AUTHOR

Dirk Borghs, Chief Executive Officer of Datwyler Healthcare Solutions, graduated as an engineer in Materials Sciences from KU Leuven University (Belgium) and gained a Master's degree in Finance and Marketing. Mr Borghs joined the Datwyler Healthcare business as Technical Manager. He later became Head of Global Quality and Engineering and then ran US Operations 2001-2006. Later, as Vice-President Strategic Projects and Global Procurement, he led planning and implementation of Datwyler's FirstLine™ manufacturing standard in Belgium and the greenfield facility in India. Mr Borghs then oversaw Datwyler's main healthcare plant in Belgium, became Senior Vice-President Operations in Europe for Datwyler Sealing Solutions, and in 2017 oversaw Global Operations and Supply Chain before being named Chief Executive Officer of Datwyler Healthcare Solutions in 2020.

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YPSOMED
SELFCARE SOLUTIONS

PAVING THE WAY TO ZERO CARBON EMISSION COMBINATION PRODUCTS: INSIGHTS FROM THE YPSOMATE ZERO CASE STUDY

In this article, Sebastian Gerner, Innovation & Business Development Manager, and Andreas Schneider, PhD, Innovation & Business Development Director, both of Ypsomed, discuss how the adoption of prefilled self-injection systems has put the drug delivery device industry at the forefront of the the global plastics challenge. The authors introduce YpsoMate Zero as a case study, Ypsomed's net-zero carbon emission prefilled autoinjector, covering how the use of alternative materials, supply chain optimisations and offsetting the remaining carbon footprint result in an eco-friendly device without compromising on usability or patient safety.

SELF-MEDICATION AND SUSTAINABILITY: TURNING THE VICIOUS CYCLE INTO A VIRTUOUS ONE

When Susanna, who has been living with arthritis for about five years, started taking her newly prescribed biologics in a prefilled autoinjector, she realised that it really did reduce pain, swelling and joint stiffness. This prompted her rheumatologist to propose the new treatment option for the coming years to stop further joint erosion. However, she soon discovered that her injection routine would lead to a considerable amount of waste.

In fact, more than 16 billion injections are administered worldwide every year. A significant portion of these injection devices heads straight for the landfill – shockingly, less than 10% of diabetes patients used specific containers for the disposal of their needles, syringes and pens. For patients living with chronic diseases, injection devices are an indispensable part of their disease management routine. Instead of burdening the environment – and unnecessarily forcing patients to adopt non-eco-friendly habits – self-care should help to preserve natural resources and contribute to minimising waste and pollution. Self-care should have minimal impact on our environment.

> "Self-care should help to preserve natural resources and contribute to minimising waste and pollution."

Easy-to-use self-injection systems contribute to shifting the point of care from the hospital to the home, and are demonstrating success in doing so. At-home treatment of chronic diseases not only improves access to healthcare and lowers overall costs, it also helps to minimise the overall environmental impact by, for example, reducing the need for travel or to use hospital infrastructure and resources. The increasing adoption of single-use and prefilled self-injection devices, however, has put the pharmaceutical industry in general, and the drug delivery device manufacturers in particular, in the public spotlight with respect to some of the most pressing issues of our time: the use of plastics and its effect on the environment.

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"The vision is clear: Ypsomed is committed to achieving net-zero carbon emissions by 2030."

There is little debate about the responsibility of the pharmaceutical supply chain to help minimise the impact of healthcare on the environment and contribute to a more sustainable future. Additionally, there is considerable scope for systemic improvements where we see healthcare-related environmental impacts. However, the environmental costs of medical devices, healthcare facilities and care concepts are often overlooked. As Simon Michel, CEO at Ypsomed states, "Every year we manufacture millions of self-injection devices. As this number continues to increase, it puts us at the forefront of plastic waste – one of the world's biggest environmental challenges. We need to act now, and send a clear signal that we are taking our responsibility seriously."

Ypsomed has adopted a corporate sustainability programme that embraces environment-friendly and resource-saving actions. The vision is clear: Ypsomed is committed to achieving net-zero carbon emissions by 2030. Step-by-step, the company is reorienting its manufacturing processes, supply chain and self-injection device designs towards a less resource-intensive, more circular mindset. Ypsomed is shifting from a linear take-make-waste economy to a circular way of thinking, embracing, wherever applicable, the three core principles proposed by the Ellen MacArthur Foundation (Cowes, UK) and others to build a positive future economy:

1. Design out waste and pollution – consider waste as a design flaw and use new materials and technologies.
2. Keep products and materials in use – enable product and component reuse, repair and re-manufacturing. Allow materials to be recovered so that they do not end up in landfill.
3. Regenerate natural systems – restore valuable nutrients to the soil and other ecosystems to enhance our natural resources.

Despite all the challenges of achieving net-zero carbon emissions by 2030,

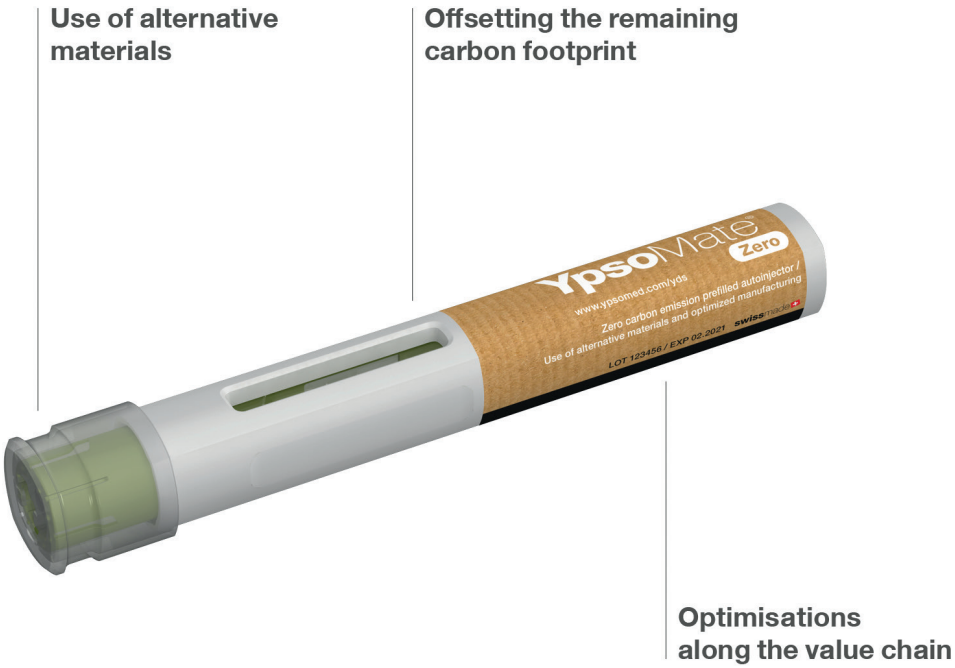


Figure 1: The YpsoMate Zero autoinjector with zero carbon footprint. The use of alternative materials, optimisations along the value chain and offsetting of the remaining carbon footprint result in a carbon emission free prefilled autoinjector without compromising on usability and patient safety.

Ypsomed has already set out on the journey to zero. This article introduces the case study of YpsoMate Zero, a prefilled autoinjector with net-zero carbon emissions and a first step towards achieving Ypsomed's net-zero carbon emissions by the 2030 goal. The case study illustrates how the use of alternative materials, optimisations along the supply chain and offsetting the remaining carbon foot print lead to an environment-friendly device offering without compromising on usability and patient safety.

"Before optimising the YpsoMate device design to minimise its carbon footprint, it was essential to gain detailed insight into the environmental impacts associated with the device as it stood."

INTRODUCING YPSOMATE ZERO – THE CARBON NEUTRAL PREFILLED AUTOINJECTOR

There are two main reasons that the YpsoMate autoinjector for use with prefilled 1.0 mL syringes was selected to have its environmental impact minimised (Figure 1). First, YpsoMate is a state-of-the-art prefilled autoinjector that provides patients with a simple and convenient automatic two-step injection procedure. YpsoMate prioritises patient safety and the ability to use the device effectively. However, its single-use nature has put the prefilled autoinjector at the forefront of the global plastic challenge, urging Ypsomed to take action. Second, YpsoMate 1.0 mL is used across chronic disease areas where patients regularly self-inject over a long period of time. Patients pull off the cap to remove the needle shield from the prefilled syringe, press the autoinjector onto the skin to trigger the injection and then dispose of the autoinjector after use. Continued YpsoMate-based self-injection leads to a considerable accumulation of waste during therapy. YpsoMate 1.0 mL, therefore, is a key priority when it comes to reducing the environmental costs of self-injection systems.

Before optimising the YpsoMate device design to minimise its carbon footprint, it was essential to gain detailed insight into the environmental impacts associated with the device as it stood. A lifecycle assessment was conducted to obtain a quantitative and systematic perspective

on the environmental costs of the two-step autoinjector over its entire lifecycle, including raw materials, manufacturing and final disposal. Figure 2 shows the YpsoMate autoinjector value chain and highlights those areas included in the case study.

Not only did the lifecycle analysis assess those process steps controlled by Ypsomed, but also included the end of life of the final assembled drug product to better understand the environmental impact associated with its disposal. A breakdown of the total carbon emission of the YpsoMate autoinjector is shown in Figure 3. The lifecycle analysis highlighted the environmental hotspots and enabled evidence-based and data-driven design optimisations.

The analysis provided two key insights that guided the subsequent optimisation efforts to minimise the environmental effects of the device. First, the materials used for the device components had the greatest impact on the device total carbon emissions. In fact, the polymer components, such as the device housing, the syringe holding unit and the components used to remove the needle guard, accounted for about 60% of the total carbon emissions of the device. Second, the analysis confirmed that the packaging materials used to ship the device components either in-house or to the final assembly sites also constituted a significant environmental impact, and were therefore a key priority. The weight of the materials used to securely package the autoinjectors is more than half of the overall device weight, and contributed to about 20% of the total carbon emissions. Interestingly, the lifecycle analysis showed that the transportation of raw materials was less critical for the environmental impact of the device.

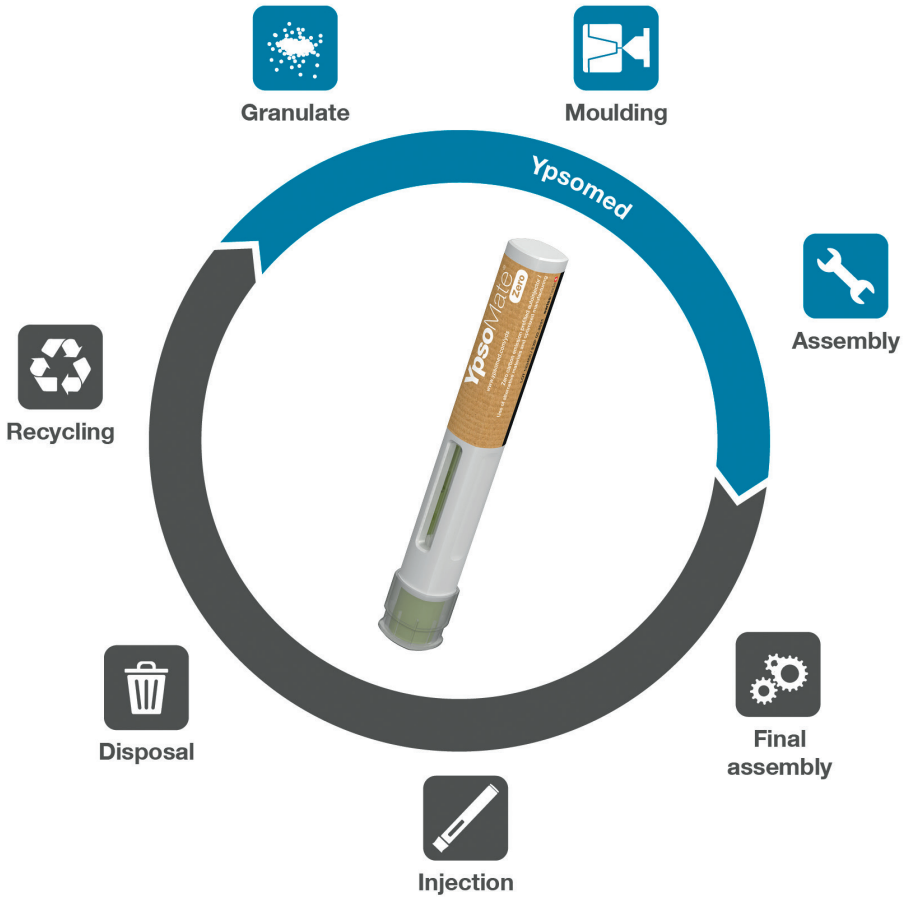


Figure 2: From vicious to virtuous circle. An introduction to the YpsoMate autoinjector value chain. The areas included in the YpsoMate Zero case study are highlighted in blue.

The lifecycle analysis thereby provided the basis for reducing the YpsoMate carbon emissions, directing the engineering efforts towards the most pressing environmental hotspots:

1. Use of alternative polymers for selected device components and packaging (e.g. device housing and packaging tray)
2. Close the loop for the packaging of device components and device sub-assemblies (e.g. trays, pallets)
3. Implement design for recycling into the development process.

The iterative implementation of the aforementioned measures was key to eliminating waste, fostering a sustainable use of natural resources, engendering resource efficiency and, most importantly, avoiding carbon emissions. As illustrated in Figure 4, several optimisation loops have resulted in a substantial reduction of the total carbon emissions.

However, a state-of-the-art injection device cannot be designed in such a way that the carbon footprint is zero. With the aim of creating a fully carbon neutral prefilled autoinjector, a separate programme is needed to offset the remaining carbon footprint. Ypsomed invests in its own programme to substitute carbon emissions. The Ahueni reforestation programme in Kenya enables the generation of carbon emission certificates while committing to the highest industry standards. Since its launch three years ago, the programme has planted 350,000 indigenous tree species to bind carbon in the long run, create new habitats for plants and animals and proactively include local communities in the project to regenerate their ecosystem.

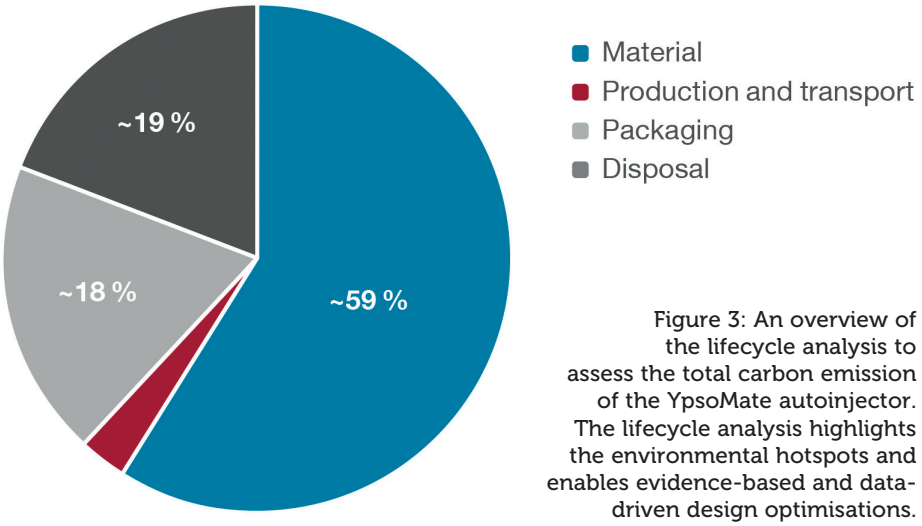


Figure 3: An overview of the lifecycle analysis to assess the total carbon emission of the YpsoMate autoinjector. The lifecycle analysis highlights the environmental hotspots and enables evidence-based and data-driven design optimisations.

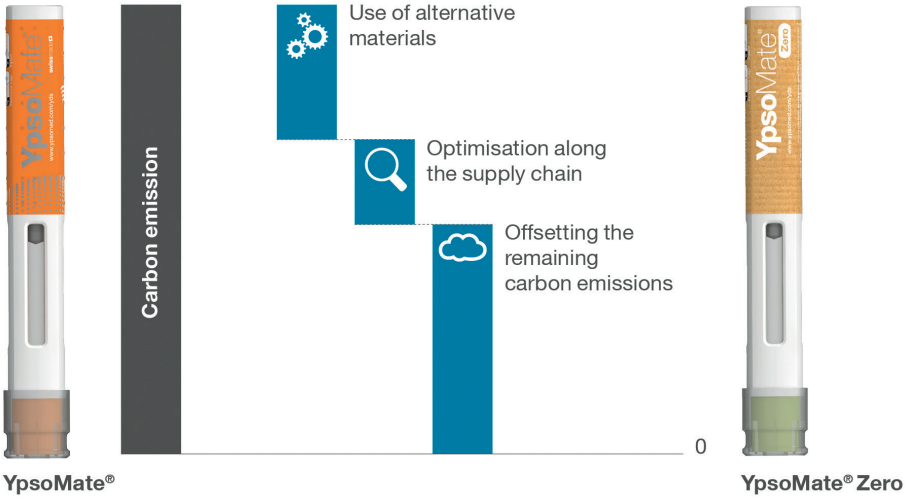


Figure 4: Transforming the proven autoinjector into a zero carbon emission device platform. The use of alternative materials and optimisation along the value chain have resulted in a substantial reduction of the total carbon emission. The Ahueni reforestation programme in Kenya, committing to the highest industry standards, is used to offset the remaining carbon footprint.

COLLABORATION TO ENABLE ZERO CARBON EMISSION COMBINATION PRODUCTS

The world's first net-zero carbon emission autoinjector paves the way towards carbon neutral combination products. On the one hand, the insights gained from YpsoMate Zero inform the overall transition to zero carbon emission self-injection device platforms at Ypsomed. On the other hand, the YpsoMate Zero also reiterates the need to bring together the commitments of partners to achieve a net-zero carbon emission combination product.

Enabling the launch of a zero carbon footprint combination product requires the involvement and co-ordination of multiple actors along the value chain in order to adopt the principles of the circular economy and remove its barriers to adoption. The journey to zero goes beyond Ypsomed's own operations, products and services. To this end, the company is fostering collaborative problem solving, shaping regulatory frameworks and promoting the circular mindset with a science-based approach. Collaboration along the value chain will help Ypsomed to enable zero carbon footprint combination products.

> "With the aim of creating a fully carbon neutral prefilled autoinjector, a separate programme is needed to offset the remaining carbon footprint."

ABOUT THE COMPANY

Ypsomed's comprehensive drug delivery device platforms include autoinjectors for prefilled syringes in 1 mL and 2.25 mL formats, disposable pens for 3 mL and 1.5 mL cartridges, re-usable pen injectors, ready-to-use prefilled wearable patch injectors and connected devices and digital services. Unique click-on needles and infusion sets complement the broad product portfolio of self-injection systems. With over 30 years of experience and pioneering spirit in the development and manufacturing of innovative injection systems, Ypsomed is well equipped to tackle one of the most pressing challenges of our time: the reduction of carbon emissions. Ypsomed anticipates the future needs of patients, pharmaceutical customers, payers and healthcare professionals, striving with its product solutions to change patients' lives and minimise environmental impact.

Ypsomed is ISO 13485 certified and all processes comply with design control and cGMP guidelines with operational QA/QC experts on site at each location. Ypsomed's US FDA-registered manufacturing facilities are regularly inspected by both pharma customers and regulatory agencies to supply devices for global markets including the US, Europe, Japan, China and India.

Get in touch with us to join our journey to zero: zero@ypsomed.com

ABOUT THE AUTHORS

Sebastian Gerner is Innovation & Business Development Manager with Ypsomed Delivery Systems. He is driving the transition of Ypsomed from a linear take-make-waste economy towards a circular economy. He is a mechanical engineer with more than 10 years of medical device experience in various medical and pharmaceutical companies.

Andreas Schneider is Innovation & Business Development Director with Ypsomed Delivery Systems. He leads a team that drives the definition and development of new drug delivery device platforms, such as next-generation autoinjectors, wearable bolus injectors, connected systems and digital solutions. Dr Schneider has published various articles and given presentations in the areas of innovation management and drug delivery. He holds a PhD in innovation management from ETH Zurich, Switzerland.

COMPANY SHOWCASE: West Pharmaceutical Services

West believes that, as a global organisation, it has a duty and obligation to contribute to a sustainable future and that each of us, working together, can make a difference. Everything we do at West supports the company's promise to make a meaningful difference – for communities, team members, customers and ultimately for patients who use West's products to help them lead longer and healthier lives. West remains dedicated to its commitment to building a diverse and inclusive workforce, and to its sustainability efforts aimed at improving the communities in which we live and work. That unwavering focus has enabled West to make a positive impact in countless ways, including through its commitment to caring for the environment and its team members, as well as giving back to communities.

> "As a company whose stated mission is to improve patient health, it stands to reason that West is equally committed to a sustained investment in creating a healthier environment."

WEST'S COMMITMENT TO THE ENVIRONMENT

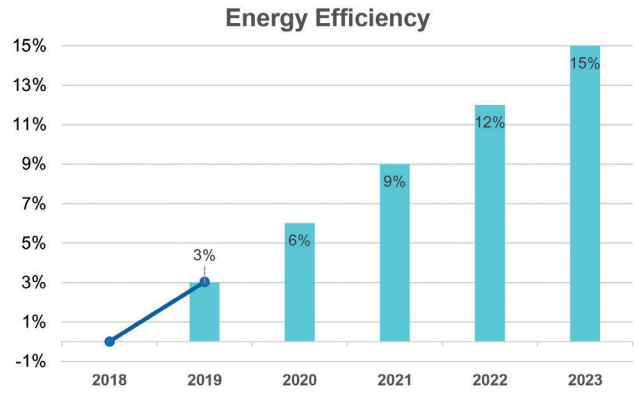
While West knows that sound environmental practices make good business sense, the underlying reasons behind the company's commitment to them are the many benefits these practices provide to our communities. As a company whose stated mission is to improve patient health, it stands to reason that West is equally committed to a sustained investment in creating a healthier environment.

West's sustainability programme is designed to target reductions in areas where the company feels it can make the greatest impact: greenhouse gas emissions, waste and increased recycling, as well as energy and water usage. Although West manages its programme at a global level, the company's manufacturing sites are also working hard to make improvements in areas where they can make a difference in their community.

In late 2019, West entered a partnership to begin a test recycling programme, with the goal of implementing this programme in multiple West US manufacturing sites in 2020. The Jersey Shore, PA, site was the first to begin recycling 100% of its rubber scrap, and West plans to expand this initiative across its network of manufacturing sites by 2021. West's six Contract Manufacturing sites recycled 98% of their waste in 2019. All of these efforts have resulted in a 15% recycling improvement over 2018, which decreases the company's waste-to-landfill total to 48%, which is in line with the reductions it needs to obtain to achieve its five-year goal set for 2023.

Progress against five-year corporate goals

Improve energy efficiency by 15% (Intensity)
over 5 years (2019-2023)



Reduce absolute emissions by 10%
over 5 years (2019-2023)

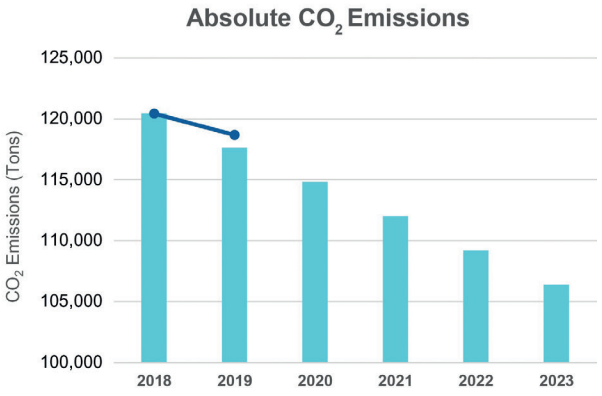


Figure 1: West's 2023 energy improvement and emissions reduction goals.

Multiple energy improvement initiatives have also yielded positive results with respect to the goal of reducing West's energy consumption, helping to shrink the company's carbon footprint. West's energy and CO2 emissions have been reduced by 7.8% and 7.1% respectively since 2018 (Figure 1). West has improved its Carbon Disclosure Project rating by no less than 500 basis points each year since it began reporting in 2013 and achieved its highest ever rating in 2019. West has also increased its environmental score with Institutional Shareholder Services Inc (Rockville, MD, US), a leading provider of governance and responsible investment solutions to the global financial community. In addition, West has maintained its Gold Standard rating from EcoVadis (Paris, France), a leader in sustainability ratings, placing it in the top 5% of reporting companies.

WEST'S COMMITMENT TO THE HEALTH AND SAFETY OF ITS TEAM MEMBERS

Although corporate responsibility is often mostly thought of as caring for the environment and giving back to local communities, West firmly believes that it also means taking responsibility for the health and safety of its team members, and working to safeguard them against work-related accidents and illnesses. West works hard to minimise the risk of incidents, injuries and exposure to health hazards, and is committed to designing and operating its facilities to provide a safe and healthy work environment.

This has never been more evident than in the current covid-19 pandemic, where West's priority since the beginning has been to care for the health and safety of its team members, and ensure that the company is implementing the most appropriate measures to create a safe working environment for team members while they are at work.

A critical component in maintaining a safe workplace begins with instilling and supporting a culture of safety – each team member must understand that they share the responsibility for workplace safety. In addition, a focus on proactive activities tied to leading indicators has helped build a culture of safety, helping to reduce and eliminate accidents. Such indicators include:

- Health and safety gemba walks
- Behaviour-based safety programmes
- Near-miss reporting
- Root-cause analysis
- Incident investigations.

Figure 2: West team members volunteering to support the Leukemia & Lymphoma Society.

West was pleased to celebrate several safety milestones in 2019, including one site which reached one million hours without any injuries, two sites that celebrated five years accident free and four sites with zero safety incidents.

WEST'S COMMITMENT TO GLOBAL AND LOCAL COMMUNITIES

Philanthropy is a cornerstone of West's culture. It anchors the company's purpose of standing by the side of its customers to help make a difference in the global community. Since its founding 97 years ago, West has fostered a culture of giving to support communities both local and global. The company's One West Team embraces philanthropy every day by making generous donations of time and resources to contribute to a healthier world.

West targets philanthropic activities and local charities to those that align with its mission in the focus areas of children, people with disabilities, healthcare and education (with a focus on STEM – Science, Technology, Engineering and Maths). The company's charitable giving framework is separated into three tiers:

- Corporate giving through direct charitable gifts made by West Pharmaceutical Services
- The Herman O West Foundation, an independently managed 501(c)(3) entity, which awards scholarships and matching gifts
- West without Borders,* a team member-led giving programme that has raised millions of dollars since its inception in 2004.

In 2019, corporate and foundation giving reached approximately US$2.1 million (£1.6 million), with more than 200 charities supported globally. West's teams continue to answer the needs of communities (Figure 2), giving nearly US$565,000, a 9.5% increase over 2018. West looks forward to continuing to nurture its team members' philanthropic spirit and implementing new philanthropic initiatives in support of local communities.

As a testament to its continued commitment to corporate responsibility, West was recently honoured to achieve several accolades, including being named as one of Newsweek's "America's Most Responsible Companies", a "Top 50 ESG Company by Investor's Business Daily", and one of Barron's "100 Most Sustainable Companies in America".

West believes in playing a significant role in making the world a better place, and does so by manufacturing high-quality products, supporting and empowering its team members, and conducting responsible operations in the communities where it does business. West takes this responsibility very seriously and never underestimates the important role the company plays in the broader community.

West recognises there is always more work to do, and welcomes the challenge of continuing to improve on the impact it makes, both now and for future generations.

**West without Borders is not affiliated with Doctors Without Borders®, which is a registered service mark of Bureau International de Medecins San Frontieres.*

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OWEN MUMFORD
Pharmaceutical Services

FROM DESIGN TO DISPOSAL: ACHIEVING SUSTAINABILITY IN MEDICAL DEVICES

In this article, George I'ons, Head of Product Strategy and Insights, Owen Mumford Pharmaceutical Services, discusses the onus on the device design industry to move towards sustainable practices, including what this entails, how it might be achieved and what benefits sustainability may bring.

Based on the article "Three perspectives on how sustainability is being achieved in the medical device market", which first appeared on Owen Mumford's Web Page in August 2020.

As our society becomes increasingly concerned with environmental protection, medical devices that are strictly single-use and disposable are a glaring issue. The medical device industry is under pressure from regulators, hospital systems, governments and consumers alike to seek more responsible and sustainable solutions. From a commercial point of view, developing sustainable medical products that continue to protect patients and healthcare workers from infection comes at a very real cost. However, companies that do not take the initiative to become more environmentally responsible risk losing access to markets around the world.

WASTE REDUCTION VERSUS INFECTION CONTROL

While reducing waste in the healthcare system is an important objective that must not be neglected, safety in healthcare environments is a critical priority. According to the European Centre for Disease Prevention and Control, healthcare-associated infection (HAI) rates run between 5% and 8% of patients in most developed countries.[1] These rates are unacceptably high, and may be exacerbated by the spread of antimicrobial resistance.[2] A further consideration is the need to prevent avoidable infections from needlestick injuries amongst healthcare workers. These safety concerns have led to strict one-use regulations around many invasive medical devices, along with mandatory legislation in the US and Europe on the use of products for needlestick injury prevention.

This tension between sustainability and infection control could not be more topical, as efforts to contain the coronavirus pandemic continue. An immediate concern for healthcare systems is to provide sufficient personal protective equipment (PPE) to frontline healthcare workers, which is frequently made of plastic material and tends to be single-use only. In fact, from

> "Taken together, the healthcare sectors of the US, Australia, Canada and England emit an estimated 748 million metric tons of greenhouse gases each year, which, if ranked alongside whole nations, would come in as the seventh largest greenhouse gas emitter in the world."

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February to July 2020, 2.3 billion items of PPE have been distributed to health and social care services in England, equivalent to that distributed in the whole of 2019.[3] This proliferation of demand, and a wider awareness of the issue due to the pandemic, may however prove to be an impetus for an urgent review of plastic waste management methods in the medical industry.

THE STATE OF PLAY

Healthcare systems currently have a sizeable environmental footprint. Taken together, the healthcare sectors of the US, Australia, Canada and England emit an estimated 748 million metric tons of greenhouse gases each year, which, if ranked alongside whole nations, would come in as the seventh largest greenhouse gas emitter in the world.[4] In Europe, legislation has helped to manage the situation by significantly altering manufacturing processes, labelling requirements and disposal restrictions, and creating instructions for end-of-life management and recycling. Although many medical devices are currently exempt from these regulations, several directives, including the Waste Electrical and Electronic Equipment Directive and Restriction on Hazardous Substances Directive, are in the process of being reviewed and could be applicable in future. In addition, as medical products become more "connected" in our increasingly digitalised world, they will also fall under the purview of legislation for devices with electronic components.

SUSTAINABILITY CHALLENGES

Currently, approximately 90% of medical device waste consists of disposable, one-time-use products or components. Efforts to reduce the volume of disposable components are constrained by the need to maintain safety standards, as discussed previously. Additionally, it is critical to ensure security of product supply; considering that in many cases, disposable products may generate the bulk of a manufacturer's revenue, the transition towards greater sustainability must be commercially viable. The risks associated with hazardous medical waste and biological contamination, as well as the high cost of product sterilisation and reprocessing, have historically prevented businesses from moving away from disposable products towards something more sustainable.

> "Many group purchasing organisations have appointed and empowered Senior Directors of Environmentally Preferred Sourcing who are successfully implementing the sustainable purchasing business case."

Traditionally, incineration has been used to reduce the volume of medical waste and destroy biohazardous materials. This process releases nitrous oxide, as well as known carcinogens including polychlorinated biphenyls, furans and dioxins.[5] Exposure to these compounds has been linked with damage to foetal and adult body function as well as the acidification of land and ocean. Replacing incineration with recycling would therefore tangibly benefit society, by reducing damage to both people and the environment. Where incineration cannot be avoided, European regulation sets strict emission limits for incinerators dealing with clinical waste.[6] Furthermore, sophisticated filtering systems are now being installed to prevent toxic fumes from polluting the atmosphere.

Sterilising devices for reuse may seem like a feasible alternative. However, it is often environmentally unsustainable, as well as being costly, as the sheer amount of energy required to carry out cleaning processes often outweighs the energy needed for the manufacturing and disposal of single-use devices. Moreover, several of the sterilisation methods which are well-established in healthcare, such as the use of glutaraldehyde and ethylene oxide, are not only harmful to the environment but also tend to be regulated by strict disposal rules. As a result, many hospitals and medical device companies are adopting less toxic methods, such as hydrogen plasma.[7]

A further obstacle to reuse is that a recycled device would be subject to the same level of scrutiny as a brand-new one under the EU Medical Device Regulation. However, manufacturers can expect further developments in this area, following the European Commission's 2019 consultation around the safety and performance requirements for single-use device reprocessing.

LEVERAGING PURCHASING POWER

On first inspection, the complex relationship between product sustainability, patient safety standards and commercial viability may appear to create an impasse. However, there is much that can be achieved and much that is already being done. The purchasing power of healthcare systems is a significant tool that can be used to influence suppliers towards taking environmental factors into consideration during manufacturing. Evidence of this can already be seen in the industry. Many group purchasing organisations have appointed and empowered Senior Directors of Environmentally Preferred Sourcing who are successfully implementing the sustainable purchasing business case.[8] Additionally, tenders within the EU increasingly include requirements for environmental credentials. As a consequence, many medical device firms are proactively publicising their environmental record and sharing their progress in this area. When assessing how these medical device manufacturers are delivering on sustainability, while taking into consideration the significant regulatory and safety concerns, three key areas of activity can be identified:

- Recyclability
- Sustainable manufacturing
- Sustainability by design.

RECYCLABILITY

As it has become clear that enabling device reuse is fraught with complications, another option is to reprocess and reuse its materials. PVC, the most widely used plastic material for disposable medical equipment, can be recycled several times without losing its critical properties. Equally, work has been done around the use of more easily recycled plastics, such as renewable polyethylene (PE) and polyethylene terephthalate (PET). For optimal gains, closed loop recycling systems must be put in place to recover waste material from hospitals and bring them into the recycling process. Considering that there is an estimated one million tons of clean, non-infectious healthcare plastic waste generated in healthcare facilities every year,[9] the benefits of these schemes would be considerable.

Further research could bring greater benefits still. Monomer extraction techniques in development enable recycled polymers to be broken down to their constituent monomers. If widely adopted, this could mean a virtually limitless recyclability of some polymers without loss in performance.[10] Finally, recycling should also extend to packaging. Manufacturers have already developed solutions such as decreasing packaging volume by favouring sealed trays instead of pouches or reducing the overall number of packaging components (Figure 1). However, they can also reduce energy consumption by assessing logistics during the design process and selecting optimum transport, especially if there is a need for controlled temperature.[11]

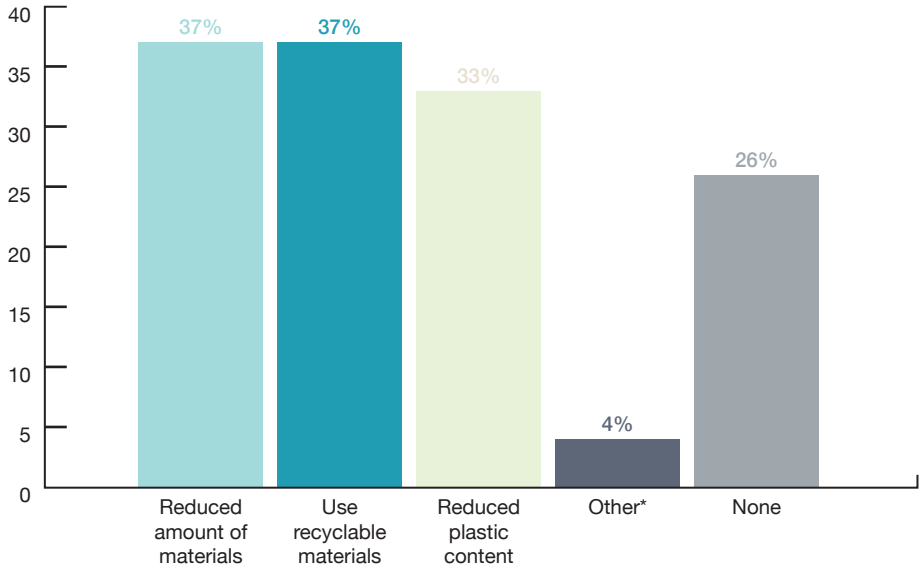

Figure 1: Responses to the question: "What changes have you already implemented to pharmaceutical packaging design and materials to provide a more sustainable alternative?" Respondents were permitted multiple answers (n=166). *Other includes: improved nonreactive materials; more reusable and biodegradable components; new way to administer; and training on critical thinking about sustainability with several groups of health professionals. Conducted by Owen Mumford Pharmaceutical Services in partnership with Pharma Intelligence.

SUSTAINABLE MANUFACTURING

Reviewing manufacturing processes plays an important role in reducing the impact of production on the environment. As well as optimising logistics, businesses can reduce water use, strengthen energy efficiency and reduce the use of polluting chemicals (Box 1). These initiatives can also help to reduce operating costs, which in turn, makes sustainability more commercially attractive. Moreover, reducing energy costs can help to finance sustainability programmes, producing further savings in the long term.

Newer generations of manufacturing technology are also likely to play a part in reducing waste, whilst simultaneously producing a raft of business benefits, such as improved productivity and shortening time to market. A good example is the adoption of 3D printing to develop and test prototypes. These can help to develop optimum product moulds more quickly, fulfil usability testing outcomes and refine production parameters to minimise raw material volumes and maximise output productivity. In sum, further technological innovation aiming to get as near as possible to "zero defect" manufacturing will, in all likelihood, produce inherent sustainability benefits.

SUSTAINABILITY BY DESIGN

From the very beginning of the design process, manufacturers already take many factors into account around the whole lifecycle of a product, from concept development and material selection, to transportation methods and end-of-life disposal. Businesses must simply add sustainability factors to their existing design procedures, making sure to evaluate energy efficiency, environmental impact, material usage and recycling. There are already resources available to support this transition. For example, existing US FDA and EMA quality system requirements cover tracking, materials safety/efficacy and disposal. Similarly, lean manufacturing methodologies can provide sustainability benefits in several areas, such as overproduction, waiting time and inventory management.

In relation to product design and engineering, there are many elements that can support sustainability (Box 2). Optimising the size of a device design and reducing the number of components can simplify the manufacturing process, reduce waste and reduce transport impact. If a product has minimal components and is easy to disassemble, this will also facilitate

BOX 1: OWEN MUMFORD & SUSTAINABLE MANUFACTURING

"Owen Mumford has adopted many onsite changes to ensure all our energy is coming from clean, renewable sources. We are also investigating a wide range of materials and additives which can reduce the energy required to process into final product. Bio-based materials can offset the carbon emitted during processing as the monomer source grows. A growing range of sources for bio-based monomers is available, such as wood pulp or sugar cane.

However, when assessing the most appropriate material for a part, the entire lifecycle of the product needs to be considered. For example: bio-degradable polymers can contaminate a recycling stream and emit methane when incinerated... and methane has a carbon emissions impact 25 times greater than CO_2."

Toby Cowe
Technology Development Group Manager R&D, Owen Mumford

recycling and make the process cheaper. An assessment of how raw materials and production methods can be better harmonised across different products may streamline the use of resources, while enabling greater task agility across production lines. Finally, for disposable products, manufacturers must review whether they could be using more environmentally friendly materials, which will reduce the level of toxic air emissions during disposal or incineration, as well as lower waste processing costs.

Most devices – especially parenteral or other invasive products – will continue to have a disposable component to meet regulatory requirements, and address safety and hygiene concerns. This does not mean that disposable medical products cannot be made more sustainable. There are many areas for improvement, such as increasing the recycling of materials, and introducing sustainability considerations in manufacturing processes and design. Additionally, device designers can look to produce products that incorporate the disposable component within a "shell" that is reliably reusable. In fact, digitally connected devices are already driving developments in this direction, as disposable electronic components would not be commercially viable or an acceptable option for the environment. Designers must therefore focus on creating a simple, repeatable interface between disposable and reusable components, without compromising device functions or efficacy.

ABOUT THE COMPANY

Owen Mumford is a major healthcare company and device manufacturer that commercialises pioneering medical products in its own brand and custom device solutions for the world's major pharmaceutical and diagnostic companies. Owen Mumford's goal is to enhance access to diagnostics, encourage adherence to treatment and reduce healthcare costs, making a world of difference to a world of people.

BOX 2: OWEN MUMFORD & SUSTAINABLE DESIGN

"Device design considerations can have a large impact on the carbon footprint of therapies. Innovative approaches have been adopted by Owen Mumford Pharmaceutical Services to remove springs from our disposables; emissions related to the manufacture, processing and shipping of metals greatly exceed that of polymers due to the higher density and forming temperatures required. Furthermore, a reduction in the amount of single-use plastic associated to each treatment whilst maintaining safe and effective usability characteristics can be achieved with careful consideration at a design stage."

Toby Cowe
Technology Development Group Manager R&D, Owen Mumford

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ABOUT THE AUTHOR

George I'ons is currently Head of Product Strategy and Insights at Owen Mumford having worked for the former Original Equipment Manufacturer and now Pharmaceutical Services division of the organisation since 2006. His current focus is on deciphering the rapidly changing pharmaceutical and biotech sectors in relation to their needs for combination products. In his previous roles in business development he worked closely alongside R&D to develop devices for a variety of global pharmaceutical and diagnostic clients. Prior to Owen Mumford George worked for Abbott (Berkshire, UK) in EMEA marketing roles in Germany, focusing on its diabetes business.

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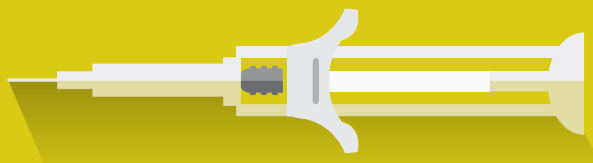

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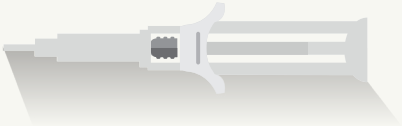

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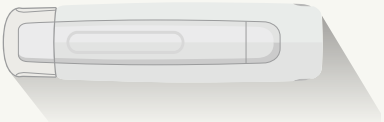
UniSafe® Auto-Injector
Simplifying reusable delivery



In development

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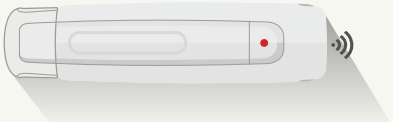

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ERIK HAEFFLER, RECIPHARM

Erik Haeffler is Vice-President Manufacturing Services & Head of Sustainability at Recipharm. He is responsible for the Group's sustainability work, as well as its focus on operational and commercial excellence. As part of his role, Mr Haefler is continuously developing a model for working with multi-site projects and is accountable for operations development across the company, including elements such as project management resources, corporate IS and project/product sourcing decisions.

In this interview, Mr Haeffler discusses how the pharma industry can balance optimising environmental sustainability with maintaining the highest safety and efficacy standard for achieving its main objective of promoting patient health and wellbeing.

Q Why is it important for pharma to be a sustainable industry? Surely healthcare is so important to people that pharma's environmental impact is secondary?

A Ultimately, the purpose of pharmaceuticals is to improve patient health and quality of life. The pharmaceutical industry is a responsible one, and this is particularly true when it comes to its environmental impact. The work our industry does is vital, but nonetheless these operations should be carried out in a responsible way to minimise any potential negative environmental impact. It's a balancing act but there are ways we can reduce the impact of operations and as an industry we are committed to exploring these options.

Q Looking at the big picture, what would you say are the most significant sources of major environmental impact that pharma can address to improve sustainability?

A Pharma has been working on environmental issues for a long time. The most significant impact on the environment comes from manufacturing pharmaceutical products on a commercial scale. Although systems and governmental regulations are well developed in Europe, the US and Japan, there are still ongoing problems in other markets, particularly in other areas of Asia, where pressure to manage damaging levels of pollution is not as concentrated.

One particular area of concern is the manufacturing of antibiotics since emissions of the antibiotic compounds can drive antimicrobial resistance. This means taking care of hazardous waste, sewage and emissions remains absolutely critical for the industry. Another area that seems to get less attention is what happens to medicines that have expired or are no longer in high demand. From an environmental perspective, it is important that these unused drugs do not follow the same routes of normal household waste. This is something that could potentially be improved in many parts of the world. It's important that authorities and governments support the industry in developing processes to help resolve this.

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Q A pharma company whose drug delivery partners and CDMOs offer sustainable products, technologies and services will produce more sustainable end products. Where can drug delivery partners and CDMOs offer that increased sustainability?

A This is something which needs to be carefully balanced. It is important to make sure we do not compromise on the medical efficacy of an end product by altering the way it has been manufactured. That being said, manufacturers should always strive to reduce any environmental impact throughout the manufacturing process and the supply chain, where possible.

Co-operation between manufacturers of end products and the original suppliers of materials is constantly developing. With this in mind, it is becoming increasingly popular for the industry to apply a "Supplier Code of Conduct" to a product, to set the boundaries and expectations regarding any sustainability matters.

When it comes to the technical aspects of pharmaceutical production, a lot of focus is being placed on scale and improving the efficiency in manufacturing processes. Improving yields from the processes means there will be less waste, and by optimising scale of production, the overall environmental impact can be reduced significantly.

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optimising scale of production, the overall environmental impact can be reduced significantly. Replacing hazardous materials is also important – new technologies for wastewater treatment and filtering of solvent emissions are constantly emerging making the processes much cleaner. In addition, supply-chain practices, such as reducing the number of suppliers involved in the production of a product, are providing opportunities for reducing transportation, which is beneficial when it comes to reducing the industry's impact on the environment.

Q Where do you think the driving forces for improving sustainability are coming from?

A Currently, the driving force for exploring greener processes is primarily coming from within the industry itself. This is a direct result of the global focus on improving sustainability, with both governmental regulations and the procurement standards from payors adding pressure for sustainability concerns to be a priority. So far, the attention from patients and healthcare professionals is limited, however this is likely to increase over the coming years.

Q Can you envisage a time where patient or healthcare professional treatment preferences could be influenced by how sustainable one option is compared to another? i.e. could sustainability be a product differentiator in competitive markets?

A Ultimately medical efficacy should be the top priority and vital medications need to remain readily available. However, there may be a situation where sustainability could be the deciding factor between two brands. In addition, there has been discussion around potentially introducing payment systems designed to give benefits to companies that can clearly show advantages from a sustainability point of view, and it is likely this will be explored further in the future.

Q In addition to regulating to enforce sustainable practices, what role can regulators play in adapting or even relaxing some regulation to enable more sustainable approaches?

A It is important that we don't start to mix assessments of safety and medical efficacy with sustainability aspects. Sustainability is vital for pharmaceuticals, but it should not be part of the medical assessment of a product. Patient safety and effective treatment needs to remain our top priority.

ABOUT THE COMPANY

Recipharm is a CDMO headquartered in Stockholm, Sweden with development and manufacturing facilities in France, Germany, India, Israel, Italy, Portugal, Spain, Sweden, the UK and the US. The company continues to grow and expand its offering for customers. Employing around 5,000 people, it is focused on supporting pharma companies with its full-service offering, taking products from early development through to commercial production. For more than 20 years, it has provided pharma expertise and managed complexity for its clients throughout the entire product lifecycle.

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