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DRUG DELIVERY & ENVIRONMENTAL SUSTAINABILITY

This edition is one in the ONdrugDelivery series of publications. 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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ROUNDTABLE: ALLIANCE TO ZERO

In this Roundtable discussion, Sebastian Gerner, Robert O'Beirn and Sabrina Gérard talk with ONdrugDelivery about the Alliance to Zero, an association for pharma and biotech supply chain companies that aims to facilitate the transition of the pharma sector to compliance with net-zero emissions.

SEBASTIAN GERNER

Alliance to Zero | YPSOMED SELFCARE SOLUTIONS

Sebastian Gerner is President of the Alliance to Zero, and 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. Mr Gerner is a mechanical engineer with more than 10 years of medical device experience in various medical and pharmaceutical companies.

ROBERT O'BEIRN

Alliance to Zero | Sharp

Robert O'Beirn is Vice-President of the Alliance to Zero, and Head of Sharp's Clinical Services and European Packaging businesses. He originally joined UDG Healthcare in 2011 as senior legal counsel and subsequently moved to corporate development, with particular focus on M&A. As a member of Sharp's senior leadership team, he also acts as Executive Sponsor of Sharp's environmental, social and governance (ESG) and sustainability programmes.

SABRINA GÉRARD

Alliance to Zero | DATWYLER

Sabrina Gérard is a Committee Member of the Alliance to Zero, and Head of Sustainability & Agility at Datwyler. She is a chemical engineer with more than 25 years of experience in lean & agile, sustainability and quality assurance. She has worked for fast-growing, global organisations in the automotive, medical device and healthcare industries. As Head of Sustainability at Datwyler she co-ordinates sustainability programmes together with employees, customers, and society.

Q What is the impact of the pharma industry on global CO_2 emissions?

SEBASTIAN

The pharmaceutical industry accounts for as much as 10% of the carbon emissions in America and 5% on a global level. That means pharmaceutical companies emit significantly more carbon emissions than the automotive manufacturing sector.[1]

Although the delivery device *per se* may not be the main driver of carbon emissions, it is the material representation of waste. It is what ends up in the hands of the patient. Drug delivery devices and primary packaging materials also account for a proportion of the CO_2 emissions of combination products based on their packaging design. So improving the design of the individual components, as well as providing environmentally friendlier packaging, will improve the footprint of the overall combination product.

ROBERT

A recent *Pharmaceutical Manufacturing* article reported industry surveys conducted in 2020 that indicated 48% of biopharma manufacturers always look for packaging that is recyclable or that can easily enter the waste stream, with 81% being likely to use energy-efficient packaging soon.[2] This reflects a rapid and significant shift in thinking by biopharma companies.

Q Please tell us how the Alliance to Zero came into being, which organisations are involved, how is it funded, and what are its overarching goals?

SEBASTIAN

The ambition of the Alliance to Zero is to enable the transition of the pharmaceutical industry to compliance with net zero goals, by launching a net-zero carbon emissions product. This jointly developed net-zero product offering will be available by 2030, with interim milestones in 2023 and 2026 (see Figure 1).

> "The Alliance to Zero was founded by eight companies along the value chain of injectable products and our main focus is on the primary and secondary packaging of the physical device."

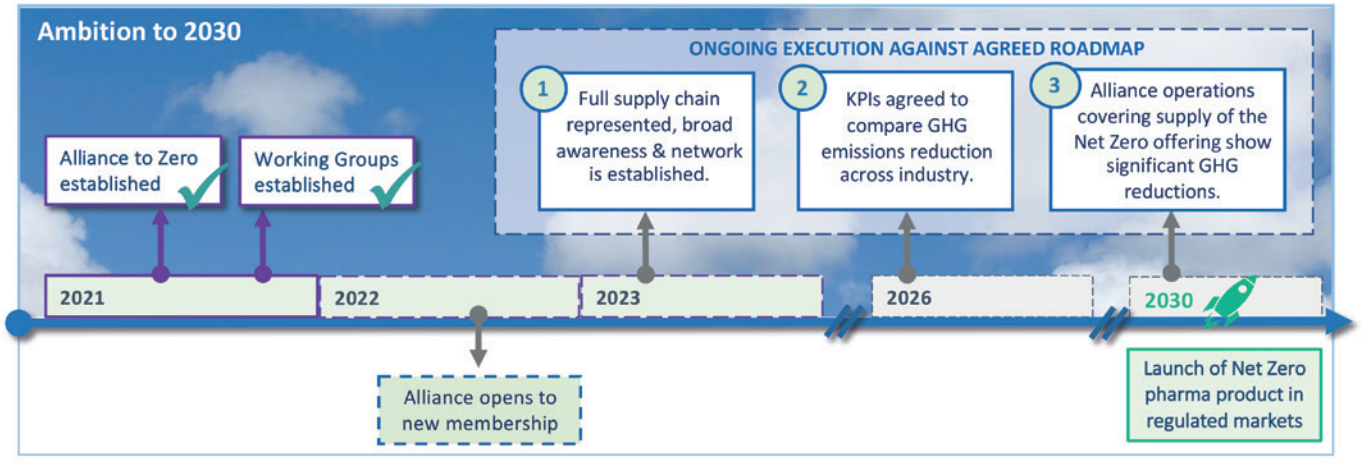

Figure 1: Timeline of the Alliance to Zero's ambition to 2030.

Therefore, at the Alliance to Zero, we are developing guidelines, creating a common language and defining measures which we can apply on footprint-reduction efforts of our collective products and services.

The Alliance to Zero was founded by eight companies (see Table 1) along the value chain of injectable products and our main focus is on the primary and secondary packaging of the physical device. So all company members are currently active in this field and provide respective product and service offerings to their pharma clients.

Each member company pays an annual membership fee, depending on its size, which is being used to sponsor projects with a common interest in order to deliver our shared vision. In particular, partnerships with academia are being established to support the common goal.

Company	Role Within the Supply Chain
SCHOTT glass made of ideas	Primary containers
DATWYLER	Container closure components
YPSOMED SELFCARE SOLUTIONS	Autoinjectors
Harro Höfliger	Assembly solutions
schreiner MediPharm	Labelling solutions
KÖRBER	Packaging machinery
Sharp	Assembly and packaging Services
HEALTHBEACON	Smart sharps containers

Table 1: Alliance to Zero founding companies.

Q How is net zero defined by the Alliance? How might a member's net zero status be certified or validated?

SEBASTIAN

Net-zero emissions is a very new term and a common understanding of net zero is to be established. The Alliance is closely following the leaders in the field such as the Science Based Targets Initiative (SBTi),[3] which is currently developing the standard for net-zero emissions. The SBTi is a partnership between CDP Worldwide (previously the Carbon Disclosure Project), the UN Global Compact, World Resources Institute (WRI) and the World Wide Fund for Nature (WWF).

Net zero describes a target of completely negating the amount of greenhouse gases (GHGs) produced by human activity, to

"Each of the member of the Alliance can attest to the increasing number of requests from clients and partners for metrics and reporting on environmental KPIs."

be achieved by reducing emissions and implementing methods of absorbing carbon dioxide from the atmosphere. From that newly established standard we will then derive specific measures for the Alliance and define KPIs which all our member companies will be expected to commit to.

Q Thinking about your company in particular, where does your organisation fit in the overall supply chain, and where are the main areas where CO_2 can be reduced?

ROBERT

Sharp offers contract commercial and clinical packaging services that include device assembly, secondary packaging, labelling, serialisation, storage and distribution so we operate at the centre of the pharma supply chain. Our clients would specify the device and packaging formats as well as materials and components. Our area of influence in terms of GHG reductions would be in the procurement of packaging materials and the management of our energy and GHG emissions across our production facility network. Sharp has made significant progress in scope 1 and 2 emission reduction, but we are at the early stages of developing a roadmap to significant reductions in our scope 3 emissions. *(See Box 1, Glossary of Definitions (next page) for more information about scope 1, 2 and 3 emissions.)*

SABRINA

Datwyler's main initiative is to become completely climate neutral for its own operations (scope 1 and 2) by 2030. Beginning with emissions of approximately 80,000 tons of CO_2eq in 2020, Datwyler is following the reduction path defined by the SBTi, which includes implementing measures to purchase renewable energy and increase energy efficiency. These actions are intended to reduce GHG emissions drastically, while simultaneously achieving forecasted business growth.

In 2021, some 40% of Datwyler's total electricity consumption at all plants worldwide will be from renewable energy sources. In Switzerland, the company already has a plant that has been producing CO_2-neutral since 2012. Datwyler has also started a project to identify and quantify scope 3 emissions, to develop measures for further reduction.

SEBASTIAN

Ypsomed has committed to achieve net-zero emissions in operations (scope 1 and 2) latest by 2030 and net-zero emissions for the entire company (scope 1–3) by 2040. Ypsomed has handed in a letter of commitment to SBTi and is currently developing the reduction pathway to the individual net zero points.

Our corporate carbon footprint, calculated for the first time in 2019, has shown that our own GHG emissions from heat and electricity consumption (scope 1 and 2) amount to just 3% of total emissions. However, 97% of the CO_2 emissions come from the upstream and downstream value chain (scope 3). The largest share is accounted for by purchased materials (in particular plastic granulate and transport containers). Therefore, it is crucial for us to work with our partners to tackle emissions where they occur.

The realisation that the materials we procure create the largest share of our carbon footprint inspired the development of the YpsoMate® Zero, launched in 2020. The YpsoMate autoinjector platform will be switched to biopolymers and the packaging design will be adapted in order to reduce emissions. The remaining emissions will be compensated with carbon removal certificates in order to offer a true first net-zero product offering. Other product platforms will follow and so contribute to the corporate carbon emission reduction pathway Ypsomed has taken.

Q What are the ways in which your Alliance to Zero members' clients and partners will benefit from you achieving net zero status?

ROBERT

Each of the members of the Alliance can attest to the increasing number of requests from clients and partners for metrics and reporting on environmental key performance indicators (KPIs). As part of the selection criteria for the awarding of new business, for example, Sharp is consistently requested to show evidence of energy rating standards at our facilities, as well as the quantification models we use to calculate our sustainability impact. Clients also want to understand how we integrate sustainability into both our governance and operational practices.

The most challenging aspect of the GHG emissions protocol is scope 3, which includes all indirect (non-energy related) emissions that occur in a company's value chain. The interdependent nature of the value chain means that the way we as suppliers manage our own GHG emissions will have an important impact on our client's ability to reach their scope 3 goals. Each member company of the Alliance has committed to delivering on a roadmap that will significantly reduce their GHG emissions, thereby making it easier for our pharma clients to achieve their scope 3 commitments. Clients will also benefit directly from the work of the Alliance to Zero as we ultimately progress towards making a net-zero product available to the industry.

> "The interdependent nature of the value chain means that the way we as suppliers manage our own GHG emissions will have an important impact on our client's ability to reach their scope 3 goals."

SABRINA

In an evolving pharmaceutical sector, achieving more sustainable outcomes can be difficult, especially for manufacturers who must cater to a more diverse marketplace. More than ever, the industry and patients require that the pharma sector make strides toward sustainability.

Among its own clientele, Datwyler has seen companies increasingly inquire about sustainability initiatives and ways in which they can make their overall supply chain more environmentally responsible. While more packaging suppliers of critical drug delivery components are making efforts to improve the sustainability of their supply chain, not many have made as many strides or as ambitious goals as Datwyler.

Clients can benefit from Datwyler's efforts knowing that the company can support them in their sustainable goals whether it be through resource-friendly production, ecodesign principles or via net-zero status. While some pharma companies have just begun inquiring about making their supply chains more sustainable, Datwyler is prepared to help them as the industry continues to move in this direction.

"Analysing platform by platform, we will have a net-zero product offering on all our products available in the near future. This will then directly reduce our customers' scope 3 emissions as they can source a product with net-zero emissions."

SEBASTIAN

Our customers are requesting carbon footprint data from Ypsomed on a product level and we are prepared to deliver on this. Furthermore not only calculating our product carbon footprints, but with the Zero Program we have a strong reduction program established. Analysing platform by platform, we will have a net-zero product offering on all our products available in the near future. This will then directly reduce our customers' scope 3 emissions as they can source a product with net-zero emissions.

Q The Alliance was only founded a few months ago. Can you talk about how it was initiated?

SEBASTIAN

Establishing the Alliance to Zero in a virtual setting (due to the covid-19 restrictions) presented a number of challenges, including the legal framework for registering the association in Switzerland, as well as starting our work without being able to meet in-person. However, in October 2021 we held our first in-person workshop, which included external input with speakers from industry. We also formed our individual working groups, to develop the key pillars of our framework including:

- Language & methodology
- Sustainable procurement
- End of life
- Machinery & processes.

These working groups are developing guidelines for each topic area, with the aim of applying them within each member company.

BOX 1: GLOSSARY OF DEFINITIONS

Climate Neutral:
Climate neutrality combines an organisation's need to account for their GHG footprint and establish a clear reduction strategy before offsetting unavoidable emissions. For companies, climate neutrality is a "point in time" statement, where historical carbon emissions are measured and offset. Compared with carbon neutrality, climate neutrality places more of an emphasis on covering all GHGs beyond carbon, and includes climate impacts beyond GHG emissions, such as radiative forcing from aircraft – often used to calculate emissions from business travel.

Climate Positive:
Climate positive, or "carbon negative", both describe a state of removing more GHGs than one emits.

Greenhouse gas (GHG):
In 1896, Swedish scientist Svante Arrhenius was the first person to investigate the greenhouse gas effect, i.e. the ability of CO_2 to trap heat in the atmosphere. Arrhenius won the 1903 Nobel Prize for Chemistry. A GHG is any gas that exhibits the greenhouse gas effect. In addition to CO_2, examples of other GHGs are methane(CH_4), nitrous oxide (N_2O), chlorofluorocarbons (CFC), and hydrofluorocarbons (HFCs) including hydrofluoroalkanes (HFAs).

Gold Standard:
Established by WWF, the Gold Standard is endorsed by more than 80 non-government organisations (NGOs). UN agencies use the Gold Standard for the development of their own carbon mitigation and sustainable development projects. The Gold Standard is now also certifying sustainable development goals.

Net Zero:
The Intergovernmental Panel on Climate Change (IPCC) defines net zero as a state where there are no incremental additions of GHGs into the atmosphere. This means that all avoidable emissions have been reduced and residual emissions have also been removed from the atmosphere. To achieve this, an organisation must:

- Reduce: plan a trajectory to reduce emissions across the entire value chain. Set a net zero target year based on science, with interim milestones on how to get there, all consistent with a 1.5 °C mitigation pathway.
- Compensate: become climate neutral by financing projects to avoid and remove emissions further
- Neutralise: once emissions have reduced to close to zero levels, eradicate unavoidable residual emissions with carbon removals to achieve net zero.

Remaining Emissions:
Unavoidable emissions which will remain after reduction efforts.

Removed Emissions:
Emissions that are removed from the atmosphere by supporting certified carbon removal projects (natural or technical solutions), such as reforestation.

Scope 1 Emissions:
Emissions from sources directly owned or operated by a specific company. For example, if a company has a fleet of vehicles that burn fossil fuel, or buildings with boilers, their emissions are scope 1.

Scope 2 Emissions:
Emissions based on energy a company purchases to operate its enterprise directly. The most common across-the-board source of a scope 2 emission is electricity consumption.

Scope 3 Emissions:
Emissions resulting from activities not directly owned by a business, but are associated with its operation. Examples include business travel, waste management, commuting, and third-party distribution.

Verified Carbon Standard (VCS):
This standard developed and administered by Verra (Washington, DC, US) is the world's most widely used voluntary GHG reduction programme.

Definitions sourced from the web site of sustainability consultant South Pole (Zurich, Switzerland). www.southpole.com

Q What are the benefits to stakeholders of the Alliance to Zero? What is the offering?

SABRINA

Ultimately, there are many parties involved in the development of a single drug to ensure that it reaches patients in a sterile, secure condition up to and throughout point-of-use. The industry and stakeholders benefit from an initiative like Alliance to Zero because it will help to create a more circular economy that promotes greater lifecycle awareness on a global scale. With more companies taking responsibility for environmental and social conditions, in addition to meeting the increasing demand for sustainability, initiatives like Alliance to Zero resonate with the future workforce. More importantly, this initiative helps to secure the environment for current and future generations to come.

ROBERT

The alliance is intended to benefit our mutual pharma clients. Through this proactive collaboration between supply chain partners we are reducing the logistical burden for those pharma companies who want to reduce their scope 3 emissions.

In the immediate term, the alliance is working to establish and validate the framework within which to achieve our net zero ambition. By mid-2022, we expect to welcome new member organisations to join the association, representing the value chain, in order to broaden our reach and help accelerate our progress to net zero.

"The Alliance is intended to benefit our mutual pharma clients. Through this proactive collaboration between supply chain partners we are reducing the logistical burden for those pharma companies who want to reduce their scope 3 emissions."

ABOUT THE ALLIANCE

Alliance to Zero is a non-profit membership association for pharma and biotech supply chain companies that aims to facilitate the transition of the pharma sector to compliance with net-zero emissions. As a working group with commonly shared goals, it engages in collaboration with academia and non-profit organisations as well as sponsoring projects. It involves, connects and co-ordinates suppliers, pharmaceutical companies, manufacturers and service providers along the supply chain of pharma products. After sharpening its vision and launching initial initiatives, Alliance to Zero will welcome new members along the value chain by mid-2022 to expand its reach and drive long-term success.

The Alliance to Zero manifesto can be viewed online here: *alliancetozero.com/manifesto*

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Alliance to Zero

Enabling Net Zero Pharma Products

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SUSTAINABILITY, WASTE & REMANUFACTURING IN THE MEDICAL SECTOR

Here, Cormac O'Prey, Principal at Kestrel Technology Consulting, discusses some of the sustainability challenges facing the medical sector, such as how to make re-use and remanufacturing viable for high-volume, low-value products, and how answers can be found by looking to successful solutions deployed by other industries.

INTRODUCTION

"Sustainability", "recycling" and "re-use" are not new ideas. Many people can still remember returning lemonade bottles for 10p apiece and putting out empty milk bottles for the milkman to collect. Some still do. So what happened? When did "use and return" become "chuck and forget"? More importantly – how do we change back? And why should we? Can we combine forgotten 20th century wisdom with 21st century circular economy innovation to stem the tide of rubbish that is clogging rivers and seas around the world? And what about us in the medical industry, and specifically drug delivery? What can we do to respond to growing public, government, patient and healthcare provider demands that we clean up our act? And how can we do it while controlling risk, without compromising safety standards and, crucially, while maintaining a profitable business?

With COP26 taking place as this article is published, there has never been more pressure on industry to reduce its environmental impact. Historically, with the priority on minimising patient risk, the healthcare sector has been considered exempt from sustainability demands. However, there is strong evidence now that healthcare is, in fact, a major contributor to global pollution and rising CO_2 levels. If ranked alongside countries, the healthcare industry would be be the fifth-largest emitter on the planet,[1] so that supposed exemption no longer holds true.

With the implementation of net zero CO_2 targets set for 2030,[2] major healthcare providers and suppliers are now taking sustainability very seriously. As UK NHS Chief Executive Sir Simon Stevens said, "While the NHS is already a world leader in sustainability, as the biggest employer in this country, comprising nearly a tenth of the UK economy, we're both part of the problem and part of the solution."

> Healthcare contributes 4–5% of all global greenhouse gas emissions, with inhalers comprising a significant portion of that."

Achieving "sustainability" in the medical sector generally covers reducing plastic product and packaging waste, CO_2 and CO_2 equivalent (CO_2E) emissions, and energy and water usage. Healthcare contributes 4–5% of all global greenhouse gas emissions, with inhalers comprising a significant portion of that – inhalers account for 3–3.5% of the NHS's carbon footprint[3] and 28% of GSK's CO_2E emissions (amounting to 8.4 MT) come from pressurised metered dose inhaler (pMDI) cannister propellants alone. As such, prioritising alternative, lower global warming potential (GWP) propellants makes sense, and progress towards this goal is being made. By volume, the GWP of current propellants is equivalent to over 3,000 units of CO_2, whereas some proposed alternatives are equivalent to less than one unit.

Changing the industry's preferred inhaler propellant will not affect product and packaging waste, however. Device manufacturers can also reduce their environmental impact by adopting sustainable design and manufacture. According to the United Nations, an 80% reduction in CO_2E emissions is achievable by adopting sustainable manufacture.[4] Although waste from devices and packaging is a lesser contributor to CO_2E emissions, they still represent a significant problem and this is the challenge we will focus on in this article.

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"Device design is intimately linked with sustainable manufacturing and reprocessing, with the product design requirements needing to reflect how a product will be managed at the end of its life."

SUSTAINABLE DESIGN AND MANUFACTURE

What is "sustainability" and how do device manufacturers achieve it? With the massive growth in interest in sustainability, variations in terminology have arisen, leading to misunderstandings and confusion. For example, "remanufacture" of single-use devices (SUDs) means very different things according to US FDA Guidance for Industry[5] and the EU Medical Device Regulation (MDR).[6]

According to the World Commission on Sustainability, "Sustainable development seeks to meet the needs and aspirations of the present without compromising those of the future." Sustainability in the context of drug delivery devices can be broadly divided into two disciplines – sustainable product design and sustainable manufacture – where CO_2E and environmentally damaging material waste is minimised. Device design is intimately linked with sustainable manufacturing and reprocessing, with the product design requirements needing to reflect how a product will be managed at the end of its life. To achieve a stable sustainable device manufacturing strategy in the long term, these elements must work in harmony, ideally offering a solid business incentive to manufacturers. Looking at successful examples of sustainable design and manufacture readily shows that a sustainable business case is just as important as a sustainable device design for long-term viability.

To develop and disseminate sustainable strategies, and to try and add some consistency and consensus, the British Standards Institution (BSI) and the International Standards Organisation (ISO) have led the way on how sustainability can be generally implemented in product design and manufacture. The BS8887 series of standards, including "BS/ISO 8887-2: Design for Manufacture, Assembly, Disassembly and End-of-Life Processing (MADE) Terms and Definitions",[7] suggests a framework and a set of standard terms to describe the relevant processes.

The framework suggests a range of alternative – but not mutually exclusive – routes for products and components that have reached the end of their useful lives based on their "residual values". At the top, products that are suitable for remanufacture represent the ideal for sustainability – a product that can be recovered with the maximum residual value intact and returned to the market in as-good-as-new condition at the original retail cost with warranties and at minimum cost to the manufacturer. For example, manufacturers of medical imaging equipment regularly have a significant portion of the component inventory used in new machines coming from previously used versions – with corresponding savings on manufacturing cost and waste generation. Going down through the options in the framework represents progressively lower levels of recovered value and therefore lower economic incentives for manufacturers to commit to these strategies.

BACKGROUND AND DRIVERS FOR CHANGE

So, if most of the environmental damage from inhalers comes from propellant gasses, why are we concerned with waste from used devices? The simple answer is because, as with many other products in many other industries, throwing away large quantities of used medical products has become unacceptable. Inhaler use in the UK alone is set to double from 2006 levels of 35 million to 70 million by 2030. With this increase in inhaler use, governments, pressured by public opinion and environmental groups, are forcing manufacturers to reduce their environmental impact. This is increasingly leading to restrictions being placed on waste, with manufacturers being held accountable for their used products.

In the medical sector, clinicians are now considering the environmental impact of therapies in their prescribing decisions, and the NHS is making environmental performance a key requirement of suppliers, targeting a 50% reduction compared with 1990's waste levels by 2028. Furthermore, instances of patients showing reluctance towards using their inhalers because of the environmental impact have been reported, and social media campaigns have been started to force medical product manufacturers to take care of their used products (Figure 1).

On a more positive note, medical device requirements documented by the MDR, FDA and UK Medicines and Healthcare products Regulatory Agency now consider how devices can be re-used without compromising safety, and medical device regulators have been directed to help manufacturers find more sustainable solutions. The language has shifted from patient safety as the sole consideration to the need for manufacturers to balance such with environmental impact. In recent industry conferences, such as Respiratory Drug Delivery and Drug Delivery to the

Figure 1: A 2019 Facebook post shared 20,000 times.

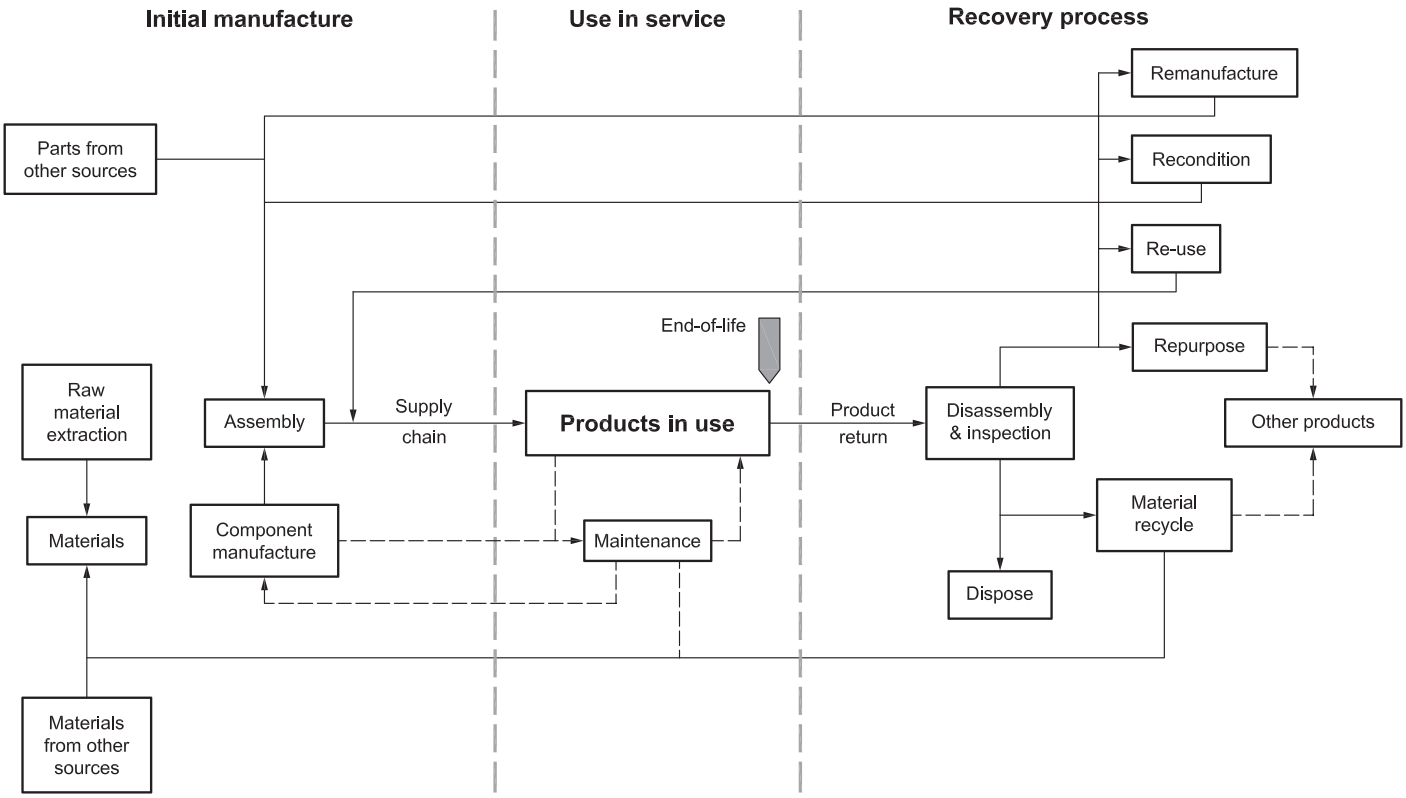

Figure 2: Cascade diagram shows decreasing residual value of used components from BS 8887-2:2009 standard (reproduced with kind permission from BSI).

Lungs, the topic of sustainability featured heavily, and collaborative working groups, such as the End-to-End Sustainable pMDI Forum sponsored by Aptar (IL, US) and Pharmaserve North West (Runcorn, UK), are being set up to find solutions.

The good news for medical product manufacturers is that many comparable solutions have already been established in other industries. Circular design and manufacture has been in use in the medical sector for decades – although more for financial benefit rather than environmental reasons. Indeed, the financial case for circular manufacturing may become more broadly relevant in the near future as the EU is due to publish the documentation for its green finance taxonomy in 2022, which aims to provide a framework for companies and public authorities to use "green bonds" to raise capital for large-scale sustainability investments.

High-value, low-volume medical imaging equipment remanufacturing has successfully recovered and re-used 80–90% of the components from previously used machines, including the "heavy iron" components such as magnets, motors and structural components that constitute much of the residual value. Indeed, anticipating re-use over many cycles, General Electric (MA, US) now specify these components with up to a 40-year design life. We can learn from this.

Manufacturers of low-value, high-volume medical products, such as surgical instruments, have tried to implement circular manufacturing, but have seen more mixed success, in some cases struggling to compete with third-party remanufacturers who can recover, clean, test and resell used devices at a lower cost than original equipment manufacturers (OEMs).[8] Partnerships between OEMs and third-party remanufacturers have been set up to play to the strengths of each partner, which is how some believe the industry will evolve. Outside the medical sector, manufacturers such as Nokia have pioneered designs that are optimised for multiple lifetimes, with parts likely to become worn or damaged being designed to be cheap and easy to replace. Another example is the chair manufacturer Orangebox, which designs its core components to be durable enough to last multiple lifetimes, with covers designed to be removed and replaced quickly using zip fasteners.

On the challenging aspect of how to manage "reverse logistics", where products are recovered and returned to the OEM for reprocessing, innovators in the medical sector have struggled with low device return rates, low yields of usable product, unpredictable recovery rates and components in poor condition. Reverse vending machine makers Tomra (Asker Municipality, Norway) have automated the process of recovering plastic drinks bottles and soda cans to reduce costs and have incentivised customers to return such waste.[9] Even recycling these low-value products now makes good business sense, and could be looked into as part of a potential solution in the medical sector.

WHAT DOES GOOD SUSTAINABLE MANUFACTURING PRACTICE LOOK LIKE?

Some drug delivery device manufacturers have operated recovery and recycling schemes in which inhalers are returned to pharmacies and separated into plastic and metal components. The aluminium in pMDI cans is recovered and plastic inhaler bodies are recycled as, amongst other things, benches and playground equipment. While such schemes reduced the number of devices going to landfill, Figure 2 shows how this sort of recycling offers little opportunity to recover much residual value and little in the way of financial return. With only a 0.3% return rate, GSK replaced its scheme with a more comprehensive approach in 2020.[10]

"Designing smart devices for multiple lifetimes and considering multiple remanufacturing cycles during the design phase could address the issue of affordability for healthcare providers."

This leads into the industry's present conundrum – the question of how to combine a sustainable device design that supports value recovery and minimises waste and CO_2 emissions with a practical and effective recovery and re-use strategy. We know what we want to do, but we haven't quite figured out how to do it.

Progress in device design is being made with DuPont (DE, US) researching materials suitable for extended lifetimes and H&T Presspart (Blackburn, UK) launching a new plasma coating process for pMDI cannisters to extend their lifespan (discussed in more detail by H&T Presspart in this issue, pp 57–60). The introduction of smart devices with their higher manufactured cost and their greater potential for environmental damage, due to their embedded electronics and batteries, is an interesting case and could stimulate the adoption of design for remanufacture and circular manufacturing models.

Designing smart devices for multiple lifetimes and considering multiple remanufacturing cycles during the design phase could address the issue of affordability for healthcare providers. If a device is too expensive to manufacture for a single three-month use cycle, amortising the cost over several lifetimes could reduce total cost of ownership to acceptable levels. Furthermore, if you can recover and remanufacture such a device efficiently, you have an opportunity to assess its condition and ensure that its performance over its next lifecycle will be satisfactory. By doing so, you can manage patient risk and get to sell the device again without the cost of having to make another one. There is also an opportunity to analyse a used device for issues, performing a valuable post-market surveillance function, and accessing embedded smart data could give valuable insights into patient population behaviour.

Clearly, when designing a device for multiple lifetimes, issues of robustness and degradation that do not apply to SUDs need to be considered. However, doing so does afford the opportunity to invest more in the design while still providing it at an affordable cost. Paradoxically, to reduce plastic waste you may need to make the design more robust by adding more plastic to its constituent components so that they last longer.

Examples of successful sustainable designs can be found in other industries, and the characteristics that make them work can be analysed and applied to medical devices. In device design, sustainability must be included in the requirements specification from day one in order to ensure that it drives the design development. Sustainability cannot be applied as an afterthought. Identifying the "core" of a device – the elements of the design that can be economically recovered with sufficient residual value and in good condition – is a key step.

Counterintuitively, existing designs may need to be split to separate the parts that can be re-used from those that cannot. For example, designing in sacrificial covers that protect valuable mechanisms but cannot be re-used themselves may make sense. Reasons for rejecting used components for remanufacture can include damage, wear, contamination, discoloration and even fashion. This may go against established design for manufacture and assembly (DFMA) principles and lead to an increase in part count but will reduce waste volumes overall, and of course, there are options, including biodegradable materials such as those supplied by Celanese (TX, US), to ensure that rejected parts do not contribute to plastic waste.

Adopting a modular design approach can be helpful in this respect, and can also provide some flexibility in updating design elements that have become obsolete. In this case, a "spiral" manufacturing model may be a better fit than a circular one, as market expectations are constantly changing such that remaking what was made yesterday may not be an option. Long-term stable designs are those where manufacturers can be confident that old parts will still be useful in the future. The Ellen MacArthur Foundation's (Cowes, UK) "Upstream Innovation – A Guide to Packaging Solutions" contains useful guidance on packaging design that could be useful in the medical sector.

Effective recovery and remanufacture is the other side of the equation and, just as in DFMA, needs to work in concert with the product design. So far, remanufacturing has largely been restricted to high-value, low-volume products because the process is largely slow and labour intensive. This is acceptable for multi-million dollar computed tomography (CT) scanners, but is unsuitable for mass-produced disposable drug delivery devices, such as inhalers or autoinjectors. To address this, research groups in Beijing (China) are investigating autonomous remanufacture to increase throughput and reduce costs, and the UK recycling industry now has advanced, high-speed waste recognition and sorting robots that are capable of recognising, picking, orientating and positioning up to 40 different types of device. Naturally, the design of devices must consider this, developing devices that can be dismantled without damage, maximising the recoverable yield, but that still prevent patients from accidentally taking their devices apart.

Medical device recycling schemes must also contend with historically low return rates. To tackle this, some companies have introduced reverse vending machines, such as those made by the aforementioned Tomra, which recognise returned products, inspect them, categorise them and reward users for returning them. Identifying individual devices is possible, helping to address the issue of traceability and reporting on what has been recovered before it goes further into the recovery process. Successful remanufacturing tends to feature a closed loop with customers so that rates of return and the age and condition of returned devices can be managed. This suggests that one-in-one-out strategies for devices, where replacements for prescription devices are

"A "spiral" manufacturing model may be a better fit than a circular one, as market expectations are constantly changing such that remaking what was made yesterday may not be an option."

issued on return of previously used ones, are ideal, but we must be realistic about likely return rates – patients lose, forget and damage devices and cannot be denied their medicine if they fail to return an old device. With environmental concern increasing among the public, participation in waste reduction schemes could be high if designed so that incentives are added and barriers to participation are removed.

Once recovered, remanufacturers need to determine how to re-use devices to meet regulatory demands for risk management and traceability while maximising yield and ensuring hygiene. There are established cleaning regimes, such as "AAMI TIR30:2011 (R2016) – A Compendium of Processes, Materials, Test Methods, and Acceptance Criteria for Cleaning Reusable Medical Devices", that can help.

FUTURE DEVELOPMENTS

There can be no doubt that there is still a lot of work to do in introducing sustainable design and manufacture in the medical sector, but neither can there be any doubt that it must be done. Manufacturers are understandably wary of changes to their operations that are as fundamentally disruptive as introducing sustainable manufacturing, and our industry is characteristically risk averse for very good reasons. Therefore, the question is how to introduce change at an acceptable rate and risk level, as well as doing so in such a way that the benefits can be demonstrated in limited trials to the entire organisation before fully committing to wholesale change.

Again, other industries can help by showing the way. Lifecycle analysis techniques can create a baseline against which change can be measured and improvements evaluated. This provides compelling, objective evidence of improvement, and successful trials in domestic kitchen products have shown a full return on investment after introducing remanufacturing inside one year. There are many organisations set up to provide support, including the Association of Medical Device Remanufacturers, the European Centre for Remanufacture, the Ellen MacArthur Foundation (who include AptarGroup among their members), the BSI, the ISO, the Nordic Centre for Sustainable Healthcare and the International Pharmaceutical Aerosol Consortium.

There is a developing international consensus, including collaboration between the ISO, the BSI and the Chinese national standards bodies. Furthermore, automated remanufacture of high-volume, low-value products, essential for reaching sustainability in medical products, is under development with UK Universities and research groups alongside groups in China – the 5th International Workshop on Autonomous Remanufacturing was held on October 16–17, 2021 at Beihang University, Beijing.

ABOUT THE COMPANY

Part of the Kestrel Consultancy Group, Kestrel Technology Consulting works with a range of UK-based and multinational client companies. The company builds deeply integrated working relationships, leading to exciting and innovative technology and product development projects. Kestrel Technology Consulting's areas of expertise include the medical (including drug delivery, surgical, home healthcare, ophthalmic, hospital equipment, emergency care and biotechnology), smart grid and metering, power distribution, switchgear, smart home, consumer and light industrial industry sectors.

ABOUT THE AUTHOR

Cormac O'Prey has been working in product development consultancy, including medical device development, in the Cambridge area since 2000. He currently runs Kestrel Technology Consulting, a company specialising in medical, healthcare, smart energy and sustainable product development. He is a long-standing member of the BSI committee for BS8887: Design for Manufacture Assembly, Disassembly and End of Life Processing.

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ON drugDELIVERY

2022 EDITORIAL CALENDAR

Publication Month	Issue Topic	Materials Deadline
January	Skin Drug Delivery: Dermal, Transdermal & Microneedles	Dec 9, 2021
February	Prefilled Syringes & Injection Devices	Jan 6, 2022
March	Ophthalmic Drug Delivery	Feb 3, 2022
April	Pulmonary & Nasal Drug Delivery	Mar 3, 2022
April/May	Drug Delivery & Environmental Sustainability	Mar 17, 2022
May	Delivering Injectables: Devices & Formulations	Apr 7, 2022
June	Connecting Drug Delivery	May 5, 2022
July	Novel Oral Delivery Systems	Jun 2, 2022
August	Industrialising Drug Delivery	Jul 7, 2022
September	Wearable Injectors	Aug 4, 2022
October	Prefilled Syringes & Injection Devices	Sep 1, 2022
Oct/Nov	Drug Delivery & Environmental Sustainability	Sep 15, 2022
November	Pulmonary & Nasal Drug Delivery	Oct 6, 2022
December	Connecting Drug Delivery	Nov 3, 2022

PHARMAPACK EUROPE DRUG DELIVERY AND PACKAGING ANNUAL SURVEY 2021

Here, Pharmapack presents the results of its annual survey and market report, covering the latest Pharmapack Innovation Index and the inaugural Pharmapack Sustainability Index, and taking stock of where the survey results suggest the pharma industry currently is, and where it is heading, in terms of innovation and sustainability.

This article was originally published as part of a market survey report by Pharmapack.

INTRODUCTION

Stimulated by the pandemic, innovation in the pharmaceutical industry has gone through a golden period of advancement and, as a result, the drug delivery and packaging markets have also seen a period of continual growth and innovation. Whether it be vials, autoinjectors, connected devices or the cold-chain storage of lifesaving covid-19 vaccines, the pharmaceutical packaging and delivery sectors have played a key role not just in fighting the pandemic but in more generally transforming the way we deliver and take medicines.

With a rise in the rate of chronic diseases and a significant number of vaccine doses being manufactured for covid-19, it is anticipated that there will be an increased demand for primary packaging, and for glass containers in particular. In fact, according to Allied Market Research, the glass segment is estimated to register the highest compound annual growth rate (CAGR), 8.5%, between 2020 and 2027.[1]

More broadly, there have been a raft of changes across the pharmaceutical drug device delivery and packaging sector in the past few years, with a continued drive by drug delivery device and packaging manufacturers towards patient-centricity. The aim being to improve the patient experience, and also to increase patient compliance and reduce attrition rates. Yet, with the proliferation of smart packaging and devices, these goals have often worked against the industry's other main trend – improving sustainability. Answering the concerns around the rising amount of non-degradable plastic waste, drug delivery device and packaging companies have sought out greener, more sustainable solutions including the use of bioplastics and blister packaging.

This article will dive deeper into these juxtapositions, evaluate the changing perception of innovation in the drug delivery device sector, and explore how far along each country is in terms of optimising the sustainability of pharma devices and medicines. Looking further ahead, we will discuss insights into which areas of drug delivery device development will see the greatest innovation over the next five years, as well as postulate what will be the most used primary oral dosage packaging.

METHODOLOGY

The report's key metric, the Pharmapack Innovation Index (Box 1), saw over 350 companies score the most innovative countries, with a further 50+ companies supporting a deep-dive analysis into the pharmaceutical drug delivery device and packaging sector as whole. Not only do the results provide key indicators of the overall strength of the industry but they also deliver insights into the

BOX 1: PHARMAPACK INDEX RESULTS AT A GLANCE

Pharmapack Innovation Index

India has seen the fastest (12%) rise in innovation while the US has extended its lead over Europe, where Germany has retaken the regional top spot from Switzerland.

Pharmapack Sustainability Index

Europe is leading on pharma packaging and device sustainability, well ahead of the US.

Pharmapack Europe

www.pharmapackeurope.com

areas that have seen the biggest year-on-year percentage rise. In total, executives from five continents – including all of the major pharmaceutical markets – provided responses, giving a diverse global perspective on the drug delivery and packaging market.

RESULTS

The report's key metric, the "Drug Delivery Innovation Index" – scored out of ten (Figure 1) – is designed to assess the perceived strength of each market's innovativeness, with the overall market perception rising by 1.81% year-on-year. This suggests, as many people would expect during the pandemic, that the last year has been a very productive time for the industry in terms of new ideas, delivery mechanisms and devices.

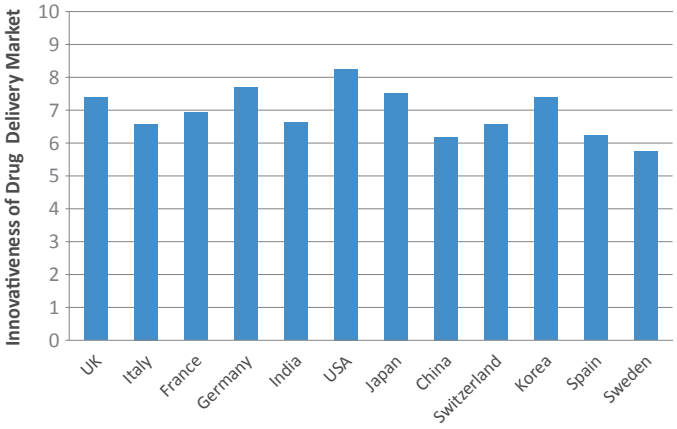

Figure 1: Drug Delivery Innovation Index 2021 (scores by country out of 10).

The US has remained unchanged at the head of the pack, maintaining its position as the world's most innovative country in the drug delivery field, with a score of 8.26. The other tier one markets, Germany (7.69) and Japan (7.52) – 2020's second and third placed economies – have both seen a slight year-on-year score increase. The UK (7.39) has moved narrowly ahead of last year's pre-eminent European market, Switzerland (7.38) – which has, surprisingly, fallen back. In fact, the UK has seen a flurry of innovative drug delivery device announcements in the last 12 months, including the much publicised and discussed acquisition of UK asthma inhaler company, Vectura – which is reportedly set to be acquired by Philip Morris (NY, US) after a number of prominent offers, including one from the private equity house The Carlyle Group (WA, US).[2]

However, by far the biggest surge came from India (6.62) – a country that had already seen a massive 25% increase in 2020 – with a year-on-year increase of around 13%. Consequently, India has moved ahead of China (6.18), Spain (6.23), Korea (6.57) and Italy (6.58) to firmly consolidate itself in the third tier of the most innovative nations. While India's rise will seem surprising to some, the country has shown significant interest in the drug delivery industry, and this is none more so reflected than by the world's first DNA vaccine, ZyCoV-D (Cadila Healthcare, Gujarat, India). While the vaccine is itself a world first, the delivery mechanism is equally novel – subcutaneous administration using a needle-free device pressed against the skin.[3] India's ongoing rise could also signal wider changes ahead, as the emerging nations begin to compete on innovation as well as cost (Box 2).

BOX 2: EXPERT PERSPECTIVE ON INNOVATION IN CHINA AND INDIA

"There has indeed been a lot of activity and interest from Indian and Chinese organisations focused on developing lookalike models of existing European or US devices, including dry powder inhalers and soft mist inhalers. Such developments could well morph into completely new devices, although it is common to see new inhaler technologies developed for a specific formulation at the behest of a pharma company. Any trend in innovations will likely also be influenced by new formulations or APIs.

As for pen injectors or autoinjectors, there may be greater scope for a device suitable to a range of drug types or formulations that can be licensed to a pharma company, and hence there may be more scope for device innovation in these areas."

Andy Fry
Founder, Team Consulting

More broadly, the back-to-back double-digit improvements in its Drug Delivery Innovation Index score indicate positive sentiments towards the developments in manufacturing and biosimilars, as well as the rise of new biotech targets that are permeating through the market into drug delivery and devices innovation. Another major driver in India's significant development within the space is the introduction of R&D initiatives such as "Start Up India'" and "Make In India", with foreign direct investment and manufacturing sites increasing significantly during the pandemic.[4]

WHAT DOES THE OVERALL SCORE TELL US ABOUT THE DIRECTION THE INDUSTRY IS HEADING?

The reputations of most markets displayed a healthy increase, perhaps reflective of the new confidence and positivity around pharma post-pandemic, and the overall index has risen 6% since 2019, which bodes extremely well for the industry. The direct impact of the pandemic has had consequences for the supply chain, especially early on, but covid-19 has also generated a plethora of opportunities across the industry.

One particular beneficiary has been digital applications and connected devices, which have seen rapid growth over the course of the pandemic. To list just a few, many countries have launched track-and-trace schemes, vaccine passports, virtual appointments and rapidly scaled up self-administrated therapies, with even the apps themselves now receiving US FDA approval. Many experts have identified apps as a potential new paradigm for mental health treatments.[5]

BOX 3: EXPERT PERSPECTIVE ON BIOSIMILARS IN EUROPE

"There are more biosimilar products in Europe than in any other market. Here you have a much stronger instinct across the health sector to adopt biosimilars to reduce the costs of treatment. However, what we are also seeing is that the numbers of biologics that are offered with devices is increasing. This is something that we have to expect and it is a positive development for injectable devices."

Dr Charbel Tengroth
Managing Director, Tengroth Consulting

In Europe, the size of the drug delivery device industry was circa US$340 million (£248 million) in 2021,[6] and the market is expected to grow by a CAGR of 5.9% until 2026, reaching $452 million. This is driven by a multitude of factors, including the prevalence of chronic diseases, increasing therapeutic options and the growth in the biologics and biosimilars market (Box 3). In particular, as a consequence of rising numbers of cancer, diabetes and respiratory patients across Europe, there is now a huge number that will require regular use of drug delivery devices for diagnosis and treatment purposes.

Another trend that is accelerating post-pandemic is the trend towards self-administration. One only needs to look at the effects of overburdened hospitals during the pandemic to see the benefits this could bring in both the long and short terms. It is perhaps unsurprising that – with an increasing number of patients now using injectable devices that can be also monitored in a home setting – the market for wearable injectors capable of delivering high-volume biologics, which are another area of recent innovation, is set to grow by $4 billion over the next three years.[7]

Understandably, the usability of devices has become a critical part of innovative medicines, with a shift in how companies are conducting R&D. Patient experience teams and real-world usability studies are now expected and no longer considered optional. The Pharmapack survey findings support this trend, with 78% of respondents stating that, with an increasing number of patients self-administrating drug therapies, "patient-centricity" is the most important factor in device design, particularly in terms of the need to "optimise safety and efficacy while minimising potential user errors".

In fact, 87% of respondents cited "patient adherence and ease of administration" as the primary consideration when manufacturing patient-centric devices (Figure 2). Other key considerations highlighted included the "size and portability of the device" (65%), "decreasing the number of dosing events" (43%) and "limiting the need for patient training" (26%). One other important consideration highlighted by industry respondents was to minimise or eliminate any pain involved in administering an effective dose – consequentially, Pharmapack's experts predict that patients will increasingly wish to switch to needle-free, painless injectable forms that are easy to use and disposable (particularly new patients).

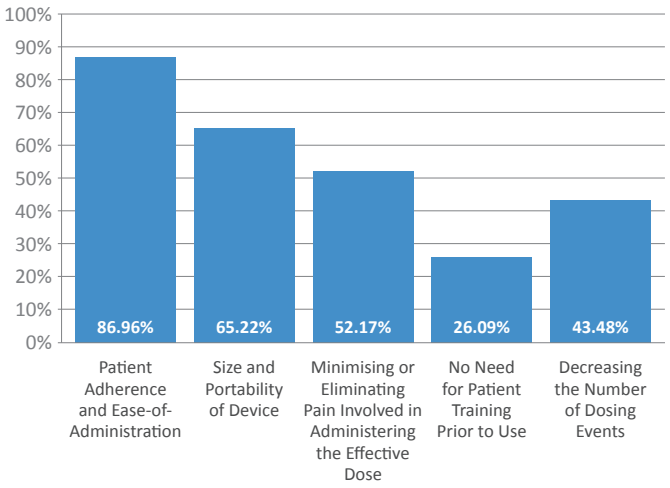

Figure 2: What are the main considerations when manufacturing patient-centric devices?

More widely, patient adherence has been an issue for many years, costing healthcare systems a significant amount across all chronic disease states. Therefore, is expected that a rise in the use of painless delivery (60%) will continue, with survey respondents identifying smart-dose injectors – those that can that confirm adherence – as the delivery form most likely to see double-digit annual growth in the next calendar year (Figure 3). Wearable injectors were also selected by half of the respondents as a device that will see double-digit growth, with drug patches (45%), smart dry powder inhalers (40%) and multidose delivery injection caps (40%) following. Significantly, the respondents reported strong percentages across all device types, which is perhaps a positive reflection of the likelihood of very strong growth in the next few years for all devices.

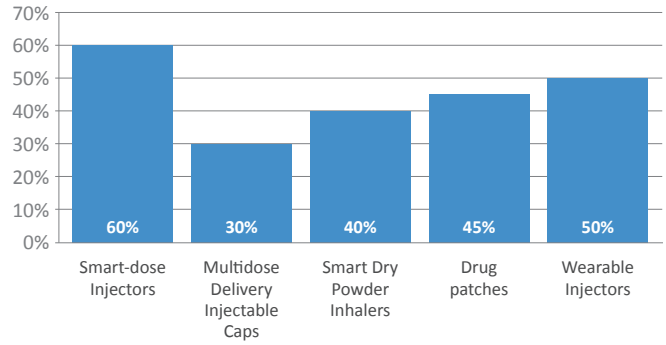

Figure 3: Which delivery form has the greatest potential for double-digit growth in 2022?

The case for smart devices continues to grow as, in addition to improved adherence, they offer the possibility for evaluation over a longer duration of time and not just in controlled hospital settings. Collecting real-time data empowers industry with data on real-world effectiveness against clinical efficacy. However, their use – primarily due to the high cost of introduction – will likely be limited to innovative medicines; they are, for example, unlikely to gain significant traction among biosimilars developers (Box 4).

CHALLENGES THAT COULD SLOW ADOPTION OF CONNECTED DEVICES

Interestingly, cost alone – the factor often blamed – was not seen by the industry as the main issue that could slow down adoption of connected devices. Instead, the complications around data

BOX 4: EXPERT PERSPECTIVE ON CONNECTED DEVICES IN THE BIOSIMILARS SPACE

"Digitalisation is probably not going to have much of an impact for some time in biosimilars, because it completely goes against affordability and market access. This is on top of electronics that will require a dedicated infrastructure and, potentially, interoperability between patients, healthcare providers and pharma companies. I think connected devices are very much catered for innovative drugs – there is more incentive for their use especially where we don't have much data on usage and adherence. However, if you have a biosimilar, you probably have a fairly good idea of what the clinical outcome is, what the work is of the treatment in terms of how and when the patients use it."

Dr Charbel Tengroth
Managing Director, Tengroth Consulting

security, privacy and processing were highlighted as potential issues that could hamper implementation in the next two to three years (Figure 4). This is an area of growing concern for both developers and pharma, as we have seen issues around hacking and, of course, devices must be interoperable with healthcare systems while simultaneously being compliant with regulations across regions. Pharmapack's experts therefore predict that, over the next few years, the industry will attempt to move towards digital standardisation to offset some of the complexities these newer intelligent devices will bring in compliance. It is even possible that there will be a push for patients to have the ability to take direct control of their data.

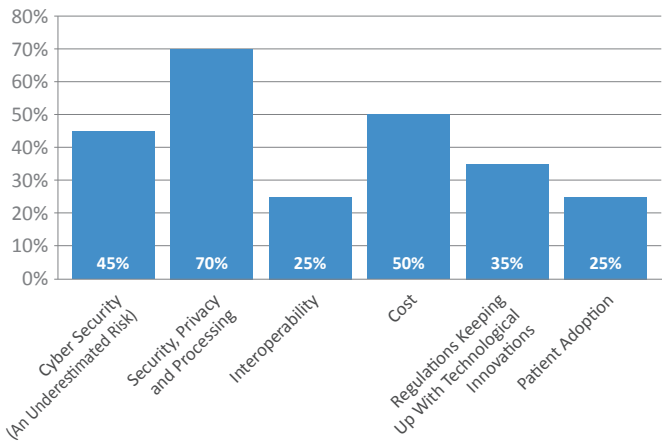

Figure 4: What is the biggest barrier facing connected devices and their widespread implementation over the next three years?

THE DRIVE TOWARDS SUSTAINABILITY

While the covid-19 pandemic has captured the attention of the world, including the pharma industry, there is also another looming issue on the horizon – climate change. Pharma has begun a drive towards sustainability in the last five years, with an increasing number of companies looking to minimise their carbon footprint, reduce waste, lessen greenhouse emissions and lessen their reliance on plastics. One major sector that has come into focus is packaging, and while packaging in pharma is used less than in industries such as food and fast-moving consumer goods, most medical packaging is derived from polymers, and the majority of medical waste is disposed of via landfill.

Governments are creating wider sustainability strategies across many industries, and pharma is no different, with a recent drive towards green chemistry initiatives to reduce the use of solvents in API manufacturing being just one example. Almost half of the survey respondents believed that investment in eco-packaging will increase by at least 50% within the next two to three years (Figure 5), and this will be largely driven by companies looking to lower their carbon footprint in line with the goals set out by the United Nations (Box 5).

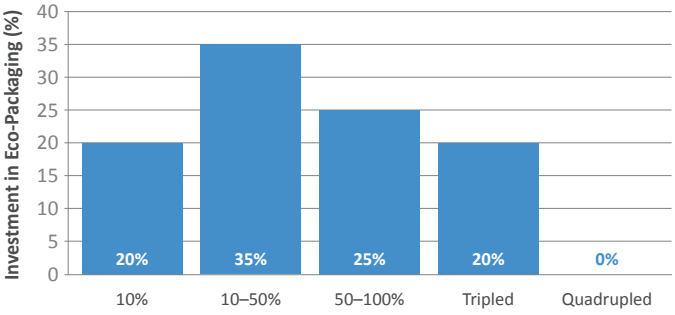

Figure 5: In the next five years, by how much will investment in eco-packaging increase?

BOX 5: EXPERT PERSPECTIVE ON SUSTAINABILITY IN THE PHARMA INDUSTRY

"With the wide range of medicinal packaging platforms available, there is a large range of choice for patients and each platform has its own inherent sustainability index, which is usually measured as a CO_2 equivalent value. Currently, there is no clear guidance on what standards the pharma industry should meet when it comes to sustainability. Healthcare providers and customers are increasingly asking about metrics regarding the carbon footprint of medical devices, medicines and packaging and this especially ties into the former's own sustainability initiatives."

Gregor Anderson
Managing Director, Pharmacentric Solutions

HOW DOES THE INDUSTRY THINK DIFFERENT COUNTRIES COMPARE FOR PHARMA SUSTAINABILITY?

Pharmapack's new Sustainability Index (scored out of 10) – created to gauge the perception of how much is being done by each country in terms of plastic use, waste reduction, device recycling and progress towards sustainability – assesses how far along each country is in terms of achieving optimal sustainability of pharma devices and medicines among its population (Figure 6). Leading the Index in its inaugural year is Sweden (6.87), whose adoption of a strategy for a circular economy in 2020 has been key in their drive towards a more sustainable approach to packaging.[8] To give just one example, Svensk Plaståtervinning (Motala, Sweden) has invested in building the world's largest plastic recycling facility, Site Zero.[9] The UK (6.04), which has implemented a tax on virgin plastic materials in disposable packaging, Germany (6.74), Switzerland (6.78) and France (6.09) are also all perceived by the industry to be leading Europe's efforts in sustainability.

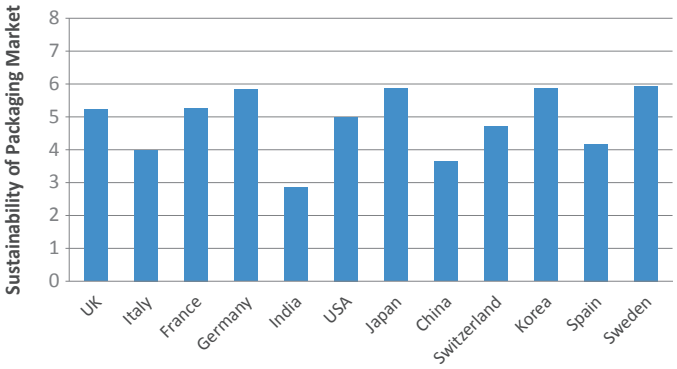

Figure 6: Packaging Sustainability Index 2021 (scores by country out of 10).

While both the governments of India and China have made sizeable efforts towards reducing carbon and environmental impacts of their pharma industries, the market has yet to be convinced, with India (3.30) and China (4.22) having the lowest perception scores by some distance. Also of note is that this is the only Pharmapack metric where the US ranks lower than the majority of European nations. Pharmapack surmises that this is likely due to the US's weaker governmental commitments, rather than a reflection of the relative commitment to sustainability of US-based drug device companies. However, the expert takeaway from this assessment has been that, in order for the industry to transition to a greener future, the global pharma industry should work together (Box 6).

However, the two dominant trends – smart packaging and green packaging – are often diametrically opposed in practicality, as smart devices tend to be less recyclable. However, an encouraging 65% of survey respondents believed that both can co-exist (Figure 7). The majority of the industry believes that "a shift towards better recycling and improved product lifespan" will help integrate sustainability goals without compromising device adoption over the next three years. However, 15% believe that consumer demands will take precedence, demanding that more sustainable and ethical products be used, while 20% believe that smart packaging will prevail as patient efficacy and adherence improvements will outweigh environmental considerations for now.

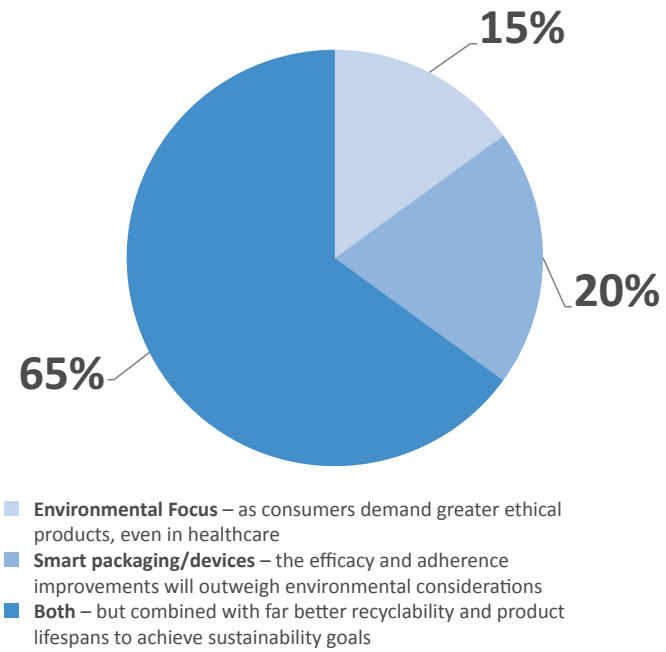

Figure 7: The two dominant trends "smart packaging/devices" and "environmental/green packaging" are often diametrically opposed. Which do you think will have the biggest bearing on product development over the next three years?

BOX 6: EXPERT PERSPECTIVE ON WORKING TOGETHER TOWARDS SUSTAINABILITY

"The whole pharma industry has to work together as an aligned partnership for solutions to be viable. This is because no single pharma company can tackle the bigger opportunities, such as recycling and standardising packaging materials and pack formats. With a joined-up industry roadmap, real change can be implemented, and this will need all stakeholders onboard. Green solutions should ultimately be a competitive advantage for all."

Gregor Anderson
Managing Director, Pharmacentric Solutions

CONCLUSION

One consequence of the pandemic is that novel drug delivery device innovation – outside novel injectors – was temporarily slowed and, as the industry returns to normality, we can expect a rise in new devices throughout 2022 (Box 7), with over half of the industry representatives surveyed expecting more than 10 new device approvals in 2022 (Figure 8). Significantly, future covid-19 vaccines will further increase the demand for injectable devices, and the pandemic has also clearly shown the benefit of both connected and self-use devices.

BOX 7: EXPERT PERSPECTIVE ON THE NEXT BIG INNOVATIONS IN DRUG DELIVERY & DEVICES

"There is a lot of benefit for patients that are taking a drug long term to not have to inject each time. Implanted systems that can slowly release a drug would be great, however, they don't really exist at the moment. Despite this, oral insulin may be nearer to becoming a reality than it was 10 years ago, and developments such as in-body implanted systems, which generate insulin are definitely growth areas.

Ocular delivery is also an area that could see more innovation in the near future, focusing on drug delivery across the blood-brain barrier to improve how quickly it gets into the system. For a while this approach appeared to fall out of fashion, however, it is beginning to be considered again as a key way to deliver into the blood. Such an approach would be particularly helpful in chemotherapy for example, as when these drugs are delivered orally or via injection, they can be harmful as they affect more than just the targeted area. Direct intra-tumoral delivery would be a brilliant breakthrough for cancer treatment, however, there are a lot of hurdles to overcome before this can be achieved, such as further developments in highly focused, targeted drug delivery."

Brennan Miles
Managing Consultant, Drug Delivery, Team Consulting
Dr Stephen Blatcher
Head of Early Stage MedTech, Team Consulting

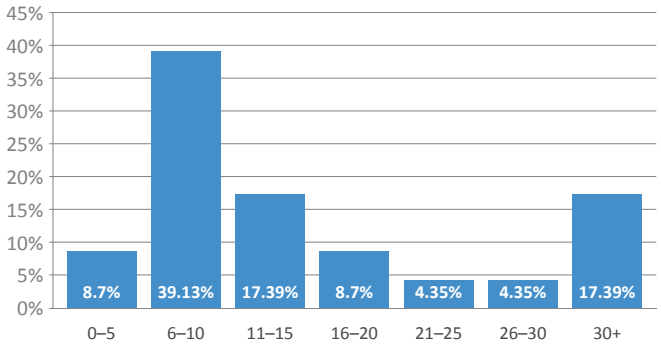

Figure 8: How many novel drug delivery devices or platforms will be approved by the FDA in 2022?

Pharmapack anticipates that innovation in devices will accelerate post-pandemic and that device manufacturers and pharma companies will increasingly collaborate to use them in conjunction with other digital assets, including apps, smartphones and computers. Ultimately, this will give patients far greater control over their own care. In the medium term, Pharmapack anticipates these efforts to start aligning with much wider access to recycling schemes so that patient adherence, which is inherently green, since it seeks to optimise the use of medicines, and sustainability gains can be made in tandem alongside therapeutic improvements.

However, the pandemic has also altered perceptions and expectations, exemplified by the increasing number of people who are now self-administrating. As this becomes the norm, companies are likely to make the patient experience the central component of drug delivery device design. Potentially emerging from this trend – in combination with connected devices – will be the use of real-time data to ensure that patient treatment can be evaluated over a longer time period, in pursuit of increased compliance.

In terms of the annual Pharmapack Innovation Index, it has been another good year for the industry, with respondents raising the overall index by nearly 2%, and India making sizeable gains and the US leading once again. Yet, in an industry so used to US leadership, sustainability goals are, in the industry's opinion, currently being driven forward by European nations. The EU's bloc-wide ability to regulate is pressing the industry to re-evaluate the materials it uses, but also, how to reliably collect and recycle these devices when, historically, virgin materials have been not only preferred but required. Pharmapack anticipates that the total lifecycle impact of devices will be talked about as the primary metric in two- or three-years' time.

Over the next few years, Pharmapack also expects medicine delivery to become more efficient as patients gain greater digital tools. However, sustainability goals may also see these very same digital tools being used to empower patients to be part of the solution by using reminders, maps and instructions on how, when and where to responsibly dispose of packaging waste and used devices.

Additional survey results not directly referenced in this article are presented in Box 8.

ABOUT PHARMAPACK

Launched in 1997, Pharmapack is a Europe-based conference for pharmaceutical packaging, drug delivery and medical devices and machinery. Pharmapack started as a biannual conference and exhibition, taking place every other year in Paris, until industry developments demanded a more frequent event to help the industry stay up to date on the latest trends, developments and regulations. In the past 24 years, the event has grown from a conference with a small table-top exhibition to an event hosting over 410 exhibitors and welcoming attendees from 75 different countries over two days.

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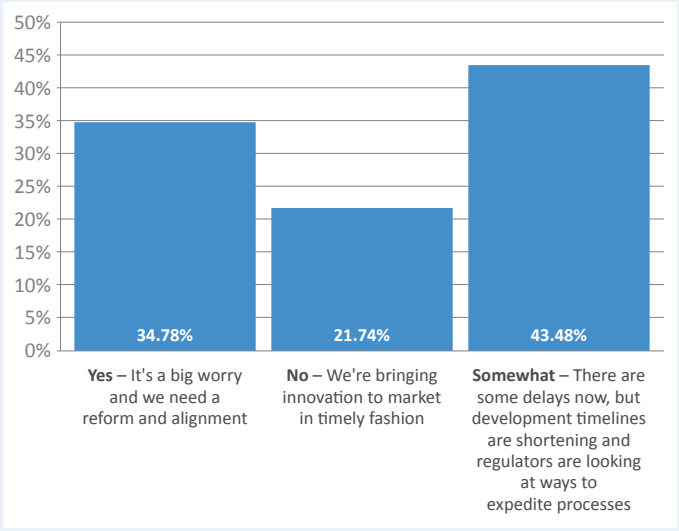
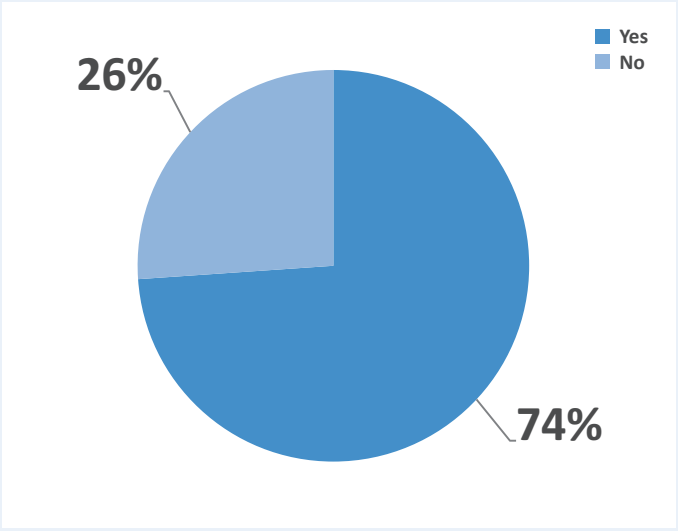
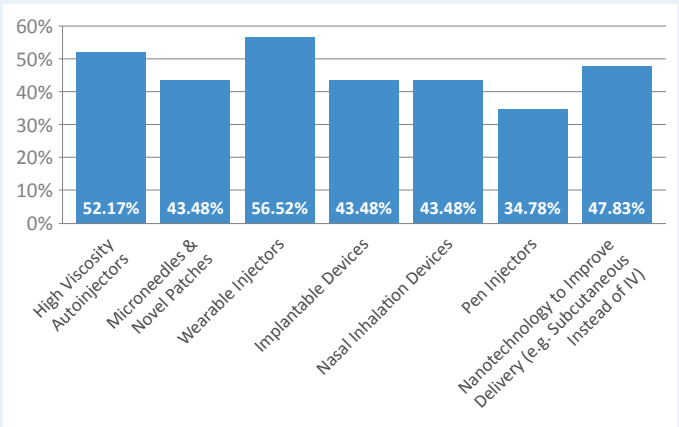
BOX 8: ADDITIONAL SURVEY RESULTS



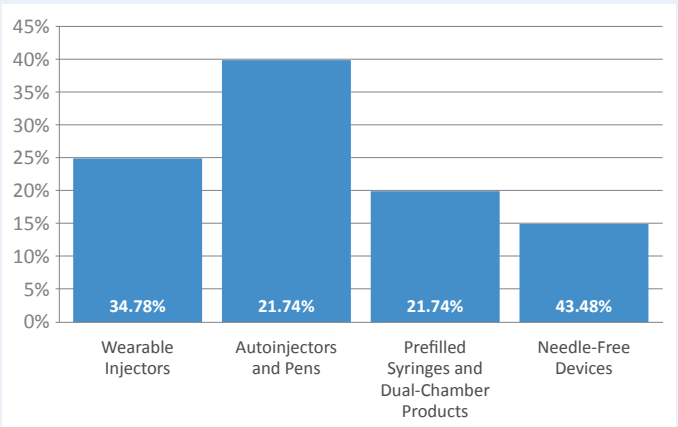
Do you think tightening regulatory requirements could constrain the growth opportunities for the drug delivery device industry?



Do you think the EU will join the Medical Device Single Audit Program (MDSAP) in the next two to three years (changing from being a pilot observer)?



What drug delivery devices will see the biggest areas of innovation to support growth in biologics over the next five years?



Which of the following product classes do you anticipate will have the most FDA approvals in the calendar year 2022?

EIGHT ESSENTIAL SUSTAINABILITY TERMS FOR THE MEDICAL DEVICE INDUSTRY

In this article, Charlie Dean, Mechanical Engineering Consultant, Kay Sinclair, Senior Consultant, and Brennan Miles, Managing Consultant, Drug Delivery, all of Team Consulting's sustainability group, provide an overview of eight terms key to a common understanding in the ongoing, and crucial, discussion surrounding sustainability.

In recent years the subject of sustainability has transcended from the discussions of the scientific and political world and permeated into our professional lives and even household conversation. This has been keenly felt in the medical device industry, where the criticality and emergency of sustainability is fast becoming a key focus. For most pharmaceutical professionals and medical device developers looking to do their part, understanding the deeper scientific and socioeconomic factors involved in sustainability may be prohibitively laborious. However, it is still important for all companies to work with a common understanding of the issue and the terms involved. This article presents a brief list of sustainability terms and how they apply to medical device development that would be beneficial for our industry to know.

1: SUSTAINABILITY

Definition

The simple definition is "the ability to maintain something on its current path or development", but Sustainability (with a capital "S") points to the modern definition widely accepted in the UN's Sustainable Development Goals (SDGs).[1] The 17 goals highlight the breadth of this term, covering not just the climate, but all manner of emergencies that threaten humanity's healthy, peaceful and prosperous existence on planet Earth – from poverty to education and more. If you're after a gold standard definition of sustainability, this is it.

> "When thinking about sustainability, many companies focus on the pressing issue of climate change. However, it is important to maintain a full understanding of the term to allow for a more holistic and strategic approach to problem solving and mitigation efforts."

How This Applies to the Industry

When thinking about sustainability, many companies focus on the pressing issue of climate change. However, it is important to maintain a full understanding of the term to allow for a more holistic and strategic approach to problem solving and mitigation efforts. This will help to reduce the chance of exacerbating one issue while rushing to solve another, or even allow companies to solve multiple problems with one well-placed policy. For example, creating manufacturing sites in multiple locations around the world can reduce the carbon footprint of a vast transportation network, while also creating jobs and boosting the economy in lower-to-middle-income regions.

Many companies incorporating sustainability into their business approach choose to follow the principle of the "Triple Bottom Line" (TBL) – a term elevating social and environmental factors to stand alongside economic factors. The TBL was, and still is, a powerful concept to enact positive change. However, it is not sufficient on its own to capture the fullness of the challenges we face. Instead, it is prudent to rely on the UN SDGs for a more comprehensive definition of sustainability.

2: GREENHOUSE GAS EMISSIONS AND CARBON FOOTPRINT

Definition

Greenhouse gas (GHG) emissions and carbon footprint are interchangeable terms relating to the total emissions caused by human activity. This could be the

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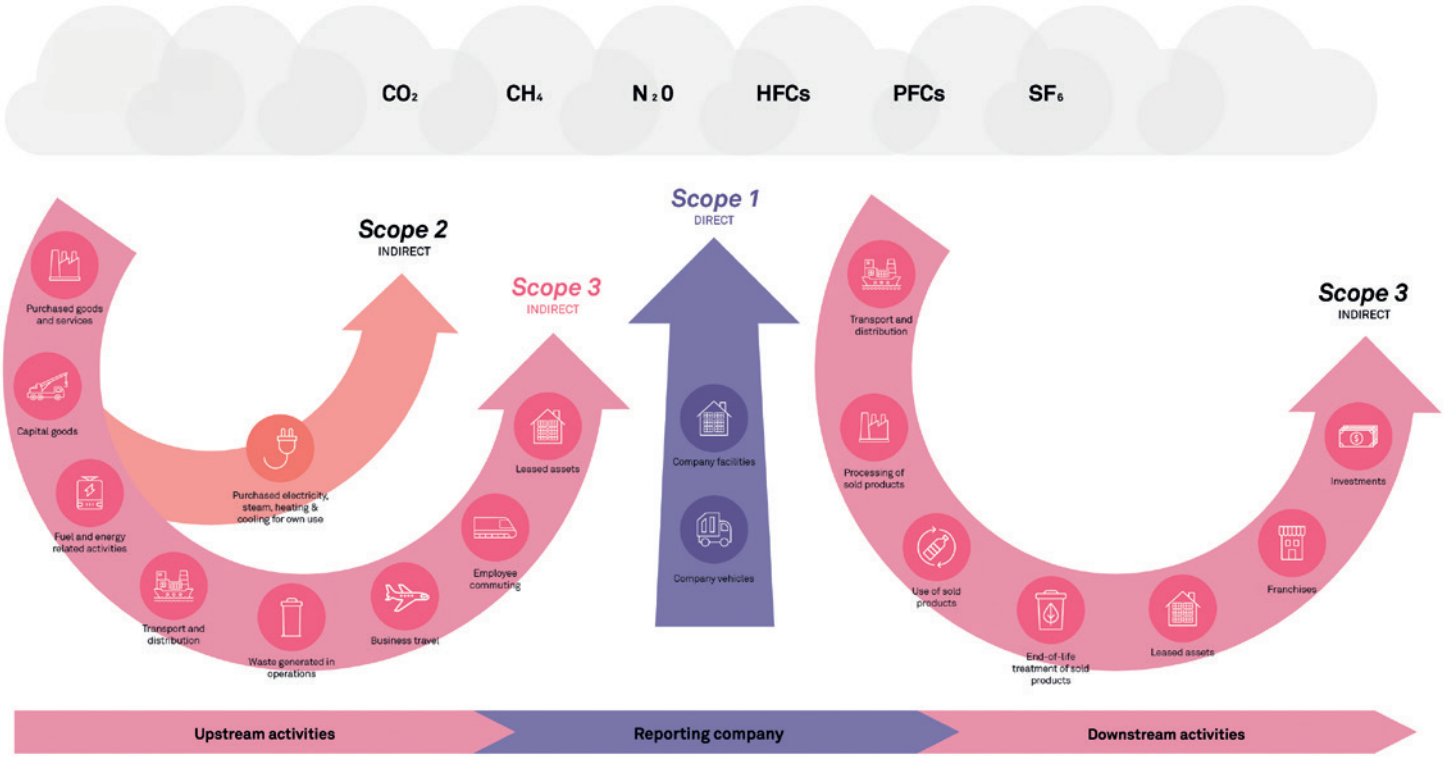

Figure 1: Overview of GHG Protocol scopes and emissions across the value chain.

> "Manufacturing processes that require electricity therefore contribute GHGs by association, owing to the method used to generate the energy required."

manufacturing of a product, driving a car or emissions from an individual's lifestyle. Methane from domesticated cattle also counts here, as rearing livestock is a human activity. While GHG emissions (or carbon footprint) is an expression of the total amount of GHG emissions, the values are typically normalised and expressed in terms of carbon dioxide equivalent, typically as grams or kilograms of CO_2-eq.

How This Applies to the Industry

There are numerous gases and gas sources that contribute to the greenhouse effect. Understanding them is key to mitigating them. The most well-known example of GHG emission is the burning of fossil fuels, which releases carbon dioxide into the air. This occurs in transportation, heating and several forms of energy generation, such as coal-fired power plants.

Manufacturing processes that require electricity therefore contribute GHGs by association, owing to the method used to generate the energy required. For example, energy intensive processes in medical device development, such as printed circuit board manufacture, have high carbon footprints. This has caused the recent trend among some organisations to bolster their on-site renewable energy in order to reduce their reliance on coal-fired energy grids.

Some gases are also emitted due to the inherent chemical or physical process involved in the healthcare industry's regular activities. For example, pressurised metered dose inhalers (pMDIs) use pressurised fluorinated gases to aerosolise a drug formulation for inhalation. These gases, such as hydrofluoroalkanes (HFAs), have especially high global warming potential. As such, the continued use of these gases in pMDIs is under heavy debate.

3: NET-ZERO CARBON TARGETS

Definition

This is a goal that a person, organisation or government sets themselves whereby they pledge to reach net-zero GHG emissions by a specified date. The term "net-zero", not "zero", is key here, as it is impossible to mitigate all emissions entirely. With every best effort there will always be legacy or residual emissions. To hit these targets, there is a need to remove emissions from the atmosphere by at least an amount equivalent to that emitted.[2]

Compared with the similar term "carbon neutrality", a key aspect of achieving net-zero carbon targets is that reducing emissions is the first priority, with carbon offsetting only being used to balance the remaining emissions. In contrast, carbon neutrality often refers to simply purchasing carbon reduction credits in order to proceed as normal, with no transformation to any proprietary operations.

How This Applies to the Industry

With governments beginning to pass laws aimed at ending global warming, it is fast becoming relevant for organisations to set their own targets to reduce emissions. What this means for each organisation will differ, making measuring emissions a key activity. The GHG Protocol is the most widely used accounting framework for quantifying and measuring these emissions (Figure 1).[3] The protocol breaks down emissions into three categories:

- Emissions directly caused by an organisation's activities
- Indirect emissions from purchased electricity or other energy sources
- All other indirect emissions from activities within the value chain.

4: CARBON OFFSETTING

Definition

The act of carbon offsetting involves removing GHGs from the atmosphere to balance against an organisation's residual GHG emissions. As mentioned prior, it is impossible to remove emissions from one's own operations entirely.

There is heavy debate between the two methods of carbon offsetting schemes:

- **Reduction schemes:** These reduce (non-proprietary) emissions through renewable energy projects, such as wind farms or solar panel projects. Purchasing credits in reduction schemes results in reducing future emissions elsewhere but does not remove emissions to balance against an organisation's own residual emissions.
- **Removal projects:** These absorb GHGs from the atmosphere, most notably through planting trees or "sequestration".

How This Applies to the Industry

With numerous opportunities for absorbing emissions from the atmosphere, it can be challenging for businesses to determine which project most closely aligns with their organisational goals and core values. While it may seem like a monumental challenge, the best approach is to start small and build from there. Aiming for a running start of measuring your emissions and removing all residual emissions may be overwhelming, which is why organisations set net-zero targets for the future and build roadmaps to achieving their goals.

> "As global warming is one of the key facets of the climate emergency, GHG emission is typically the impact category of most interest. However, there is great value in being aware of the other categories so as to not create more problems by rushing to solve only the most obvious one."

5: CIRCULAR ECONOMY

Definition

Developed by the Ellen MacArthur Foundation, the "circular economy" is a novel methodology for driving system change for a more sustainable economy. Instead of the linear cradle-to-grave or "take-make-waste" industrial model, the circular economy aims to redefine industry with a "cradle-to-cradle" approach (Figure 2).[4]

How This Applies to the Industry

Applicable to numerous industries, this system aims to address a number of environmental issues, primarily surrounding the depletion of natural resources and excessive generation of waste. It encourages going back to the drawing board and rethinking product lifecycles to embed recycling, repair, re-use, refurbishing, maintenance and other approaches with the aim of making more efficient use of resources and energy, as well as minimising waste and pollution.

The circular economy shifts the focus from purely a product design-oriented solution to the climate emergency, to more of a service design-oriented one. A sustainable design is unlikely to be achieved through product design alone.

Figure 2: Ellen MacArthur Foundation – Circular Economy.

6: LIFECYCLE ASSESSMENT

Definition

Lifecycle assessment (LCA) is a widely recognised (ISO 14040:2006) environmental management framework for assessing the environmental impacts of a product or service. Often misinterpreted as being a tool only for analysing a product's carbon footprint, LCA is more appropriately used for a wide range of impact categories, with GHG emissions being only one of many. Other uses for LCA include assessing:

- Land use
- Water use
- Resource efficiency
- Hazardous and toxic material waste
- Heavy metal content (HMC).

As dictated in ISO 14040, the principles of LCA involve four key stages:

- Goal and scope definition
- Inventory analysis
- Assessment
- Interpretation.

During the goal and scope definition stage, it is critical to be clear which impact categories are of most relevance, usually determined by where the impacts are regarded as being highest, or perhaps where there is most opportunity for mitigation. As global warming is one of the key facets of the climate emergency, GHG emission is typically the impact category of most interest. However, there is great value in

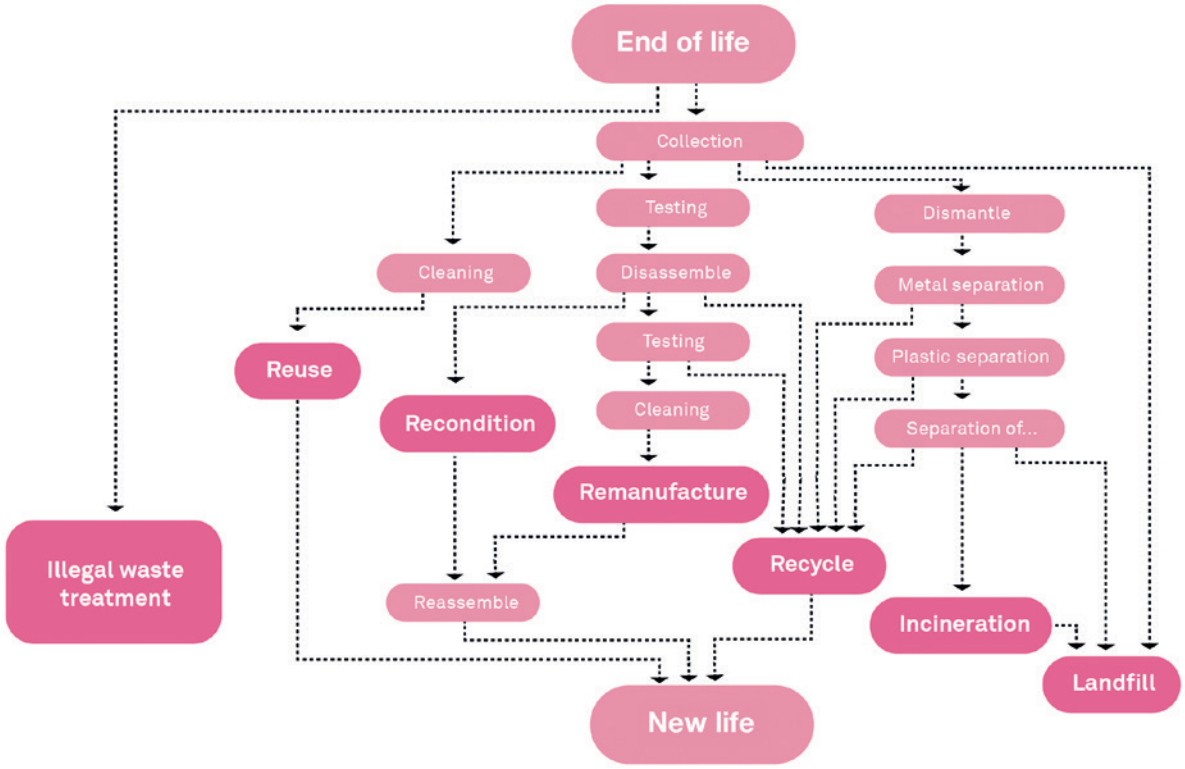

Figure 3: Overview of end-of-life options and crucial steps in the end-of-life treatment.

being aware of the other categories so as to not create more problems by rushing to solve only the most obvious one.

How This Applies to the Industry

Minimising a medical device's environmental impact is a complex, multi-variable and highly technical challenge. LCA is a widely used and methodical way of managing this process by providing quantitative insights into device or drug development to drive environmentally friendly choices.

7: BIOPLASTICS

Definition

Bioplastics are polymeric materials derived from biomass sources. These biomass sources are typically renewable sources that can either be waste from food and agricultural processes, or derived from sources specifically used for polymer resins, such as castor beans.

There are two key advantages of using such plastics. Firstly, they aren't made from fossil fuels, which are a depleting resource that requires millions of years to form. Secondly, the carbon footprint of producing biopolymers, from planting a seed all the way to formulating plastic resins, is typically much lower than with fossil fuel-based plastics. There is also a possible benefit that the biomass sources may also sequester atmospheric carbon during their growing stages too.

How This Applies to the Industry

Bioplastics is a fast-growing industry, with more and more bioplastic resins being made available, even for medical device applications. As demand increases and confidence grows in these technologies, the supply can be expected to increase too. Experimentation may be required in order to incorporate such materials into device development, but considering these materials as part of device design may yield a more sustainable product.

> "As governmental legislation and regulatory requirements evolve, medical device manufacturers are being required to take more responsibility for the full lifecycle of their products."

8: DESIGN FOR END OF LIFE

Definition

This design practice is concerned with designing a product with the end of its life in mind. It aims to build an understanding of what disposal or end-of-life processing is most relevant to the product. Having this mindset allows for more sustainable design choices to help reduce the environmental impact of medical waste. This can include aspects such as design for disassembly, recycling, re-use, remanufacture, energy recovery, repair and more (Figure 3).

How This Applies to the Industry

Alongside GHG emissions, medical device waste is another cause for concern. Due to its clinical nature, medical device waste is typically disposed of outside of municipal or domestic waste streams, most often in medical waste incinerators. Conventionally, design efforts are usually focused on design for manufacture and for commercialisation, with the product's end of life often being an afterthought.

Designing for end of life is of increasing importance, particularly at earlier phases of medical device development, such as the concept generation phase. There is also the opportunity to reduce the carbon footprint of subsequent generations of products, as recycled material feedstock can have lower associated emissions than virgin materials. As governmental legislation and regulatory requirements evolve, medical device manufacturers are being required to take more responsibility for the full lifecycle of

their products. The new expectation is set to be that you should be ready to look after your product from the start to the end of its life.[5]

SUSTAINABILITY IN MEDICAL DEVICE DEVELOPMENT

There is no easy path towards fully sustainable medical device development. For any progress to be made, however, it will be important for companies to join the discussion with a common understanding of the issue. As innovations in sustainable development progress, and as regulations, standards and legislation evolve, we can hope to see some meaningful progress reflected in the medical device and pharmaceutical industry.

ABOUT THE COMPANY

Team Consulting is a leading medical device design and development consultancy focusing on the pharmaceutical and healthcare industries. Team provides advice, support and device development solutions for its clients across a broad range of briefs, from establishing sustainable development strategies for new technologies or device platforms, through to full device development and manufacturing support. Focusing only in the medical space, Team's domain expertise can be translated into successful outcomes that are both regulatory compliant and designed for end users.

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ABOUT THE AUTHOR

Charlie Dean is a consultant within the mechanical engineering group at Team Consulting. Within his work on drug delivery products, he combines analytical skills with manufacturing knowledge to optimise device concepts for production and market. Mr Dean has a special interest in how to incorporate sustainability initiatives into medical device development, using tools such as lifecycle assessment to understand and mitigate a product's environmental impact. He has a BEng in Mechanical Engineering from Loughborough University (UK) and a MSc in Biomedical Engineering from the University of Surrey (UK).

Kindeva
DRUG DELIVERY

SIX INHALER SUSTAINABILITY MYTHS – AND WHY THEY MUST BE BUSTED

In this article, Louise Righton, Global Strategic Marketing Leader – Inhaled Drug Delivery at Kindeva, busts six sustainability myths about inhalers.

The 26th UN Climate Change Conference of the Parties (COP26) is being held in the UK from October 31 to November 12, 2021. The COP26 summit brings parties together to accelerate action towards the goals of the Paris Agreement and the UN Framework Convention on Climate Change.[1]

Countries are being asked to come forward with ambitious 2030 emissions reductions targets that align with reaching net zero by the middle of the century. The UK was the first country to pledge to reduce carbon emissions by 78% by 2035.[2] The UK NHS stated its aim to be the world's first net zero national health service for the emissions it controls directly, aiming to become net zero by 2040, with an ambition to reach an 80% reduction by 2028 to 2032.[3]

It is recognised that healthcare is a significant contributor to the global carbon footprint – this has been calculated to be equivalent to 4.4% of net emissions in 2014.[4] While more than half of these emissions are from energy use, medicines also contribute; inhalers, particularly pressurised metered-dose inhalers (pMDIs), have come under scrutiny due to the environmental impact of the propellants used. While this scrutiny is positive because it will encourage change, much of the debate is narrowly focused on the comparative global warming potential (GWP) of different device types. 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

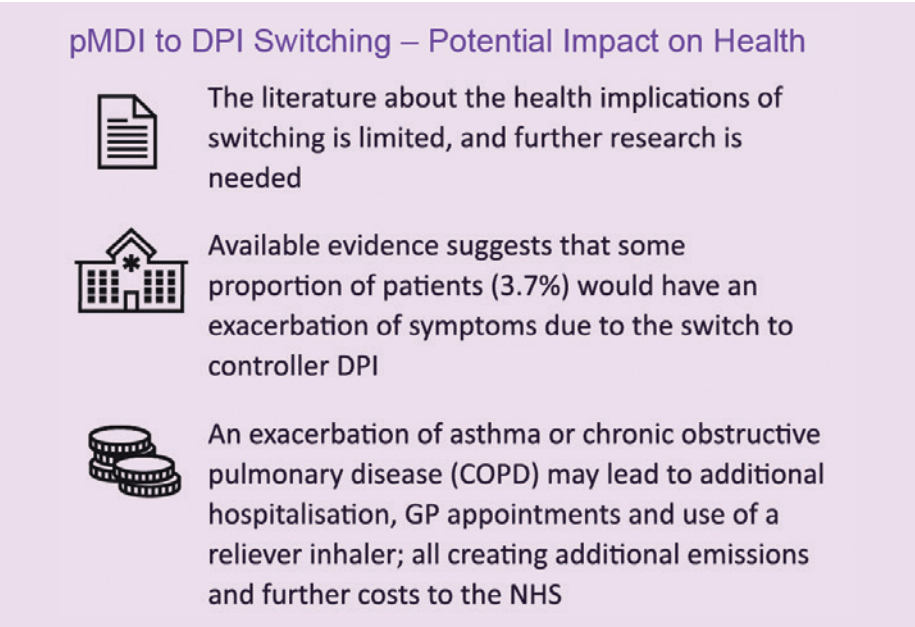

Figure 1: Switching has the potential to create additional emissions and further costs to the NHS.[7]

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"The NHS has identified the inhaler market as one area of decarbonisation to help reach its net-zero target, citing that pMDIs account for 3% of all emissions."

(DPIs) and soft mist inhalers (SMIs), are categorically superior to pMDIs, regardless of patient considerations (Figure 1).

For example, the NHS has identified the inhaler market as one area of decarbonisation to help reach its net-zero target, citing that pMDIs account for 3% of all emissions.[3] This has led the NHS to put prescribing targets in place to promote the rapid uptake of DPIs by switching patients from pMDIs in the non-salbutamol market. This is to be achieved by financially incentivising prescribers. From October 2021, the Investment and Impact Fund (IIF) is rewarding increased prescribing of DPIs and SMIs where clinically appropriate, such that by 2023–2024, only 25% of non-salbutamol inhalers prescribed will be pMDIs.[5] This is a significant reduction from current usage patterns – in the UK, 70% of all inhalers prescribed are pMDIs,[6] which includes a significant 61% rate of pMDI prescribing in the non-salbutamol category.[7]

This focus on reducing the carbon footprint of the inhaler market by switching from pMDIs to alternative devices may have unintended negative consequences for the NHS's net-zero ambition.[7] For all inhaler types, there is an impact on the environment to consider at each stage of the inhaler lifecycle, from manufacturing, supply and usage by the patient to appropriate disposal when the labelled number of doses have been taken or the inhaler is no longer needed.[8] A recent paper produced by the International Pharmaceutical Aerosol Consortium (IPAC), which was established to represent the industry in navigating the Montreal Protocol in the late 1980s, and of which Kindeva (formerly 3M Drug Delivery Systems) was a founding member, proposes that the most effective approach to the global environmental challenge surrounding inhalers is for healthcare systems to adopt a holistic, patient-outcome-based approach. This approach would aim to reduce the carbon footprint of patients using inhaled treatments while simultaneously supporting improvements in patient care and reducing the environmental impact of medical treatments at all stages of the lifecycle.[9]

Kindeva Drug Delivery has a legacy of advancing the environmental sustainability of inhaled medicines. A pioneer in hydrofluoroalkane (HFA)-based formulations for pMDIs, Kindeva developed the world's first chlorofluorocarbon (CFC)-free pMDI (launched in 1995). This innovation was a milestone accomplishment that delivered step-change improvements in the environmental impact of inhaled drugs, and Kindeva remains at the forefront of environmental progress today. The pMDI industry is making great strides in the transition to low GWP propellants, with HFA-152-a from Koura (Cheshire, UK) and Honeywell's (NC, US) HFO-1234-ze(E) the current candidates to replace existing propellants HFA-227ea and HFA-134a.[10]

Nevertheless, despite the industry's commitment to decarbonisation, in the form of investment in reformulation and manufacturing technology,[11–15] a narrative has evolved that pMDIs are inherently "bad" and must be replaced as quickly as possible by alternative inhaler types. There are several flaws in the argument that the solution to the carbon footprint of respiratory disease is to be found in a rapid switchover from pMDIs to DPIs. Therefore, the prevailing "myths" must be examined and addressed to achieve the shared industry vision of a decarbonised inhaler market.

Myth 1: For Most Patients, DPIs Are More Effective Than pMDIs, and Patients Prefer Them

Proponents of the "pMDI to DPI switch" method of decarbonising the inhaler market will often selectively cite studies that seemingly prove that DPIs are more effective than pMDIs and that patients prefer them. This myth is leveraged to promote a rapid switch from pMDIs to DPIs in the non-salbutamol segment. The pMDI is then pigeon-holed solely as a solution for reliever medication (short-acting beta agonist, or SABA). In fact, the relative efficacy of different types of device – particularly pMDI compared with DPI – has been studied extensively by researchers for decades. Systematic reviews and meta-analyses show no significant differences in effectiveness across devices in general.[16–18] Recent head-to-head randomised controlled trials and population studies show a set of applications for which pMDIs are currently the device proven to be significantly more effective, or at least as effective, as DPIs.[19–24] For a complex medical challenge, pMDIs are a crucial option for physicians. The literature does not support the myth that pMDIs have a role to play solely in delivering SABA therapy.

"For a complex medical challenge, pMDIs are a crucial option for physicians. The literature does not support the myth that pMDIs have a role to play solely in delivering SABA therapy."

Myth 2: Patients Should be Made Aware of the Carbon Footprint of Their Inhalers and be Encouraged to Switch From pMDIs for Environmental Reasons

Matching the patient with the right inhaler is a complex decision that the clinician must judge and should not be overly carbon led. Guidelines from the Global Initiative for Asthma and the Global Initiative for Chronic Obstructive Lung Disease emphasise this.

Asthma and chronic obstructive pulmonary disease (COPD) patients with stable disease should have continuity of inhaler device.[25] Suddenly asking the patient to switch from a device that is working to a new device for carbon-led reasons, not medical reasons, can have negative consequences: patients can lose confidence in their treatment,[26,27] they can suffer a reduced perception of disease control[28] and they can even lose trust in their health practitioner and health system.[29] Empirical findings and best practice suggestions consistently advise against switching away from established, functioning treatments without a clear, clinical objective.

Myth 3: A Minority of Patients and Some Young Children are Unable to Use DPIs, but the Majority of Patients Find Them Easier to Use as They Require Less Co-Ordination Than a pMDI, Leading to Greater Adherence

An essential element of optimised disease management is the training and correct usage of devices.[30] While the handling of all pMDIs requires the same approach, different

"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."

types of DPI pose different challenges to patients.[31] 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.[32] 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.[33–35] Some previous studies show pMDIs are associated with better disease control and treatment adherence among subjects with asthma and that they have equivalent treatment satisfaction to DPIs.[36]

Incorrect usage can be particularly problematic for patients who are prescribed multiple DPIs because it can be challenging to train patients to use devices with different designs – some incorporating reservoirs of powder, others requiring single-use loading with a capsule, for example. It has been suggested that physicians should avoid prescribing multiple devices requiring different handling and dosing techniques.[37] 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.

Myth 4: pMDIs are the Only Inhaler Type With an Environmental Impact and Should be the Focus of Sustainability Policies

Propellants are only one part of the story – we need a shared understanding of each product's lifecycle and its total environmental impact so that we can expand the discussion from a single focus on GWP to a more holistic approach to sustainability. The industry-led CFC-HFA transition made major improvements in the sustainability of pMDIs, and facilitated the introduction of more DPIs, expanding patient and clinician choice. With a wider choice of devices on the market, an environmental policy must go beyond propellants and 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. In the quest to reduce GWP, we must not overlook environmental impacts such as human toxicity, fossil depletion and marine eutrophication. A recent study found that an HFA-152a pMDI inhaler has the lowest impacts for 10 out of 14 environmental categories considered, while the DPI is the worst option for eight impacts.[38]

The development of pMDIs with low GWP propellants will raise the bar on sustainability, and manufacturers and stakeholders must rise to the challenge of sustainability through the product and patient lifecycle. We have an opportunity as an industry to address the wider sustainability picture and broaden the thinking beyond propellants.

Myth 5: Another Advantage of DPIs is that they have Dose Counters, so the Patient Knows How Many Doses are Left and Doesn't Throw Away a Part-Full Inhaler, Thereby Minimising Wastage

The majority of pMDIs now use a dose counter to ensure minimal wastage. 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. Kindeva believes this new dose counter delivers benefits throughout the

"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."

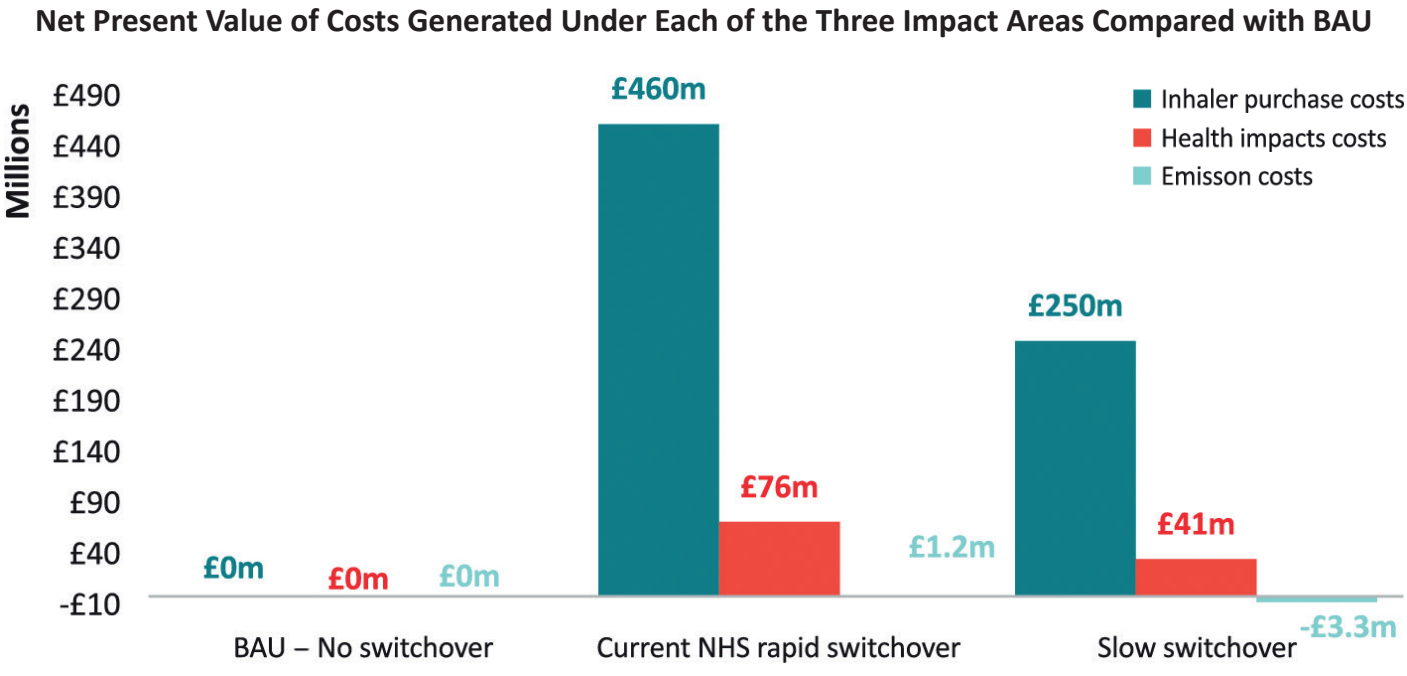

Figure 2: Assessing the economic impact of the NHS's pMDI to DPI switch policy versus business as usual and a slower switchover.[7]

value chain – the simplicity of assembly, compatibility with a broad range of actuators and valve types and the robust reset of dose counting – and also represents a marked sustainability improvement by reducing plastic use. The industry must recognise that these improvements are possible through the regular cycles of innovation, and it must continue to challenge itself on sustainability.

Myth 6: To Decarbonise the Inhaler Market Quickly, we Need to Switch as Many Patients as Possible From pMDIs to DPIs, Thus Reducing the Carbon Footprint of Each Patient and Achieving Net Zero

A recent study found that the NHS's rapid switchover policy is unlikely to result in a substantial reduction in carbon emissions, compared with the no policy implementation alternative, and will likely result in rising costs of treatment and an adverse impact on patient health (Figure 2). The study included an academic literature review that suggests that about 3.7% of switched patients will have one additional exacerbation resulting from the switch, leading to additional hospitalisation and GP appointments, and use of a reliever inhaler, all creating additional emissions and further costs to the NHS.[7]

CONCLUSION

In order to ensure a smooth transition to low GWP pMDIs, and to maintain the pMDI as a key delivery platform that many patients and prescribers rely on, there are a number of unhelpful "myths" surrounding the sustainability of inhalers, which have become the prevailing narrative and which must be countered. The industry is fully committed to introducing pMDIs containing low GWP propellants as soon as is practicable, and stakeholders need to support this aim. Current policy to reduce pMDI prescribing in the non-salbutamol segment may result in the unintended consequence of slowing down the introduction of new propellants across both the non-salbutamol and the salbutamol segments, the latter being reliant upon pMDIs. Robust sustainability strategies require a holistic, end-to-end view of product design, lifecycle analysis and patient impacts. Decarbonising the inhaler market cannot be optimally achieved by a rapid reduction in pMDI prescribing – a more holistic view must be adopted for the good of the environment, patients and health systems.

ABOUT THE COMPANY

Headquartered outside St Paul, MN, US, Kindeva Drug Delivery is a leading global contract development and manufacturing organisation in the pharmaceutical industry. Kindeva provides unique technologies and quality services to its customers, ranging from formulation and product development to commercial manufacturing. Kindeva focuses on complex drug programmes, and its current offering spans inhalation drug delivery, transdermal drug delivery, microstructured transdermal systems (microsystems) and connected drug delivery. Kindeva employs approximately 900 people at six facilities worldwide.

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SUSTAINABILITY WITH THE ARIA AUTOINJECTOR: A LIFECYCLE ASSESSMENT

In this article, Emil Fraenkel, Sustainability Engineer and Bjarne Sørensen, Director, Front-End Innovation, both at Phillips-Medisize, consider the sustainability of re-usable and disposable autoinjectors, its implications in adding connectivity to drug delivery devices and how it has been an important consideration for Phillips-Medisize in the development of the Aria re-usable autoinjector.

This article is a continuation of the case put forward by Phillips-Medisize in ONdrugDelivery Issue 113 (Oct 2020).

INTRODUCTION

In September 2019, Health Care Without Harm (HCWH) published a report that estimated that the global climate footprint for healthcare is equivalent to 4.4% of global net emissions (2 gigatons of CO_2 equivalent based on 2014 data from HCWH).[1] To put these numbers into perspective, the healthcare industry produces twice the level of greenhouse gas emissions compared with the aviation industry.[2] Recognising this impact, the healthcare industry is following other industries in developing and deploying sustainability initiatives throughout the value chain. To date, much of this work has focused on sustainability initiatives aimed towards optimising the manufacture of drug product, such as using less energy and water, but often ignored the total impact of each product and supply chain on overall sustainability.

Looking at just one part of the supply chain or product lifecycle in isolation, and only measuring a few of the environmental problems associated with it, is simply not sufficient. However, leading pharmaceutical companies now have well-defined strategies for product stewardship and environmental impact reduction, setting deadlines as aggressive as 2030 for achieving their sustainability targets – improving not only sustainability of their own operations but demanding that all parties throughout their value chain do so as well. Achieving sustainability is challenging, especially for an industry where plastics make up approximately 85% of medical equipment, and approximately 90% of medical device waste consists of disposable, one-time-use products or components.[3]

THE CASE FOR RE-USABILITY IN HEALTHCARE

The HCWH report aligns its findings with the Greenhouse Gas Protocol (GHGP), categorising healthcare emissions into three groups or "scopes":[4]

1. Direct emissions from healthcare facilities
2. Indirect emissions from purchased energy
3. All other indirect emissions that occur in the value chain, including both upstream and downstream emissions.

Overall, the paper found that fossil fuel consumption is at the heart of healthcare's emissions due to it being

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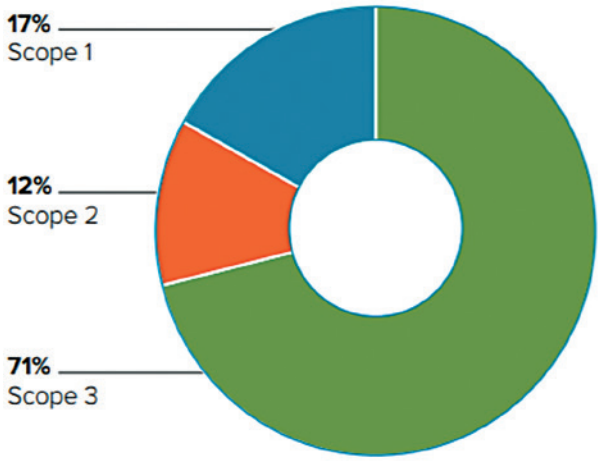

Figure 1: Classification of GHG emissions in healthcare.

"A significant portion of the medical device industry generates the bulk of its revenue from the sale of disposable products or components, including finished autoinjector devices and their associated components."

integral to the energy supply, raw materials, manufacture and transport of healthcare operations. Figure 1 showcases the findings; 17% of healthcare emissions are produced on site (Scope 1), 12% come from purchased energy (Scope 2) and 71% come from indirect emissions (Scope 3) – predominantly from the global supply chain involved in the production, transport and disposal of goods and services, including medical devices and instruments. As a result, manufacturers of medical devices and instruments are coming under increased scrutiny from healthcare providers and pharmaceutical companies looking to achieve better sustainability across their value chains.

A significant portion of the medical device industry generates the bulk of its revenue from the sale of disposable products or components, including finished autoinjector devices and their associated components. This business model has proved to be particularly attractive as it decreases the risks associated with contamination and inappropriate re-use, as well as the high costs associated with product reprocessing and sterilisation.

In the highly regulated medical device industry, many manufacturers see the demands of sustainable design as yet another unwelcome design restriction. Engineers and designers need to focus on compliance with strict regulatory guidelines and meeting intense time-to-market pressures. Some perceive the need for sustainability as hampering material choice and impeding innovation. The possibility of legal liability and lengthy product development cycles has also slowed the adoption of sustainable practices in the medical device industry.

Many devices, particularly invasive ones, will almost certainly continue to have a disposable component to comply with safety regulations. However, taking a new approach to the design process could have a significant and positive impact on the environmental sustainability of medical devices, including autoinjectors – the primary focus of this article.

Waste management is one of the biggest challenges facing sustainability-friendly initiatives. People tend to throw things away, instead of re-using or recycling them, leading to increased environmental impact from waste going to landfill or incineration. Or even worse, discarded products can end up outside regulated waste management systems with serious consequences for natural ecosystems and wildlife.

"The impact of product and process design on greenhouse gas emissions can be reduced if products are made usable for longer periods of time."

The impact of product and process design on greenhouse gas emissions can be reduced if products are made usable for longer periods of time (Figure 2). By creating devices that consumers can use for longer, companies can reduce the frequency at which their products are discarded. Products with increased longevity inherently lead to less pollution and lower risk of waste ending up where it can have an adverse impact on nature.

Experts in the field frequently make use of qualitative arguments to promote sustainability initiatives but, ultimately, we need to investigate and measure the actual quantitative environmental impact of the product/device. The most widely accepted method of achieving this is via a lifecycle assessment (LCA). This rest of this article will provide insights into the environmental performance of Phillips-Medisize's Aria, a re-usable, electronic autoinjector, compared with the disposable autoinjectors that are typical to today's drug delivery device industry.

AUTOINJECTORS

Autoinjectors are an important case for considering innovations that can improve medical device sustainability. These devices have become increasingly common in the treatment of chronic diseases, as they offer the convenience of safe self-administration in the patient's home. With around 50 approved drug-autoinjector combination products on the market, the dominant design has become that of a disposable, spring-driven device, with manual needle insertion and

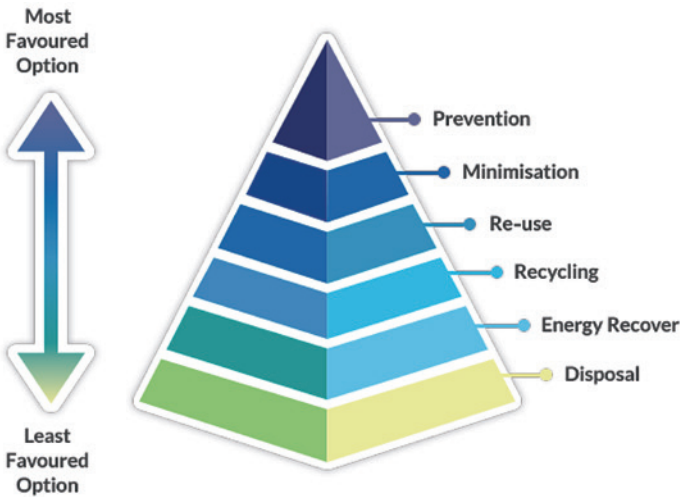

Figure 2: Waste hierarchy highlighting re-use and recycling over energy recovery (incineration) and disposal.[5]

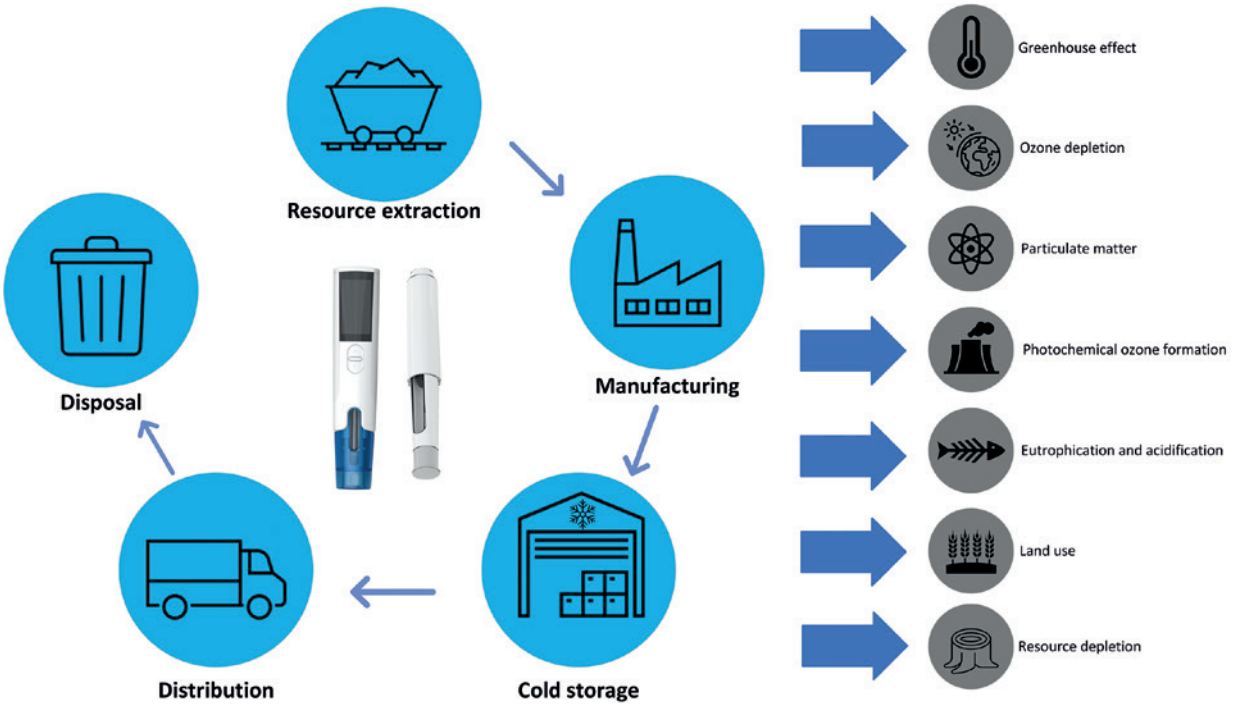

Figure 3: LCA includes analysis of impact categories standard to the strategy at each point within a device's lifecycle.

removal, shield-triggered activation and passive needle protection. Although the approach has been favoured, as it has been seen to provide optimal safety, usability and convenience at an acceptable cost, changes in market needs are starting to challenge this approach. High on the list of these newly prominent needs is the need to better address sustainability.

LCA is a standardised, cradle-to-grave, analysis technique used to assess the environmental impacts associated with all the stages of a product's lifecycle, from raw material extraction through materials processing, manufacture, distribution, use and disposal. Cold storage is added as a lifecycle stage in this study, as the drug often needs energy-intensive cooling prior to use. Figure 3 provides a pictorial depiction of how LCA is carried out in practice.

LIFECYCLE ASSESSMENT – SCOPE OF ANALYSIS

Aria is a new smart autoinjector platform being developed by Phillips-Medisize to meet important emerging needs in the self-injection market, including improved device sustainability. The autoinjector consists of a re-usable electronic power unit, which replaces the spring-powered drive in a mechanical device, coupled with a disposable cassette that contains the prefilled syringe and provides needle safety, using a moveable shield similar to most disposable devices. The cassette can accommodate both 1 and 2.25 mL prefilled syringes. There are two main models, both of which include Bluetooth connectivity:

- **Aria**, which has a simple user interface
- **Aria+**, which offers several advanced features, including a graphical user interface.

"Aria is a new smart autoinjector platform being developed by Phillips-Medisize to meet important emerging needs in the self-injection market, including improved device sustainability."

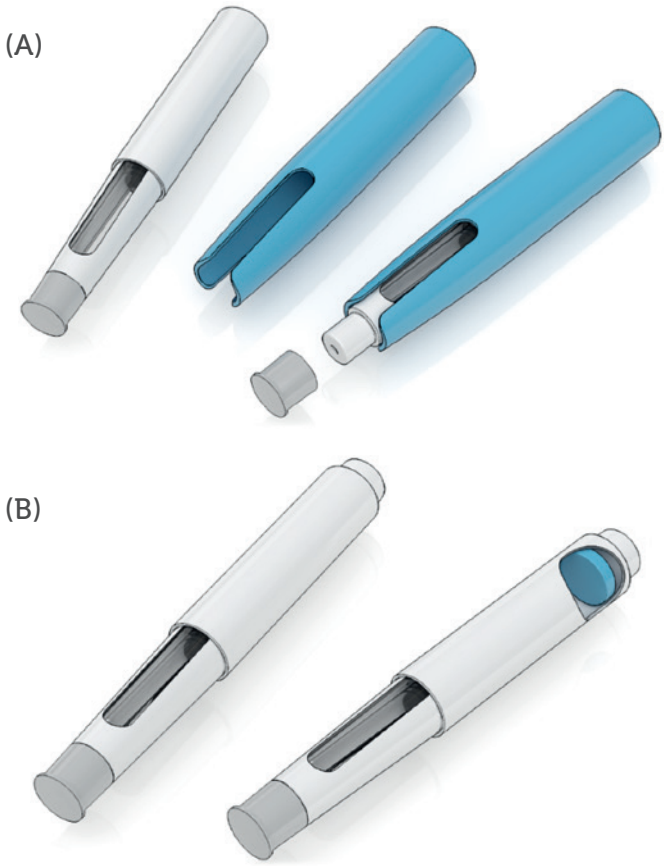

Figure 4: (A) Illustration of an autoinjector with a re-usable connectivity sleeve. (B) Illustration of an autoinjector with a disposable connectivity solution.

Figure 5: Material composition of the Aria+ semi-reusable autoinjector, for both 1 and 2.25 mL delivery volumes, compared with three typical disposable autoinjectors. The material composition of a re-usable connectivity sleeve is compared with that of a disposable connectivity module.

The LCA method used for the study described in this article is based on the ILCD 2011 midpoint+ developed by the European Commission[6,7] and the Ecoinvent 3.0 inventory database.[8] The study followed relevant standards (ISO 14040 and 14044) and underwent critical review by an independent third party to ensure fair conclusions and compliance with the standards. The study focused on the Aria+ model, as it is the less sustainable of the two models, and considered both 1 and 2.25 mL cassettes. For comparison with the Aria, three common disposable autoinjectors were included in the assessment. Finally, the study also evaluated two connectivity technologies (Figure 4):

- A re-usable "add-on" sleeve
- A single-use "add-in" module that is assembled into the disposable autoinjector during manufacture and disposed of with the device after use.

The data on the Aria+ and connectivity add-ons were derived from Phillips-Medisize designs and data for typical disposable autoinjectors obtained from the analysis of commercially available devices to determine the material composition, and then interpolating information regarding manufacture, distribution, use and disposal of the devices. A limitation of the study is that the assembly process was not included for any of the devices.

Several impact categories were included within the scope of the LCA. These impact categories group different emissions into one overarching environmental effect. Each impact category was assessed throughout the LCA for each design type, allowing an apples-to apples comparison of the device design. This study focused on the following impact categories, as they were considered to have the greatest influence on environmental sustainability for the overall device design:

- Greenhouse effect
- Particulate emissions
- Ozone depletion
- Photochemical ozone formation
- Acidification
- Marine eutrophication
- Freshwater eutrophication
- Depletion of abiotic materials
- Land use.

WASTE PER INJECTION

Figure 5 illustrates the material composition of the different devices evaluated in this LCA. Most autoinjectors use a prefilled syringe with a glass barrel and steel needle, which are well characterised in terms of compatibility with drug products and hence are more difficult to replace with more sustainable materials. As such, it is more interesting to consider the use of plastic and metal in the autoinjector itself. The amount of these materials used increases with the dose size and are a key aspect of the overall device design.

Notably, the Aria cassette uses less material than a typical disposable autoinjector. This is primarily due to Aria's lack of a spring; naturally, not needing a spring means less metal in the cassette, but it also means less plastic, as not needing to contain a compressed spring means the cassette does not need to be as rigid as a typical disposable autoinjector. When comparing 1 and 2.25 mL systems, the impact of a semi-reusable device format is even more striking, with the plastic used increasing by 39.8%.

While these calculations provide a simple means of demonstrating waste reduction, assessing the true waste produced by a re-usable device is, in reality, more complicated. Waste reduction depends not only on materials used and product design but also on how many times the device is used throughout its operational life. Therefore, considering waste in terms of "waste per injection" is the more appropriate approach.

Waste per injection associated with a disposable autoinjector is simply the complete autoinjector, as the entire device is discarded after just one injection. On the other hand, the waste per injection for a re-usable autoinjector is defined as:

$$\textit{Waste per injection} = \textit{Cassette} + \frac{\textit{(Reusable device)}}{\textit{(Total injections over device lifetime)}}$$

The Aria re-usable autoinjector has a specified lifetime of 550 injections and, in a best-case scenario, this limit would be reached during the intended three-year lifetime of the device. However, the study considered a more realistic base-case scenario of weekly injections over a three-year period, equating to 156 injections.

This dosing regimen was used to calculate waste per injection for the Aria+, which was then compared with that of today's typical commercially available disposable autoinjectors. The study took packaging (secondary and tertiary) into account,

as well as the instruction leaflet that would usually be provided with the device. As Aria+ is an electronic device, the analysis also included a charger and a more comprehensive user manual than the instructions for a disposable device. Figure 6 illustrates waste per injection, expressed in weight per material type.

The results highlight that about 30 g of waste is associated with the Aria re-usable autoinjector on a per injection basis, with the electronics only contributing 0.25 g per injection. Waste for the disposable autoinjectors was in the 60–70 g range for 1.0 mL devices and 80 g for 2.25 mL devices, depending on the particular commercial device considered. This represents a reduction of approximately 50–60% reduction in per injection waste for the Aria+ re-usable autoinjector, compared with typical disposable autoinjectors.

ENVIRONMENTAL IMPACT

Whereas the re-usable Aria contributes to less waste per injection than disposable autoinjectors, it does contain electronics, which have a higher environmental impact. The following results include the full lifecycle for each of the autoinjectors, including optional connectivity features, and provides a full perspective of the environmental impact in each of the principle environmental impact categories assessed.

Figure 7 illustrates the impact of the re-usable Aria compared with three typical disposable autoinjectors, also highlighting the added burden of including re-usable connectivity with the disposable autoinjectors (hashed bars). The results are illustrated as contributions to environmental impact for the disposable 2.25 mL autoinjector, which was chosen as baseline because it has the highest impact in most categories.

The results show that the Aria autoinjector has a significantly lower environmental impact in seven out of the nine assessed impact categories. Freshwater eutrophication is higher for the Aria, compared with the disposable autoinjectors studied, due to potential sulphidic tailings

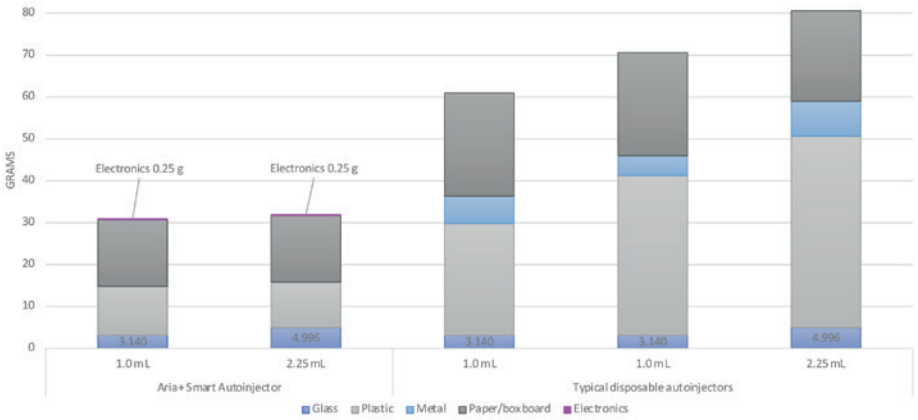

Figure 6: Waste per injection of the Aria+ semi-reusable autoinjector, compared with typical disposable autoinjectors. For the purposes of this analysis, waste per injection was determined assuming a weekly injection for three years, corresponding to a total of 156 injections.

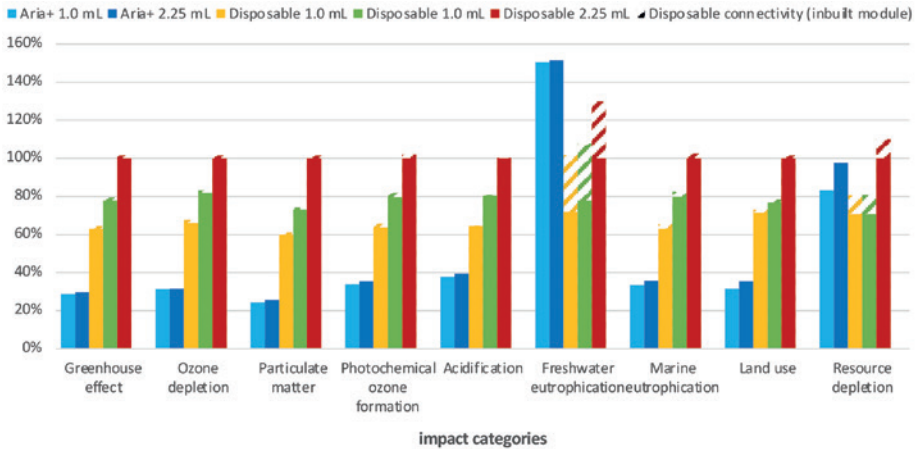

Figure 7: Percentage contributions to each of nine impact categories evaluated in the LCA. The hashed bars indicate the effect of incorporating connectivity features with a re-usable connectivity sleeve.

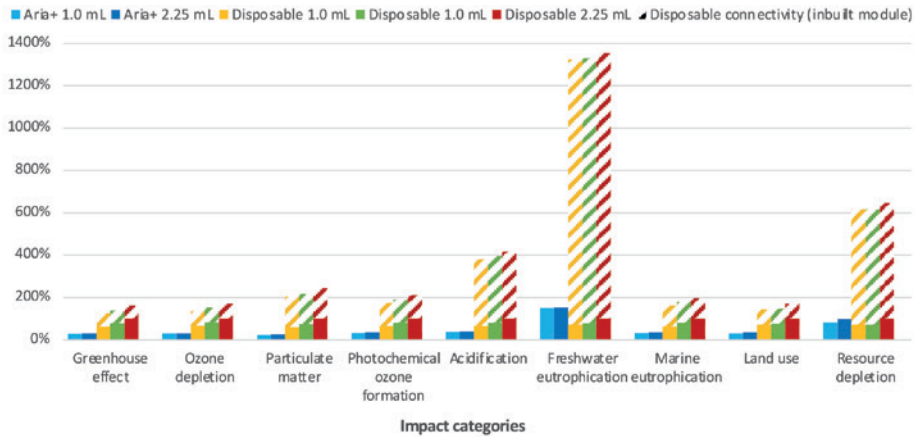

Figure 8: Percentage contributions to each of nine impact categories evaluated in the LCA. The hashed bars indicate the effect of incorporating connectivity features with a disposable connectivity module.

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"From these preliminary LCA results, it can be concluded that the re-usable Aria autoinjector has the lowest overall environmental impact in the majority of impact categories and can therefore be considered a more sustainable solution than typical disposable autoinjectors, assuming a weekly injection regimen."

(waste material remaining after ore processing) associated with the mining of metals for the electronics. The rare earth metals used in the electronic components also lead to the Aria autoinjector having a greater environmental impact than both of the 1.0 mL disposable autoinjectors for resource depletion, though it should be noted that the Aria has a lower or equivalent environmental impact to the 2.25 mL disposable autoinjector in this impact category.

For disposable autoinjectors, the inclusion of a re-usable connectivity sleeve increases the device's impact on freshwater eutrophication and resource depletion, due to the additional materials used in the sleeve electronics. However, when a disposable connectivity module is included in the analysis, the environmental burden increases significantly. As shown in Figure 8, inclusion of a disposable connectivity module leads to a significant increase in the environmental impact in all nine categories, and up to a more than 1,300% increase in freshwater eutrophication.

Disposable connectivity can therefore be seen to be challenging from a suitability perspective, compared with other available solutions. Although the add-on sleeve solution lowers the environmental impact compared with a disposable connectivity module, it requires the user to change it from one device to another, increasing user burden, meaning a user may omit this step and hence lose usage data, limiting the value of the connectivity sleeve and the connectivity features it provides.

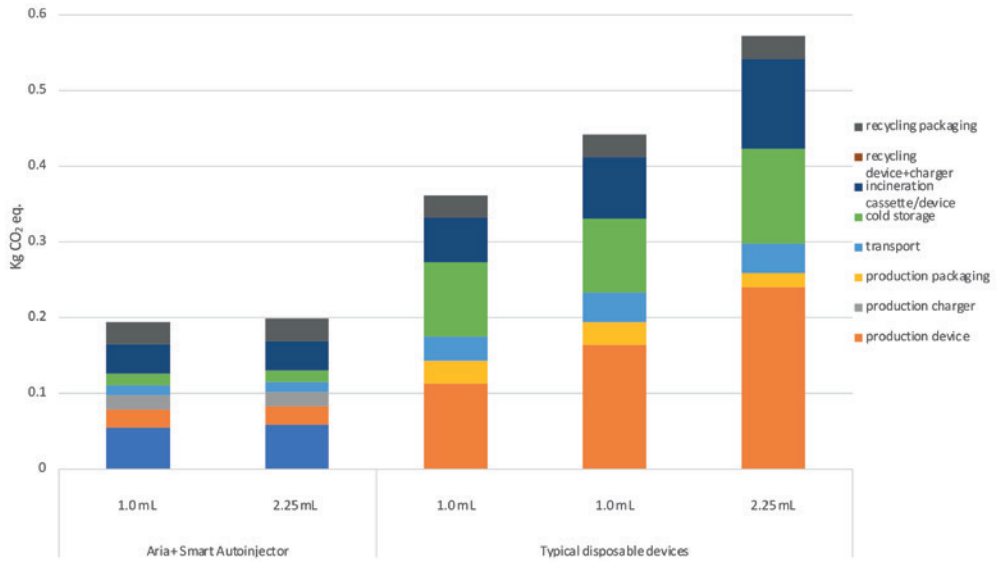

Figure 9: Per injection breakdown of contributions to the greenhouse effect for each of the devices evaluated in the LCA. As shown, drivers for the reduction of greenhouse gas emissions for the Aria+ autoinjector were savings from device production, cold storage and device/cassette incineration.

From these preliminary LCA results, it can be concluded that the re-usable Aria autoinjector has the lowest overall environmental impact in the majority of impact categories and can therefore be considered a more sustainable solution than typical disposable autoinjectors, assuming a weekly injection regimen. Furthermore, when connectivity is added in as a device feature on disposable autoinjectors, whether a re-usable sleeve or disposable module is used, the data demonstrate that the Aria provides the best solution, from a sustainability standpoint.

Although beyond the scope of the current work, it is also worth noting that connectivity itself can also have positive impact on sustainability if it can reduce other environmental impacts, such as face-face consultations, hospitalisations and drug wastage.[9]

BREAKDOWN OF CONTRIBUTIONS

To further probe the environmental impact of the devices evaluated in the LCA, we can consider the cause of the emissions for each impact category. For simplicity, Figure 9 only presents the results of contributions to the greenhouse effect, also called a CO_2 footprint (the full LCA study investigated all impact categories in this fashion). The results confirm an overall lower contribution to the greenhouse effect by the Aria re-usable autoinjector. The impact from device production is slightly lower when comparing the 1 mL disposable autoinjectors, but significantly lower in comparison with the 2.25 mL disposable autoinjector.

It is interesting to note that the Aria re-usable autoinjector has a lower contribution to the greenhouse effect for the post-production value chain activities (transport, cold storage and disposal) when compared with typical disposable autoinjectors. This is because Aria can be re-used 156 times for the weekly injections considered in the analysis, based on the study model, and therefore these contributions are split across those multiple injections. Greenhouse gas emissions due to the disposable cassette are significantly lower, as the device and cassette both use less material, weigh less and have a smaller volume, the last of which is important for cold storage.

As previously mentioned, per-injection calculations for Aria were based on a weekly injection model (156 injections over the device's lifetime) – for re-usable autoinjectors, the sustainability performance depends on how many times the device is re-used over its lifetime. By contrast, the environmental impact of disposable autoinjectors remains fixed because the device is always discarded after a single use. As such, to identify the most sustainable drug delivery device, pharmaceutical companies need to consider a therapy's treatment protocols, and the total number of injections required over a relevant period. Evaluating greenhouse gas emissions, per injection, over the lifetime of a 2.25 mL Aria device, compared with a typical 2.25 mL disposable autoinjector, allows prospective users and pharmaceutical companies to see the true environmental impact of the Aria re-usable autoinjector.

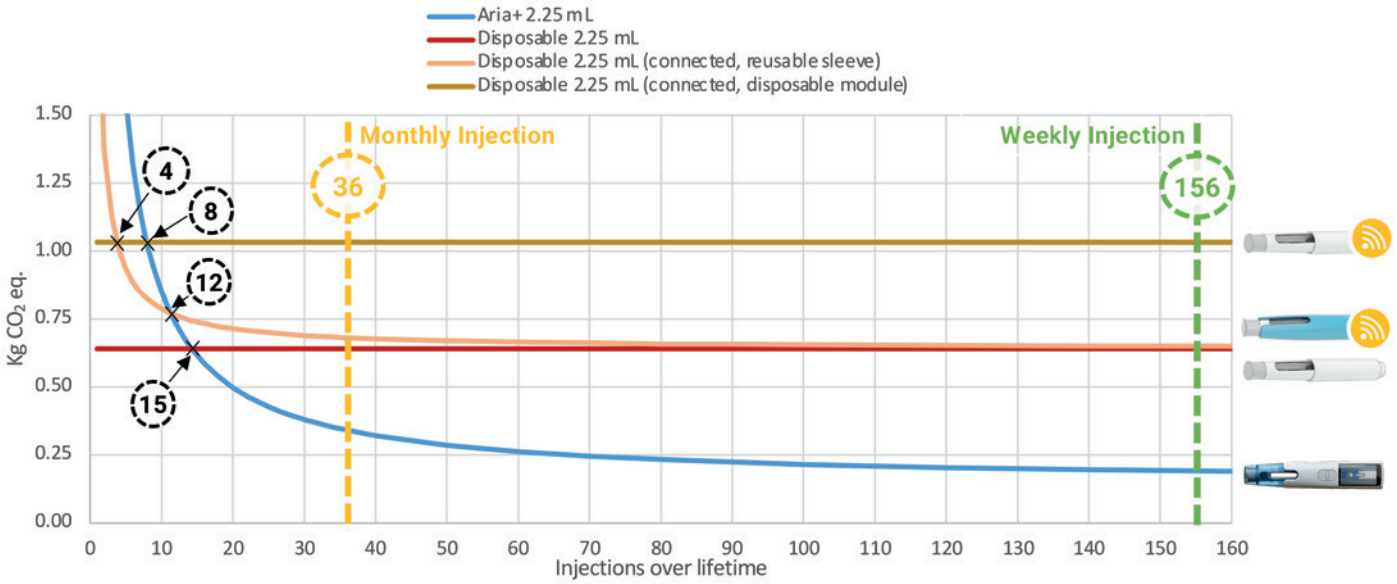

Figure 10: Correlation between injections over lifetime and impacts on the greenhouse effect for the 2.25 mL autoinjectors evaluated in the LCA.

Figure 10 highlights how the greenhouse gas emissions, per injection, decrease over the lifetime of a 2.25 mL Aria autoinjector. While a decrease is also observed for a typical autoinjector used with a re-usable connectivity sleeve, the emissions associated with Aria are roughly half that, even in a scenario where only monthly injections are considered. When weekly injections are considered in the model, emissions associated with Aria are less than half those of a disposable device paired with a re-usable connectivity sleeve. In contrast to devices with re-usable components, Figure 10 also shows how devices designed to be entirely disposable have a fixed per-injection emission profile – no improvement in the emission profile is observed.

From a treatment perspective, the results seem to suggest that if a patient only needs up to 15 injections in total, a disposable autoinjector may then be the better choice from a sustainability perspective. However, when connectivity is included, a disposable autoinjector in combination with an in-built connectivity module only has a better sustainability solution for up to four injections, and a disposable autoinjector in combination with a re-usable sleeve is better for four to eight injections. For more than 12 injections, Aria provides the most sustainable solution. Finally, considering two treatment scenarios, a monthly and a weekly injection regimen over three years, the re-usable Aria autoinjector is shown to have the lowest CO_2 footprint.

> "For re-usable autoinjectors, the sustainability performance depends on how many times the device is re-used over its lifetime. By contrast, the environmental impact of disposable autoinjectors remains fixed, because the device is always discarded after a single use."

CONCLUSIONS AND FUTURE WORK

It is evident from this work that the expectation of Aria as a more sustainable approach to self-administration of drugs for chronic diseases has been qualified by the use of an industry-standard lifecycle assessment. Furthermore, we have shown in other work that, in achieving this, Aria has not compromised other important requirements for autoinjectors around convenience, ease of use and safety. Pharmaceutical companies have also recognised these benefits and, importantly, so have users in the human factors studies that Phillips-Medisize has carried out.

ABOUT THE AUTHORS

Emil Fraenkel is a Sustainability Engineer at Phillips-Medisize, based in the company's Development Centre in Denmark. Mr Fraenkel holds an MSc in sustainable product development and is passionate about resolving environmental issues in the pharmaceutical industry. At Phillips-Medisize, Mr Fraenkel works with quantitative sustainability assessment, practices lifecycle assessment and drives product sustainability initiatives.

Bjarne Sørensen, is a Director of Front-End Innovation at Phillips-Medisize, based in the company's Development Centre in Denmark. With more than 35 years of experience within Product, Strategy and Business Development, Mr Sørensen has a very visible track record within different business areas. At Phillips-Medisize he participates in customer programmes, typically involving electronic injectors and connected health systems. He is also deeply involved in new electronic platform programmes, especially on conceptual, technical and sustainability aspects.

As connectivity becomes more important in drug delivery, the fact that this can be built into reusable electronic autoinjectors, such as Aria, creates further sustainability and/or usability advantages over similar solutions for disposable devices.

Phillips-Medisize has found the LCA approach to be very insightful in developing the device concept and design and as it progresses into clinical and commercial manufacture, and plans to repeat the calculations to support optimisation of production and distribution logistics. The company also plans to use LCA to consider more sustainable design and manufacture as a lifecycle opportunity for Aria as the availability of more sustainable materials and processes become available. Phillips-Medisize also plans to expand the work to other device platforms and programmes.

ABOUT THE COMPANY

Phillips-Medisize, a Molex company, is an end-to-end provider of innovation, development, manufacturing and post-launch services to the pharmaceutical, diagnostics, medical device and speciality commercial markets. Post-launch services include a connected health app and data services. Backed by the combined global resources of Molex and its parent company Koch Industries, Phillips-Medisize's core advantage is the knowledge of its employees to integrate design, moulding, electronics and automation, providing innovative high-quality manufacturing solutions.

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SUCCESSFULLY BALANCING THE NEEDS OF THE PLANET WITH THE NEEDS OF THE PATIENT

Here, Christophe Marie, Global Product Sustainability Director, and Taylor Price, Manager, Global Sustainability, both at AptarGroup, and Julien Storz, Director of Business Development, Consumer Healthcare, at Aptar Pharma, chart the commitments and progress made to date by Aptar in achieving its sustainability targets. The authors also provide examples of integrated, circular economy initiatives undertaken by Aptar Pharma at a product solution level and comment on concrete commitments that can be made to further progress towards sustainability.

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NO ONE IS ALONE IN THE JOURNEY TOWARDS GREATER SUSTAINABILITY

Industry continues to transition away from the traditional, linear model of "take-make-consume-throw away" and adopt the values of the circular economy, where waste and pollution are designed out of product lifecycles. Furthermore, business leaders are increasingly aware of their responsibility to define their company's own sustainability-related commitments and targets, and to ensure strategies are backed by authentic, measurable action. As such, with the sustainability credentials of the drug delivery sector coming under increasing scrutiny, learning from the experiences of other organisations or parent companies is one way to achieve this goal.

Aptar's sustainability strategy considers the impact of its business from the perspective of people, product and the planet (Figure 1). Within that, the circular economy concept stands alone, defined by a self-contained vision and specific goals and targets, even though the principles of the circular economy touch all aspects of the business. Therefore, a key goal for Aptar is to show leadership through the implementation of innovative measures that will increase recycled content within products while improving recyclability, re-usability and compostability while also phasing out substances of high concern. The ultimate goal is to significantly reduce the volume of plastic ending up as waste. Collaboration with expert sustainability partners plays a crucial role in achieving this goal, ensuring that the company can improve upon what it understands and measures.

One such partnership is Aptar's involvement with the Ellen MacArthur Foundation (Cowes, UK), a non-profit organisation with a mission to accelerate the transition to a circular economy. Since 2019, Aptar has been an active member of the foundation's "New Plastics Economy Global Commitment". With their guidance, Aptar has led a recyclability work group with the foundation's CE100 Network and piloted Circulytics, a tool which helps companies assess their circularity.[1]

Aptar's work with the Ellen MacArthur Foundation is complemented by its involvement with other global organisations focused on driving the circular economy. This includes membership of the World Business Council for Sustainable Development (WBCSD) (Geneva, Switzerland), through which Aptar has contributed to the quantitative, universal and transparent circular transition indicators (CTI) framework, designed to

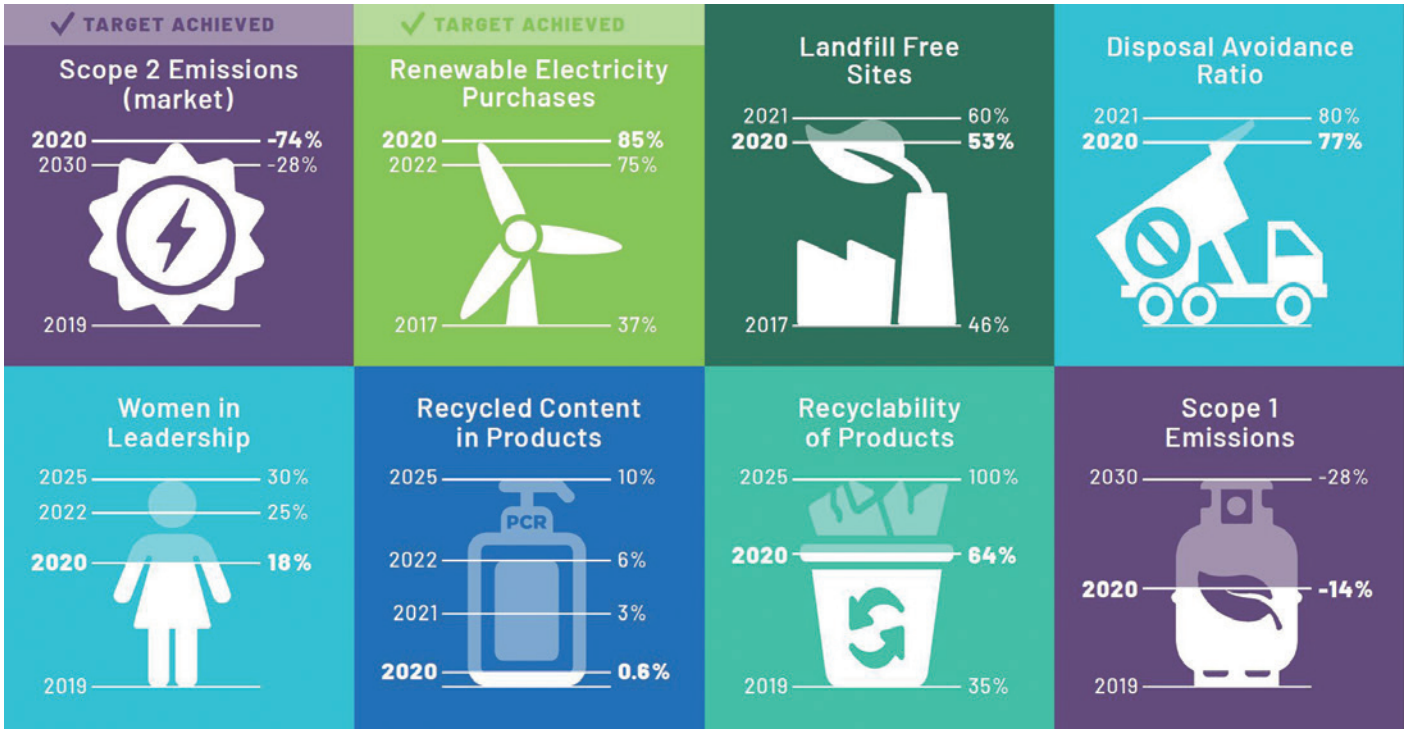

Figure 1: Aptar Group's public sustainability commitments, designed to support the wider circular economy initiative.

measure circularity and create a common language for all stakeholders. Aptar has also participated in the piloting of a Social Organisational Lifecycle Assessment (SO-LCA) tool with the United Nations environment programme.

The wider Aptar Group has expertise in the food, beverage, beauty, personal care, home care and active packaging sectors. As such, Aptar Pharma is able to benefit from considerable company-wide learning opportunities and initiatives, including cross-organisational collaborations that have sped up development times and derisked projects. More specifically, the highly regulated nature of the pharmaceutical market in which Aptar Pharma operates means that introducing ever more sustainability measures can only be achieved in line with the stringent parameters designed to guarantee product safety and efficacy, and to safeguard patient welfare. The following case studies highlight how Aptar Pharma continues to push its sustainability agenda forward within the limits of this framework.

ECO-DESIGN AND PRODUCT LIFECYCLE ASSESSMENTS

To enhance understanding of how products could impact the environment, Aptar has developed an Eco-Design Tool that incorporates Lifecycle Assessment (LCA) functionalities. Further improved in 2020 by adding additional enhancements, the company's newly optimised LCA tools help product designers evaluate the inputs, outputs and potential environmental impacts of an entire product system throughout its lifecycle (according to ISO 14040) – from raw-material extraction through processing, manufacturing, distribution, use, re-use and maintenance through to disposal or recycling.

The key performance indicators measured by the LCA include CO_2 footprint and recyclability, with Aptar's development processes now including use of the LCA tool for all new Aptar Pharma product development projects.

This centrally developed, integrated initiative is an example of the company's commitment to deliver holistic, enterprise-wide improvements, rather than isolated and fragmented initiatives. This approach to continuous cross-functional improvement has enabled advancements in several product areas.

> "To enhance understanding of how products could impact the environment, Aptar has developed an Eco-Design Tool that incorporates LCA functionality."

AIRLESS+ DERMAL DELIVERY – ACCEPTED, ACCESSIBLE, AVAILABLE AND RECYCLABLE

The focus on sustainable design embodied in the Eco-Design Tool, has helped lead to important product breakthroughs at Aptar. An example is Aptar Pharma's Airless+ range of highly recyclable products for dermal drug delivery, which addresses the need for greater patient protection, as outlined in the new US Pharmacopeia (USP) <661> "Plastic Packaging Systems and their Materials of Construction", by using medical-grade resins.

From a sustainability perspective, the Airless+ packaging ensures low amounts of residual product thanks to its high evacuation rate, which in turn supports product longevity. Additionally, as the range could be processed in existing recycling streams, it meets cyclos-HTP's (Aachen, Germany) certification requirements – Airless+ has a rating of "Class AAA", with a 96–98% "excellent recyclability" rate (for raw, natural packaging without décor and label) due to using only moulded components and no metal parts. More information is available

directly from Aptar Pharma with respect to specific information regarding the regional application of the cyclos-HTP certification.

Airless+ is processed in existing recycling streams and is manufactured in a facility that has achieved ISO 14001 and ISO 50001 certifications (Figure 2A). This facility has also achieved the International Sustainability Carbon Certification (ISCC) PLUS, which is only awarded by employing a thorough internal traceability process along the entire supply chain, taking a "mass balance approach" to trace the flow of materials that are being mixed during production. This constant monitoring and counting approach makes it possible to trace the level and characteristics of circular and/or renewable content in the final product.

BAG-ON-VALVE – RECYCLABLE CONTINUOUS DISPENSING SOLUTION

Bag-on-Valve (BOV) continuous dispensing technology is another packaging application where patient care and the circular economy can both be achieved in equal measure. Widely recognised to deliver a cleaner, superior application through complete separation of product from propellant, Aptar Pharma's BOV technology is also recyclable, as with the Airless+ range, achieving the cyclos-HTP qualification for "good recyclability" of the raw packaging (Figure 2B); specifically the certification was approved for Aptar Pharma's BOV 30 mL, Pacifica Actuator and Aptar Pharma's BOV 400 mL, Nasal EP Actuator including the cap and a standard aluminium can (more information is available directly from Aptar Pharma).

THE FUTURE LOOKS BRIGHT FOR FULLY RECYCLABLE MONO-MATERIAL PUMPS AND TUBES

Mono-material-based products are key in unlocking further gains in recyclability. In May 2021, Aptar announced the launch of the fully recyclable mono-material pump, Future, which has been designed using exclusively polyethylene (PE) material. Future is certified by cyclos-HTP and is graded class "A" by RecyClass (Brussels, Belgium) – a cross-industry initiative to establish traceability and a harmonised recycling approach in Europe.

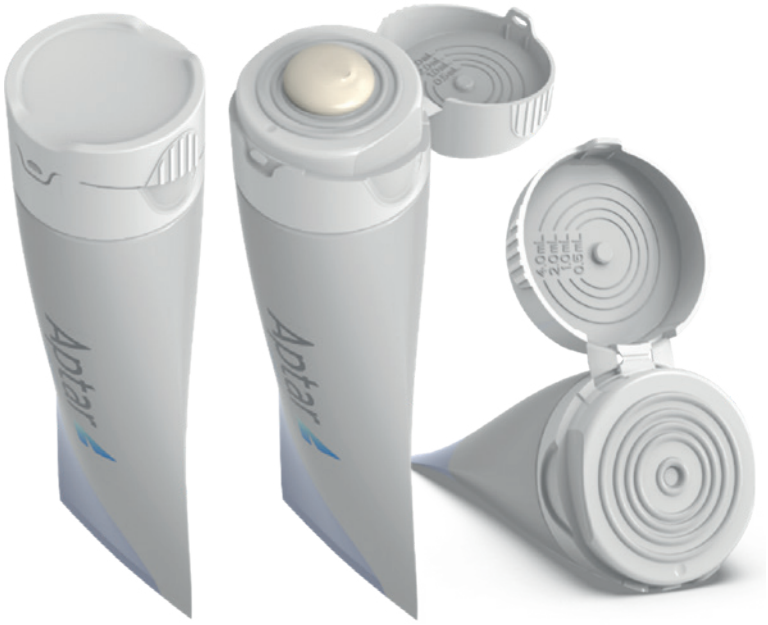

Figure 3: Proventu, Aptar Pharma's first mono-material tube.

Figure 2: (A) Aptar Pharma's Airless+ product range, manufactured according to ISCC PLUS standards, has an excellent recyclability (cyclos-HTP AAA). (B) Aptar Pharma's BOV products with cyclos-HTP certification grade A.

Further cross-functional collaboration within Aptar Pharma includes the recent launch of Proventu, the company's first mono-material tube for pharma (Figure 3). Using only polypropylene (PP), Proventu eliminates the need for a separate elastomer valve and incorporates a tethered cap, making it fully recyclable, while also preserving bulk integrity with a no-suck-back function. Proventu does not require any compromise from a user perspective, as it provides a no-mess, user-controlled application, one-handed closing and a dose measuring function. Proventu is also available with a child-resistant, senior-friendly (CRSF) option.

Aptar continues to develop innovative solutions that utilise mono-materials, having identified them as a key element of their recyclability strategy. Much like its commitment to source and using renewable feedstock, as outlined further in this article, Aptar sees this as a crucial aspect of its sustainability approach.

CREATING A SUSTAINABLE ALTERNATIVE MATERIAL AT SOURCE

A key focus for any sustainability commitment in the pharmaceutical sector must be the identification and implementation of resins that can reduce that impact. Right now, there are three available sustainable options for resins.

"A key focus for any sustainability commitment in the pharmaceutical sector must be the identification and implementation of resins that can reduce that environmental impact."

Mechanically recycled post-consumer resin (PCR) is a plastic sourced from waste that has been mechanically reprocessed for use in the manufacturing of new products. Although Aptar's other businesses already use this material, mechanically recycled PCR is not yet able to meet all the regulatory and qualitative requirements needed for pharmaceutical use.

Chemically recycled PCR originates from plastic waste that cannot be recycled mechanically, such as coloured, multilayered or multi-material packaging and films. These materials can be recycled into a pharma-grade material that fulfils regulatory requirements, but is currently only available in limited quantities. However, the sustainability benefits are compelling; the process mitigates against fossil fuel depletion, contributes to waste management and reduces the CO_2 emissions associated with incineration. As momentum continues to build behind the chemical recycling process, it is anticipated that higher volumes will be available as early as 2025.

The third option is the use of resins and chemicals from renewable feedstock, such as residue oils, fats and sustainably produced vegetable oils. As with chemically recycled options, pharma-grade polymers and chemicals can be achieved without impacting fossil fuel depletion; indeed, the process limits CO_2 emissions in the atmosphere, contributing to a more circular economy. Both chemically recycled material and resin from renewable feedstock are managed through a mass balance accounting system and require a specific certification scheme, such as ISCC PLUS.

With a supply chain established and feedstocks demonstrating compatability with the sector's specific regulatory requirements, these renewable resins will continue to emerge as a more sustainable option for pharma partners.

SHAKING UP THE pMDI INDUSTRY WITH A SUSTAINABLE ALTERNATIVE PROPELLANT

While developments such as this introduce greater potential for the sustainability of medical products in the future, when it comes to pulmonary drug delivery, decarbonisation efforts right now are dominated by a central challenge: how to move away from propellants such as hydrofluoroalkanes (HFAs) HFA P227 and HFA P134a and towards newer, lower impact approaches. Crucially, this challenge must be overcome without losing sight of two fundamental priorities: ensuring patient safety and supporting regimen adherence. The restriction on F-gases, including hydrofluorocarbons (HFCs) and HFAs used as propellants in pressurised metered dose inhalers (pMDIs), has been made official through the Kigali Amendment (2016) to the Montreal Protocol, which seeks to phase down the use of HFC/HFAs by 85% by 2047 across most countries.

Many drug delivery and pharma companies, including Aptar Pharma, are committed to defining the next phase of the pMDI market. HFA P152a and HFO1234ze are two potential alternative low global warming potential (GWP) propellants with compelling environmental cases. HFA P152a is entering its final year of an exhaustive full-inhalation propellant toxicology study and has raised no adverse findings so far. Although there are still important safety hurdles to be overcome before HFA P152a can be introduced as part of a marketable product, the current outlook is promising from a safety perspective.

"When it comes to pulmonary drug delivery, decarbonisation efforts right now are dominated by a central challenge: how to move away from propellants such as HFAs HFA P227 and HFA P134a and towards newer, lower impact approaches."

It is promising from a sustainability angle too, with research presented by the University of Manchester (UK) showing that replacing HFA P134a with HFA P152a would reduce the climate change and global warming impacts of inhalers in the UK by 90–92%.[2] HFO1234ze provides an even lower global warming potential (approximately a 99% reduction), as well as having a lower flammability concern. However, the long-term toxicology profile of HFO1234ze remains uncertain, with limited data available within the public domain to date. Aptar Pharma is working with both propellants with various collaborative partners, with both propellants offering exciting alternative pathways from a formulation stability perspective and a sustainability perspective.

A CIRCULAR ECONOMY REQUIRES SUSTAINABLE EFFORT AND INVESTMENT

The journey towards a circular economy has only just begun and there remains much work to do. The drug delivery sector has a real opportunity to make a meaningful and sustainable contribution and, to that end, Aptar has committed to some very clear, measurable, science-based targets. Firstly, to reduce absolute Scope 1 and 2 greenhouse gas emissions (GHGs) by 28% by 2030 and to reduce absolute Scope 3 GHG emissions by 14% by 2030. Secondly, by the end of 2021, more than 60% of Aptar's manufacturing locations will be Landfill-Free certified through the company's internal certification programme, and Aptar will achieve at least 80% disposal avoidance of operational waste globally. Thirdly, Aptar will continue to work towards the target of 100% renewable energy usage, having already surpassed its original 2022 goal.

FOR TODAY, FOR TOMORROW, FOREVER

As the famous Chinese proverb states, "A journey of a thousand miles begins with but a single step". Aptar Pharma, as a forward-looking provider of drug delivery solutions, embraces its obligation to innovate in a way that successfully delivers on the needs of the patient while minimising the impact on the planet. As an individual company and as an industry, it is imperative to take the initiative, make those first steps and implement the measures that will introduce the benefits of the circular economy.

This is not a journey any organisation has to take alone. Access to resources, precedents and collaborative partners is greater than it has ever been. Methods for benchmarking, continuous improvement and measurement are also well established.

For Aptar Pharma, the benefit of forming part of a sustainably focused group has allowed and enabled some innovations to be delivered quickly, and without risk, to the benefit of the company's pharma partners, patients and the planet. Other innovations are close to completion, while some remain in their infancy. Whatever the stage of development, it is important to keep in mind the ultimate goal – addressing social and environmental imperatives that create purpose and shared societal value, so that future generations may benefit from Aptar's work.

It is Aptar's deep commitment to create solutions that respect the environment, conserve natural resources and improve life on earth. As a leader in the drug delivery industry, it recognises, embraces and is determined to continue to lead the way in creating a circular economy, with repeatable and positive effects on people, the planet and products.

ABOUT THE COMPANY

For pharma customers worldwide, Aptar Pharma is the go-to drug delivery expert, providing innovative drug delivery solutions across a wide range of delivery routes, including nasal, pulmonary, ophthalmic, dermal and injectables. Aptar Pharma Services provides early stage to commercialisation support to accelerate and derisk the development journey. With a strong focus on innovation, Aptar Pharma is leading the way in developing connected devices to deliver digital medicines. With a global manufacturing footprint of 14 GMP sites, Aptar Pharma provides security-of-supply and local support to customers. Aptar Pharma is part of AptarGroup, Inc. (NYSE:ATR), a global leader in the design and manufacturing of a broad range of drug delivery, consumer product dispensing and active materials science solutions.

ABOUT THE AUTHORS

Christophe Marie is Global Product Sustainability Director within the Aptar Innovation Excellence Team, leading the Solutions Pillar of Aptar's sustainability strategy. Mr Marie's primary goals include building and driving a strategy to achieve the commitments made by Aptar through the New Plastics Economy Global Commitment, which is led by the Ellen MacArthur Foundation in collaboration with the UN Environment Programme. Prior to his product sustainability role at Aptar, Mr Marie was part of Aptar Pharma from 2002 to 2018, where he held various positions within the R&D and Global Market Development teams.

Taylor Price is Manager, Global Sustainability at AptarGroup Inc. Recently named "2021 Rising Star" by Plastic News, Ms Price is an expert at delivering results on Aptar's global sustainability strategy. Her work includes robust strategy setting, sustainability reporting, communication and supplier engagement. She also works to advocate for a circular economy to address social and environmental imperatives that create purpose and shared societal value.

Julien Storz is Director of Business Development within Aptar Pharma's Consumer Healthcare (CHC) division. He holds a bachelor's degree in business administration and has over 19 years of medical industry experience. Mr Storz joined Aptar Pharma and the CHC global market development team in 2019, where he is responsible for supporting business development efforts across numerous application fields in addition to driving CHC sustainability efforts.

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Working daily to improve the health of our patients and our planet

As a leader in drug delivery, Aptar Pharma works daily to deliver innovative technology platforms that have a positive impact on patients and the planet.

In line with our public sustainability targets for Beauty + Home and Food + Beverage products, Aptar Pharma continues to invest in renewable feedstock resins, further develop mono-material-based products and prepare for the introduction of new low GWP propellants in the pMDI market.

Furthermore, our focus on sustainable design has enabled us to make important product breakthroughs with both our Airless* dermal drug delivery range and our Bag-on-Valve (BOV) continuous dispensing technology, both achieving cyclos-HTP recyclability certifications with AAA and A classifications, respectively.

It is Aptar's deep commitment to create solutions that respect the environment, conserve natural resources, improve life on earth, and safeguard patient welfare. Because for us, helping to keep the planet and its people healthy shouldn't be a compromise.

A journey of a thousand miles begins with a single step. To find out how Aptar can help you on your sustainability journey, to learn more about our initiatives and to read our 2020 Corporate Sustainability Report, visit **www.aptar.com/sustainability**

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Aptar pharma

DATA-DRIVEN SUSTAINABILITY IN AUTOINJECTOR DEVELOPMENT

In this article, Frederick Gertz, PhD, Manager, Data Science, and Yves Steffen, Global Sustainability Director, both of SHL Medical, outline the company's approach to sustainability, involving leveraging the experience of its data science department to enhance the output of its sustainability department.

What does it truly mean to be sustainable and how can we achieve it? SHL Medical is not alone in asking these questions. Going beyond the obvious reduction in carbon footprints, sustainability encompasses a whole multifaceted paradigm for operating a company. If the UN Global Compact Principles are used as a guideline, it encompasses climate, social justice, education, health and equality, to name just a few areas.[1] For SHL, the goal remains the same – how to produce products in such a way that leaves the world a better place, for the planet and its people. To that end, SHL has found the best way to be more sustainable is to keep its footprint small to begin with.

> "SHL has derived an interesting partnership between its data-science efforts and its sustainability efforts."

Over the decades, SHL has made great efforts to increase its efficiency, to incorporate lean thinking and implementations into its production and supply, and to leverage the most cutting-edge automation and information technologies. This continuous improvement process has shown that sustainability *is* efficiency – and the company's goals are not hindered by its aim to be a sustainable company.

In this holistic approach to sustainability, SHL has derived an interesting partnership between its data-science efforts and its sustainability efforts. Since one of the goals of the data-science department is to enhance internal processes and improve efficiency, SHL has begun marrying the efforts of the two areas to bring new insight to its sustainability initiatives while also helping it to maintain its leading position as a solutions provider of autoinjector devices. These efforts have helped expand the company's data-driven decision processes beyond pure business decisions. SHL is uniquely positioned to provide this sort of value due to its vertically integrated structure and 30 years of experience in the field.

THE CONVERGENCE OF DATA AND SUSTAINABILITY

So how does the data-driven portion of an operation meld with the sustainability areas? The answer is best found in both past innovations for process development and also in future areas. Many companies today focus their control methodology on statistical principles, with the Six Sigma approach being the most commonly observed within the industry. The techniques aim to improve quality by limiting variation within the process so that a consistent product is almost always produced. Six Sigma techniques for control strategies came from Japan in the 1970s and were popularised by car manufacturer Toyota. In that same era, another Japanese school of quality was also being developed by Genichi Taguchi. His proposed system for quality incorporated *loss functions* as a sort of mathematical description of the impact that each measured characteristic would have on a certain outcome.

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In brief, loss function refers to a mathematical description of a preferred outcome using the data currently generated in the company to quantify how far away the current situation is from the ideal. What is interesting about this methodology is that much of the debate around it is centred around the discussion of what the loss function should maximise. For most corporations, the answer is usually either quality or revenue or something similar. Mr Taguchi thought otherwise and believed that "social good" was to be maximised. Built into the mathematical function that Mr Taguchi described, known as the "Taguchi loss function", were variables associated with social wellness and benefit.

The data-science team has begun developing ways to incorporate this aspect of thinking into SHL's own control plans and quality improvement initiatives, with optimisations focused not just around typical quality outputs but also incorporating aspects of energy efficiency and human efficiency. In fact, much of this has led the way for research in using data science in production environments. Already, companies have used the large data outputs from their internal manufacturing execution systems to derive areas of increased energy efficiency. In the manufacturing of moulded plastics in particular, where the entire plant essentially operates as a large heat exchanger,[2] there are numerous opportunities to improve cycle times, energy use and effective heat transfer to lower carbon footprints. Similarly, these areas are further enhanced when they are leveraged to reduce scrap rates, ensuring that as little material as possible is wasted throughout the production process.

These areas of optimisation may seem familiar – and that is because they are. Energy efficiency, scrap rate and higher throughput are all areas that any company would strive towards to improve their production output during their normal

"Sustainability initiatives and thinking in the organisation help SHL by providing it with additional robust parameters on which it can optimise."

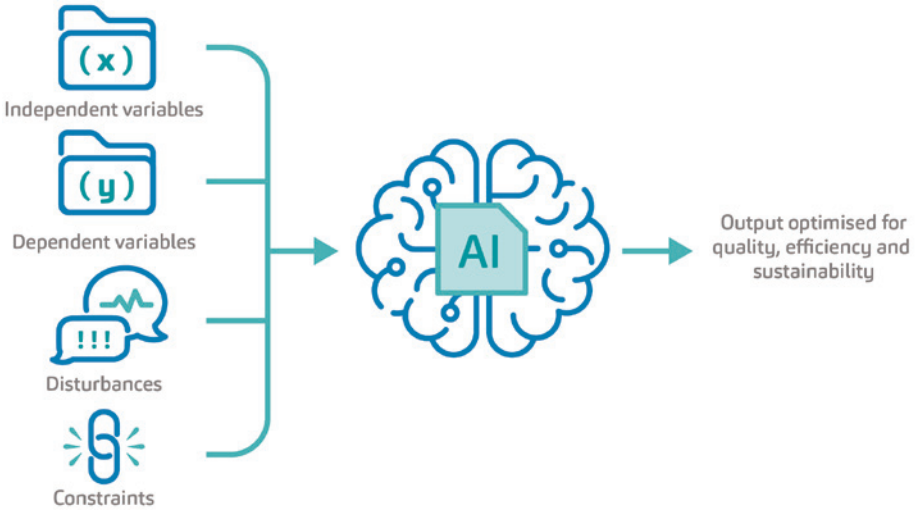

Figure 1: Diagram depicting how AI can use large amounts of data to produce value from a variety of disparate sources.

continuous improvement process. The areas also highlight how these sustainability efforts are in no way removed from the typical operations of any modern manufacturing operation. Sustainability issues can in some corporations be seen as a burden, an additional obstacle that must be overcome, but SHL has seen that these endeavours are in fact an additional pathway to success.

Sustainability initiatives and thinking in the organisation help SHL by providing it with additional robust parameters on which it can optimise. This robustness can give additional performance indicators to maximise, and further help highlight how production improvement efforts are having effects beyond just the financial bottom line. The additional parameter for project success makes some decisions easier. For example, if two options seem essentially equal, the company can now select the one that has the greatest effect on its sustainability goals. These types of avenues and endeavours can be a great enhancement to any company's data-driven efforts, and SHL continues to embrace these techniques.

AI-ENHANCED SUSTAINABILITY INNOVATION

Factory-based artificial intelligence (AI) implementations have also shown a large performance increase over standard techniques, particularly in areas where automated controls are being used. The use of AI within the tool chain of programmable logic controls can allow for drastic increases in efficiency (Figure 1). A good example of this is in the control of asynchronous motors, where machine-learning techniques from neural networks to genetic algorithms have been used, and shown to consistently outperform standard controllers.[3] For many operations, this is incredibly exciting as the intuition of many factory managers is that the switch to electric-based motors had already drastically increased performance, and they are under the impression that further increases in efficiency are just not available to them.

"The use of sustainable materials and techniques can even be a source of innovation."

Further, the use of sustainable materials and techniques can even be a source of innovation. By using generative methods and a variety of other cutting-edge techniques, much research has investigated the use of AI to help solve design problems. A better-known use of these solutions has been in the area of materials science, where high-dimensional materials spaces can be defined using a variety of different input factors. These high-dimensional spaces are well suited for solutions from new AI techniques, such as attention-based networks,[4] and can allow companies to iterate on many materials to find one that is not only best suited for their design but also well suited for their sustainability goals. In this way, companies might explore multiple alternatives that they might not have originally considered, allowing for innovative use of novel materials.

> "It is easy to say that you desire to have your entire factory run more efficiently but, in a practical sense, you will need to choose your battles."

TWO SIDES OF THE SAME COIN

In the interest of corporate and global welfare, SHL is keen to encourage others to adopt its so-called data-driven approach to sustainability. But once you combine the efforts of these two, now seemingly well-aligned teams together, the next step is how best to leverage them to have real-world impact.

One of the first goals of any such marriage is to work together to define success. Your sustainability team, depending on their maturity, will either have predefined metrics for success or will be currently forming them. In the latter case, the data-science team can play an important part in providing reasonable goals – ones that truly help the initiative as well as ones that are reasonably obtainable. Once the agreed-upon metrics have been determined, whether it be related to waste, energy use or carbon footprint, to name but a few, the data-science team can begin to work on helping prioritise your goals. Using energy savings as an example, it is easy to say that you desire to have your entire factory run more efficiently but, in a practical sense, you will need to choose your battles.

Here is where data science is truly beneficial. By combining information across your entire manufacturing space and using cost functions related to your sustainability goals, your team can begin to optimise and, most importantly, prioritise which areas of the operation not only use the most energy but also are most capable of being changed to a more efficient status. Using this data, as well as real-time analytics, the sustainability team can immediately begin selecting areas with the highest impact and visualise those changes to highlight their benefits.

It is also important to highlight that choosing these goals in no way must be misaligned with business goals. Using well-developed methods from operations research, and understanding the company's current financial models and projections, the team can also optimise to have the smallest impact on those plans – and even find areas to enhance some of those opportunities. Most companies will find that about 1–2% of their bottom lines[5] get attributed to environmental areas. But with this complete data model, those numbers can be significantly enhanced. Furthermore, this cross-departmental look, with strong analytics and improvements underlying the efforts, can also highlight something truly important for the sustainability team – its ability to enhance the revenue of the company through its objectives.

SHL'S SUSTAINABILITY GOALS

Former Unilever Chief Executive Officer Paul Polman once said: "We cannot choose between [economic] growth and sustainability – we must have both."[6] To this end, SHL has endeavoured to create "win-win" scenarios where it is able, through its data-driven methodology, to find areas where improvements in sustainable growth also improve the company's market competitiveness. It is implementing innovative initiatives across its portfolio and sites, with the goal of making all its products inherently sustainable. These sustainability initiatives cover not just the product design, development and production streams but also secondary and tertiary packaging, as well as other supply-chain activities (Figure 2).

SHL continues to strive to be not just a leader in autoinjectors but also a leader in sustainable manufacturing across a variety of different sustainability targets. The company considers its combination approach – leveraging the experience of its data-science department to enhance the output of its sustainability department – as a novel offering and it hopes its experience helps highlight the possibilities for other teams looking to provide a production environment that ultimately serves both company goals and also shared objectives for global social responsibility.

ABOUT THE COMPANY

SHL Medical is a world-leading solutions provider in the design, development and manufacturing of advanced delivery devices, such as autoinjectors and pen injectors. It also provides final assembly, labelling and packaging services for leading pharmaceutical and biotech companies across the globe. With locations in Switzerland, Taiwan, Sweden and the US, SHL has successfully built a strong international team of experts that develops breakthrough drug delivery solutions for

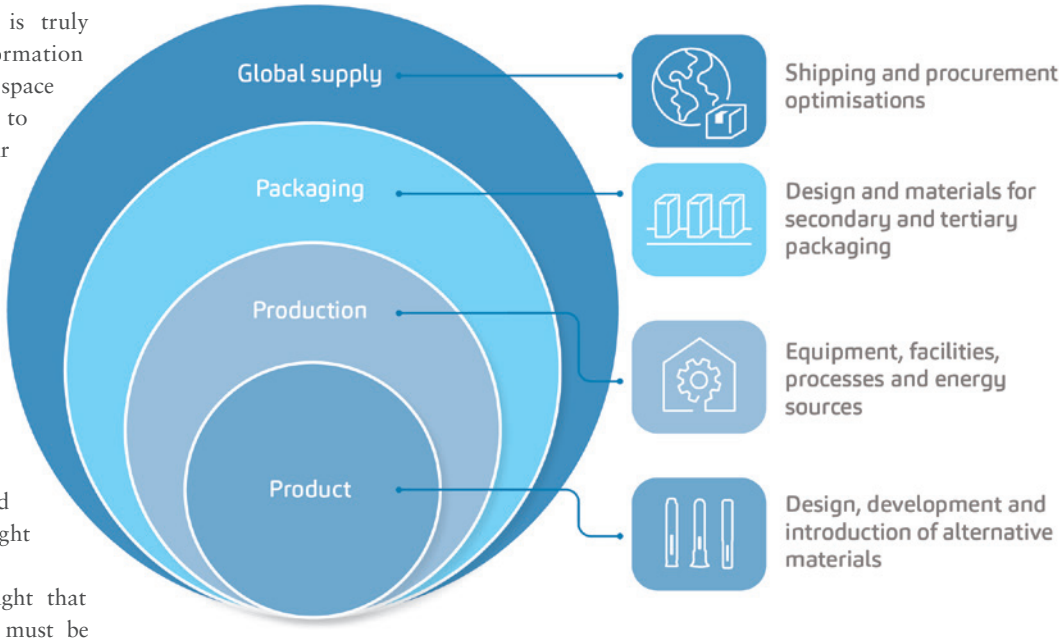

Figure 2: A visual depiction of the highly dependent nature of autoinjector development from design to production to delivery.

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ABOUT THE AUTHORS

Frederick Gertz, PhD, is the Manager of Data Science at SHL Medical. His focus in the company is facilitating data-driven methods across the organisation and providing unique insights from data using a variety of techniques, including artificial intelligence and deep learning. Prior to joining SHL, Dr Gertz worked in the medical device start-up space, where he focused on bringing novel processes and techniques, including machine learning, into the biotech industry. He holds a PhD in Electrical Engineering from the University of California, Riverside (CA, US) where his research focused on biophysics and spintronics

Yves Steffen is Global Sustainability Director at SHL Medical. He heads SHL's sustainability programme, driving key initiatives that encompass the three focus areas of product, people and planet. He is a seasoned professional with over 16 years of experience in the pharmaceutical industry. His knowledge and expertise cover broad areas concerning medical devices, combination products and alternative materials for secondary packaging. Prior to joining SHL, Mr Steffen was the head of Novartis's Packaging and Device Commercialisation department, focusing on the commercialisation of medical devices and combination products.

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H&T PRESSPART

PLASMA TECHNOLOGY – THE FUTURE OF RESPIRATORY DEVICES

In this article, Jacqueline Green, Global Business Development Manager at H&T Presspart Manufacturing, discusses how H&T Presspart's plasma treatment process can provide a future-proof and sustainable solution for some of the issues associated with suspension formulations in the respiratory device industry.

Metered dose inhaler (MDI) formulations typically exhibit two main failure modes: drug degradation and drug adhesion, both of which occur as a result of the formulation interacting with the metal canister. In order to address these issues, a matrix of canister solutions has been established over time.

> "To meet both the demands of sustainability and MDI canister design, H&T Presspart has developed a proprietary plasma treatment process that provides a sustainable, future-proof and cost-effective solution."

However, there is an increasing focus on sustainability across all industries and sectors of society, which has led to an imperative for more sustainable drug delivery solutions. In this context, the majority of these alternative cans may fall short of expectations, due to increasing environmental regulations and cost pressures.

H&T Presspart's plasma treatment process that provides a sustainable, future-proof and cost-effective solution. This process addresses the main issues encountered with formulations in the industry, with its ever-challenging and increasingly complex molecules, combinations and propellants.

FORMULATION CHALLENGES

H&T Presspart has a 50-year history of manufacturing aluminium canisters for pressurised MDIs (pMDIs). This experience has informed the company's efforts to tackle the two main failure modes that some formulations can exhibit. As mentioned prior, the first of which is drug adhesion, where drug sticks to the internal surfaces of the canister. This failure mode is encountered specifically in suspension formulations.[1,2]

The second is drug degradation, where increased impurity levels are observed as the drug deteriorates over time due to interactions with natural oxides and organic residues present on the internal surfaces of the canister. This is evident in solution formulations and reduces the shelf life of the product as a result. Both of these failure modes result in reduced drug content, meaning that the patient can receive less than the prescribed dose.

With increasingly complex formulations and molecules being developed, as well as improvements in propellants and the need for more sustainable, future-proof solutions, the role of the canister has transformed from merely providing safe containment for the drug product to being an integral part of the drug delivery system itself, increasing the importance of drug-canister interfaces.

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"In order to prevent or reduce drug degradation, canisters need to provide a barrier between the exposed aluminium on the interior of the can and the formulation."

TRADITIONAL COATINGS AND SOLUTIONS

In order to prevent or reduce drug degradation, canisters need to provide a barrier between the exposed aluminium on the interior of the can and the formulation. One solution is to use an alternative substrate – stainless steel, rather than aluminium – for more aggressive formulations. Another solution is to anodise the aluminium cans, removing the natural oxides and organic residues and replacing them with a structured anodised aluminium layer.

However, in most cases, these solutions are only useful for solution-type formulations, and do not address adhesion issues. Furthermore, anodising only slows degradation, rather than preventing it. There is also an increased cost involved with these kinds of cans due to the more expensive stainless steel material and the anodising process.

Figure 1: H&T Presspart's automated MDI plasma canister manufacturing cell.

An alternative solution is spray coating with fluorinated ethylene propylene (FEP), which provides both a barrier and low surface energy. However, once again, this solution presents cost and sustainability issues. With all this in mind, Presspart partnered with Portal Medical (Cambridge, UK) to develop a solution that addresses both aggregation and degradation, but also provides superior performance characteristics at a lower variable cost than the alternatives, with no supply or legislative barriers, and freedom to operate across all drug candidates in all markets. This solution is Presspart's patented plasma canister (Figure 1).

PLASMA TECHNOLOGY

In general terms, plasma is known as the fourth state of matter. Solids plus energy produce liquids. If energy is added to liquids, they produce gases. Plasma, an ionised gas, is produced when radio frequency energy is applied to free electrons in the gas causing ions and electrons to co-exist, which creates performance surfaces whilst maintaining bulk strength properties.[3] Plasma, or fluorocarbon polymer (FCP), is a nanolayer on the internal surface of the canister. This is different to traditional coatings, as plasma is not a substance applied directly onto the interior can surface – it is a change to the molecular structure of the canister interior, covalently, and inseparably, bonded to the aluminium surface. With the treatment limited to the internal surface of the can, label adhesion and filling line performance are not compromised.

Budesonide Study – An Example

The chemical stability of a 50 µg budesonide solution formulation contained within five alternative canisters was tested and compared. Figure 2 shows the results following 1-month (40°C/75% RH) and 3-month (40°C/75% RH) storage (valve-up and valve-down).

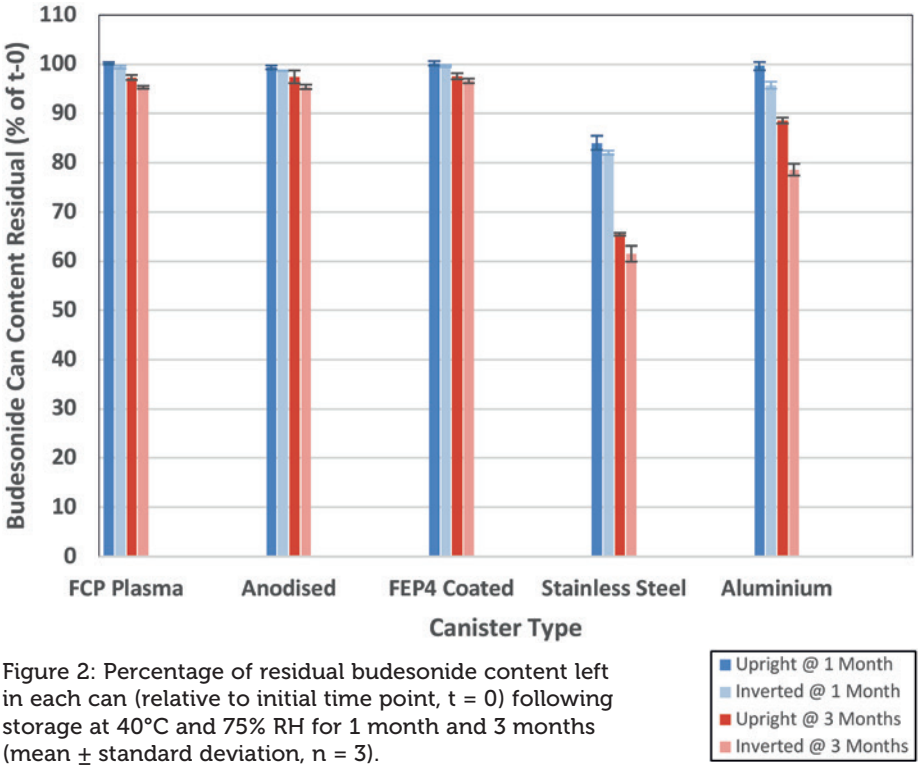

Figure 2: Percentage of residual budesonide content left in each can (relative to initial time point, t = 0) following storage at 40°C and 75% RH for 1 month and 3 months (mean ± standard deviation, n = 3).

For the budesonide solution study, surface-treated canisters outperformed stainless steel and plain aluminium canisters, showing high integrity and an inert relationship with the formulation and, therefore, less degradation with the treated can types. This was the case for both the initial and 3-month time points.

Fluticasone Propionate Study – An Example

In a second study, aerodynamic particle size distributions (APSD) were evaluated for plasma, FEP and plain canisters with regard to a 125 µg fluticasone propionate suspension formulation (Figure 3).

The data show that at the initial time point, the plasma canister outperformed the FEP and plain canisters for APSD testing, showing improved performance and less adhesion with plasma canisters.

SUSTAINABILITY

Plasma has the advantage of being able to form a nanolayer on the canister interior without the need for mass heating, due to the very high energies that can be confined

> "With the plasma treatment process being a single-stage, low-energy process, the energy consumption is 50% less than that for spray coating."

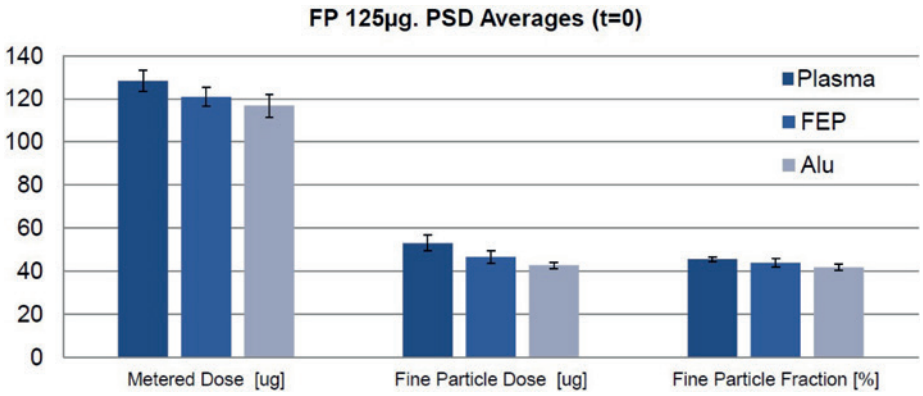

Figure 3: Data obtained at the initial time point for three canister types (mean ± standard deviation, n = 4).

thinly and consistently across all contours and high-aspect ratios of the canister. The lack of required heating means that a standard, thin-walled canister is able to be used, resulting in 30% less aluminium usage than traditional coating methods, which dictate the use of a thick-walled canister – and therefore increased costs.

With the plasma treatment process being a single-stage, low-energy process, the energy consumption is 50% less than that for spray coating. This reduced energy means that the carbon footprint of plasma canisters is significantly less than that of FEP-coated and anodised canisters (Table 1).

The lack of solvents used for plasma treatment means that there are no harmful emissions or measurable extractables or leachables. It is likely that the solvents and chemicals used for spray coating and anodising processes will fall under REACH "Registration, Evaluation, Authorisation and Restriction of Chemicals"

Can Type	CO_2 Per Million Cans (Kg)
Plasma	143
Anodised	900
Spray Coated	1,445

Table 1: CO_2 values for treated can types, per million cans. Data from H&T Presspart.

(REACH) or similar regulations in the coming years, which will not be the case for plasma, ensuring these canisters are a future-proof solution.

CONCLUSIONS

The ever-increasing challenges with pMDIs arise from more complex and combination formulation developments, cost-reduction

initiatives and the more recent pressure within the pharmaceutical industry around the need for improved sustainability.

Although propellant changes have the potential to improve the sustainability of pMDIs, there are also improvements that can be made by changing components. Analytical tests have demonstrated that plasma-treated canisters can provide improvements for both adhesion and degradation compared with plain, stainless steel, anodised and FEP-coated cans when used in conjunction with both budesonide solution and fluticasone suspension formulations.

Overall, the use of a Presspart plasma canister provides the most sustainable treated can option and tackles the two failure modes associated with pMDIs – improving pMDI performance and providing the most cost-effective, future-proof treated canister.

ABOUT THE COMPANY

H&T Presspart specialises in industrialising drug delivery devices and components. The company's products include medical devices, MDI components and a comprehensive range of dose-counting technologies. The company has over 50 years' experience and a worldwide reputation for competence, quality and innovation in the pharmaceutical sector. H&T Presspart's Inhalation Product Technology Centre and New Product Development Centre support its customers in the design and development of new inhalation products, devices and strategic initiatives. H&T Presspart, part of the Heitkamp & Thumann Group, has four European manufacturing sites, in Germany, Spain, Switzerland and the UK, with sales offices in China, India, Singapore, South America and the US.

ABOUT THE AUTHOR

With a strong pharmaceutical and analytical background, **Jacqueline Green** currently works as Global Business Development Manager at H&T Presspart, providing technical expertise and support on every aspect of MDIs with a specific focus on plasma MDI cans and sustainability.

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OWEN MUMFORD
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FORMULATION DEVELOPMENT AND DRUG DELIVERY: JOINED AT THE DEVICE

In this article, Julie Cotterell, Marketing Manager at Owen Mumford Pharmaceutical Services, discusses the major factors at play driving the direction of innovation in the subcutaneous drug delivery space, with a particular emphasis on the push towards patient self-administration.

The growth of the parenteral drug-device combination product market has been fuelled by a number of driving factors over the last couple of decades, in particular, longer life expectancy and the associated need for a greater number of patients to practise self-administration, as well as the increase in biologics and biosimilars, which have now captured 10% of the total biologics market value in Europe, according to a 2020 report by IQVIA. This stimulus has been felt both on the formulation and the device design sides.

Propelled by these key drivers, formulation science has therefore been developing along a series of key trajectories including the needs to:

- Develop greater biologic stability
- Reduce injection pain and frequency
- Allow for larger volumes of injectate
- Diversify drug delivery as well as improve ease of use for patients.

GREATER BIOLOGIC STABILITY

Ensuring the stability of biologic formulations is a challenge that requires the consideration of a number of elements. Interactions between the formulation and excipients, the primary container, oxygen and light, as well as any exposure to high extrusion or shear forces, are just some factors that may affect stability.

One of the methods undertaken to achieve greater stability and better facilitate subcutaneous injection has been the development of new excipients. However, use of these excipients presents a new set of challenges, such as interaction between the excipient and the silicon used to lubricate glass primary containers. Recently, there has been significant innovation in this area, from novel glass coatings to enhance stability to the use of innovative plastic primary containers that aim to minimise protein aggregation in biologics caused by silicon.

> "Extending shelf life beyond the typical two-to-three-year range with post-launch stability studies can provide a significant commercial advantage."

Extending shelf life beyond the typical two-to-three-year range with post-launch stability studies can provide a significant commercial advantage. While storage at below room temperature is an option to extend shelf life, this route relies on patients remembering both to keep their drug refrigerated and to remove it before use. This is especially important in the case of biologics, where low temperatures increase viscosity, making the injection potentially more painful. Additionally, there are implications in the supply chain

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where cold chain conditions may be required for these products. With all new excipients, it is therefore critical to be aware that solving one issue may well cause others elsewhere – only an holistic approach can truly benefit development.

INJECTION FREQUENCY AND THERAPY ADHERENCE

As patients are increasingly enabled and encouraged to self-administer their medication in the home, the focus on patient convenience has also heightened. As a consequence, reducing injection frequency has become an area of focus for the industry, seeking to provide increased patient convenience and thereby improve therapy adherence. As a result, various novel drug-device combination products, including long-acting and extended-release formulations, have been developed. An increased focus on the patient experience – especially for those who self-administer – earlier in the drug development process provides a more patient-centric approach with wide-ranging benefits, including patient reassurance, comfort, convenience and usability. Regulatory pressure is also providing a significant push in this direction.

Increasing drug viscosity can also help to reduce injection frequency, but can have implications for administration – the needle length and gauge may have to be adjusted, there may be increased pain on injection and there may be an increase in the required injection time or device-hold time that may be inconvenient or even impossible for the patient to manage. Furthermore, there is the constraint posed by suitability and compatibility of the selected drug delivery device with the formulation.

"As patients are increasingly enabled and encouraged to self-administer their medication in the home, the focus on patient convenience has also heightened."

LARGER VOLUME PLATFORM DEVICES

In recent years, there has been a move from 1 mL up to 2 mL injectate volumes, and some exploration of 3 mL and higher, for subcutaneous delivery to reduce injection frequency. New excipients are also being trialled to enable the administration of larger volumes, thus reducing frequency of delivery. These may in turn permit the administration of >2 mL volumes and therefore require larger syringe sizes. Having a platform device that can easily accommodate both 1 and 2.25 mL prefilled syringes, as well as a variety of fill volumes, is a distinct advantage and allows flexibility throughout both development and commercialisation. Autoinjectors that have a two-phased, independent needle insertion and dose delivery can provide an improved and more consistent patient experience during the administration process, even for volumes up to 2 mL.

"Greater choice of delivery device allows formulation experts to explore a variety of options – from formulation changes in early clinical studies to the creation of a range of differentiated products, each providing their own tangible patient benefits."

DIVERSIFICATION

Greater choice of delivery device allows formulation experts to explore a variety of options – from formulation changes in early clinical studies to the creation of a range of differentiated products, each providing their own tangible patient benefits. The range of subcutaneous delivery devices is broad, running from safety devices for prefilled syringes to disposable and re-usable autoinjectors, through to wearable injectors, each of which may also have the capability to add connectivity and thus enable the transfer of key patient data and monitoring of therapy compliance. In addition to this, giving the patient choice of delivery method and device can help increase patient confidence and reassurance, positively impacting compliance to their therapy regimen.

While wearables have attracted a lot of attention, they are not yet mainstream, except in diabetes treatment. Challenges remain within formulation development that need to be addressed for successful adoption of wearables. However, the outlook for wearable devices is positive, as they have strong potential to provide a more convenient and comfortable means to deliver therapies to patients.

EASE OF USE

The need to simplify the use of devices to facilitate patient self-administration sometimes finds itself at odds with the technological potential of new devices. On the one hand, there is the emergence of connected devices, which are designed to help improve patient therapy adherence through better support and enabling monitoring by healthcare providers, while on the other hand, there is a trend towards more complex devices with additional features, such as variable injection speed and depth settings. However, the need to keep complex features and user steps to a minimum is paramount, as devices need to be simple and intuitive in order to both minimise user errors and encourage adherence. Simpler, more streamlined

devices that focus on the functionality needed for effective drug delivery, such as efficient end-of-dose indicators, are instead more likely to prove successful on the market than those featuring over-engineered features that, in practice, may confuse patients more than help them.

A MORE SUSTAINABLE FUTURE

Formulation and drug delivery device design and development are inextricably coupled and must respond to the same drivers, so it is unsurprising that the same trends are driving innovation on both fronts. Taking a holistic view of device and formulation right from the design and development stage is critical to ensure positive outcomes from both a commercial and a therapeutic perspective. Finally, sustainable design and development of devices have become increasingly important over the last decade, with governments, regulators, patients and consumers all calling for the industry to "go green". As such, mitigation of environmental impacts relating to manufacturing and waste products, and formulations with a less frequent dosing schedule are becoming increasingly popular options.

"Sustainable design and development of devices have become increasingly important over the last decade, with governments, regulators, patients and consumers all calling for the industry to "go green".

ABOUT THE AUTHOR

Julie Cotterell is Marketing Manager at Owen Mumford Pharmaceutical Services and has over 20 years of sales and marketing experience in regional, national and global roles. She has a wealth of knowledge across several different aspects of drug delivery and the associated devices, with a particular interest in bringing products to market that can allow patients to be treated as simply and effectively as possible. Before joining Owen Mumford in 2018, Ms Cotterell worked for both pharmaceutical and medical device companies, including Baxter, BD and Smith & Nephew.

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 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.

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STRATEGIES TO ACHIEVE LONG-TERM SUSTAINABILITY

In this article, Peter Soelkner and Thomas Otto, both Managing Directors at Vetter, discuss how the pharmaceutical service provider focuses on sustainability.

The history of Vetter started with a simple pharmacy in a late Gothic, half-timbered house in Ravensburg city centre in Germany, which is still there today and serves as a reminder of the first entrepreneurial steps taken by founder Helmut Vetter in the 1950s.

The pharmaceutical service provider produces injectable drugs for its customers in the pharmaceutical and biotech industries that are vital for patients around the world. Among them are medications for cancer, multiple sclerosis and rheumatoid arthritis, as well as treatments for rare diseases. Vetter employees 5,500 staff in Ravensburg and Langenargen in Germany, as well as at sites in Austria, the US and Asia.

The company has remained down-to-earth and is proud of its roots in the region, which have enabled it to achieve significant growth. Since its foundation, Vetter has consistently pursued its path as a family-owned business that focuses its activities on the well-being of patients and takes a long-term view. The topic of sustainability plays a central role for the organisation on many levels – it aims to improve the quality of life of millions of patients worldwide in a sustainable manner. At Vetter, responsibility towards both patients and society are inseparably linked.

> "Since 2014, all Vetter's German sites have been operating with green power from hydroelectric plants."

COMMITMENT TO CLIMATE PROTECTION

The understanding that global carbon dioxide emissions must be sharply reduced has continued to grow worldwide. Vetter recognised this need early on and has been using green technologies for many years, while also making continuous investments in climate protection. For example, since 2014, all Vetter's German sites have been operating with green power from hydroelectric plants. The company reached another milestone last year when it achieved carbon dioxide neutrality in all its corporate activities at every German site, and has since gone on to achieve carbon neutrality worldwide (Figure 1).

In view of the high quality standards and numerous regulatory requirements in the pharmaceutical industry, residual emissions cannot be completely avoided. This makes it all the more important for companies to compensate for this by supporting climate protection projects. These projects are subject to strict criteria – for example, the

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Figure 1: All Vetter sites around the world are carbon dioxide neutral.

> "Vetter has its environmental, energy management and occupational safety activities certified on a regular basis."

exclusive production of renewable energies, including wind, solar or biogas. Vetter also has its environmental, energy management and occupational safety activities certified on a regular basis.

The Center for Visual Inspection and Logistics in Ravensburg (Figure 2) is a good example of Vetter's sustainability strategy. It combines the operation of an environmentally friendly biogas block-type thermal power station with the use of geothermal energy and surplus energy, as well as photovoltaic systems. In this way, a sustainable energy concept is consistently implemented. The site has already won a prestigious international industry award for its efforts as a "factory of the future".

FOCUS ON SUSTAINABLE MOBILITY

But sustainability initiatives don't always have to be high-tech. Vetter is also breaking new ground when it comes to healthy mobility and creating a greener region. For example, the company offers its staff members a leasing model for e-bikes and bicycles. Vetter also encourages its workforce to collect green kilometres by participating in initiatives such as "Green Ways to Work". The company recognises that cycling is a great way to do something good for both yourself and the environment at the same time – and it is pleased with the enthusiasm its employees have shown for the campaigns and their many benefits.

Figure 2: The Ravensburg Vetter West site honoured as a "factory of the future".

For cyclists who have worked up a sweat on their way to work, showers are available in the Vetter buildings. In addition, the company has invested in cycling infrastructure such as modern bicycle parking facilities with battery charging stations for e-bikes and on-site kits for minor repairs (Figure 3) – all intended to make switching to bicycles even more attractive.

Baden-Wuerttemberg's Minister of Transport Winfried Hermann has expressed open support for the project, stating that "The efforts of sustainability have been advanced here with commitment and initiative, which is important for the sustainable development of economic and living spaces." Staff members can use electric bicycles between the individual sites – a model project in co-operation with Technische Werke Schussental.

Figure 3: Vetter has invested in modern bicycle parking facilities with battery charging stations and repair kits.

"The company is constantly working to keep its ecological footprint as small as possible."

CULTURE OF RESPONSIBILITY

Companies have many ways to act in a sustainable manner and make sustainability a significant part of their corporate philosophy. High standards in the areas of environment and energy use, as well as health and occupational safety, are just as much a part of Vetter as social commitment, diversity and education. The company is constantly working to keep its ecological footprint as small as possible. As a family business with a long-term focus, Vetter sees this as an important component of its social responsibility – not just for today but also for future generations.

ABOUT THE COMPANY

Vetter is a family-owned, leading global CDMO with production facilities in Germany, Austria and the US. Currently employing more than 5,500 individuals worldwide, the company has long-term experience in supporting biotechnology and pharmaceutical customers, both large and small. Vetter's services range from early-stage development support, including clinical manufacturing, to commercial supply and numerous packaging solutions for vials, syringes and cartridges. As a leading solution provider, Vetter appreciates its responsibility to support the needs of its customers by developing devices that contribute to increased patient safety and convenience, as well as enhanced compliance. Great importance is also given to social responsibility, including environmental protection and sustainability.

ABOUT THE AUTHORS

Peter Soelkner has been a Managing Director of Vetter since June 2008. He graduated from the University of Dortmund (Germany) in 1992 with a degree in chemical engineering and earned an MBA from Columbia University (NY, US) in 2001. Before joining Vetter, he held positions in Germany and North America at Sartorius AG and Sartorius North America Inc in research and development, marketing and key account management, as well as general management roles.

Thomas Otto assumed the position of Managing Director at Vetter in December 2002. He began his employment at Vetter in the early 1990s as a project engineer. From 1995 to 1999, he was Manager of Packaging Materials Development and, from 2000 to 2002, he headed the R&D department. Mr Otto graduated with an engineering degree in packaging technology and print processing in 1990.

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IMPORTANT CONSIDERATIONS WHEN DESIGNING FOR SUSTAINABILITY

In this article, Michael Kiely, Principal Device Development Engineer, Gerard Linnane, Engineering Services Director, and Justin Carroll, Development Engineer, all at Jabil Healthcare, discuss how implementing a thoughtful design-for-sustainability process can ensure medical devices not only improve patients' lives but are also kinder to the environment.

A recent study from Deloitte suggests that sustainability is a major issue for most customers in 2021.[1] It reports that 32% of consumers are "highly engaged" with adopting a more sustainable lifestyle and 28% have stopped buying certain products due to ethical or environmental concerns. Younger generations are seen to be the most apt to adopt sustainable behaviours, with 50% saying they have reduced how much they buy and 45% have stopped purchasing certain brands because of ethical or sustainability concerns.

The most common way consumers demonstrate their commitment to sustainability is by avoiding single-use plastics (61% of people). The single-use medical device reprocessing market was valued at US$1,858 million (£1,358 million) in 2018 and is expected to register a compound annual growth rate of about 15% during the forecast period of 2019–2024.[2] Yet still approximately 90% of medical device waste comes from disposable, single-use components or products.[3]

Regulations and standards such as the Waste Electrical and Electronic Equipment; Restriction on Hazardous Substances; Registration, Evaluation, and Authorization of Chemicals; and the Energy Using Products have already positively impacted the sustainability of medical devices containing electronics. However, aside from meeting regulatory requirements, medical device manufacturers have typically not led the way in driving sustainability and sustainable product design, citing obvious challenges around cost, safety, functionality, usability and convenience.

The introduction of new regulations, increased consumer awareness of the environmental impact from medical waste and a sense of responsibility from companies to produce eco-friendly drug delivery devices has driven a rise in sustainability goals and policies in the medical and pharmaceutical industries. There are now programmes in place to reduce medical device waste by returning used devices for recycling, repurposing, refurbishing and re-use. These programmes present device companies with additional challenges such as establishing a safe means of returning the devices with a low burden on the user and developing infrastructure to introduce the returned devices safely and efficiently into the circular economy.

As medical device manufacturers navigate the many regulatory hurdles to approve a refurbished or multi-user medical device,

> "A design for sustainability process should cover the entire product lifecycle – from design to disposal – and needs input from all stakeholders."

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there is also the obstacle of patients accepting treatment with a refurbished device. For now, it is unlikely that the medical device industry will transfer to a model where refurbished or multi-user medical devices are the norm. But to meet their sustainability goals, there are many small improvements that will make a big difference when introduced to the product lifecycle.

A process where design for sustainability is an integral part of the conceptual design process will ensure that environmental and sustainability considerations are elevated to a similar level as regulatory, functional and business requirements. A design for sustainability process should cover the entire product lifecycle – from design to disposal – and needs input from all stakeholders.

THE EARLY-STAGE DESIGN PROCESS

Jabil Healthcare has an established early-stage design process that meets regulatory design control requirements and supports optimisation of medical device design for large-volume manufacturing (Figure 1).

This process commences with concept selection, where all potential concepts are reviewed and optimised into one selected design. The selected concept is then brought forward to the detailed optimisation stage, where subject matter experts from a range of disciplines (e.g. manufacturing, assembly and electronics) work with the design team to further improve the device design for each area. Following implementation of these optimisations, analytical tools, such as mould flow, tolerance analysis and finite element analysis simulations, along with final material selection, are conducted prior to the design being released for prototype manufacture. By integrating design for sustainability into its established early-stage design process, Jabil can have maximum impact on the sustainability of the device with minimal impact on project timeline and cost. However, this decision-making process for optimising sustainability needs to be informed and data driven, as we will discuss here.

> "Establishing specific, measurable and attainable sustainability goals within the device requirements is a key contributor to success."

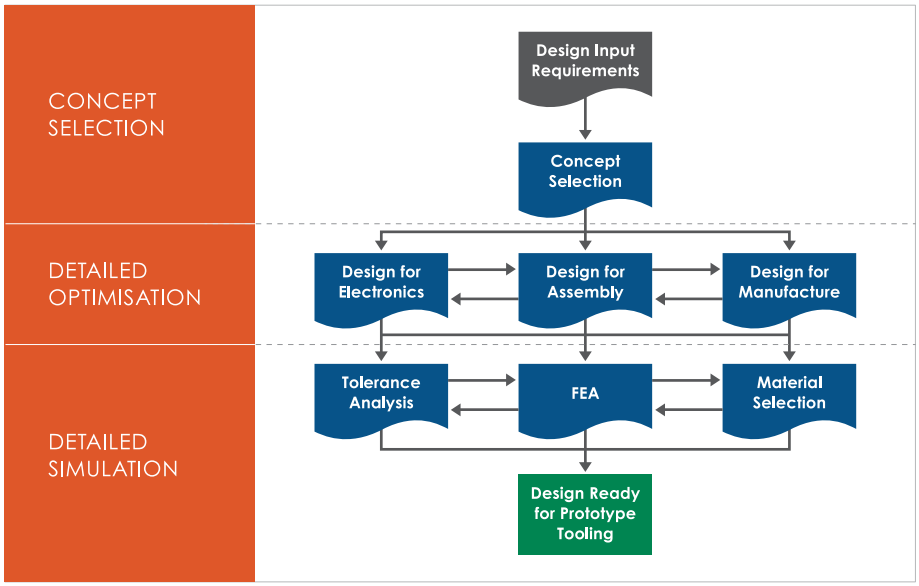

Figure 1: Early-stage design process elements.

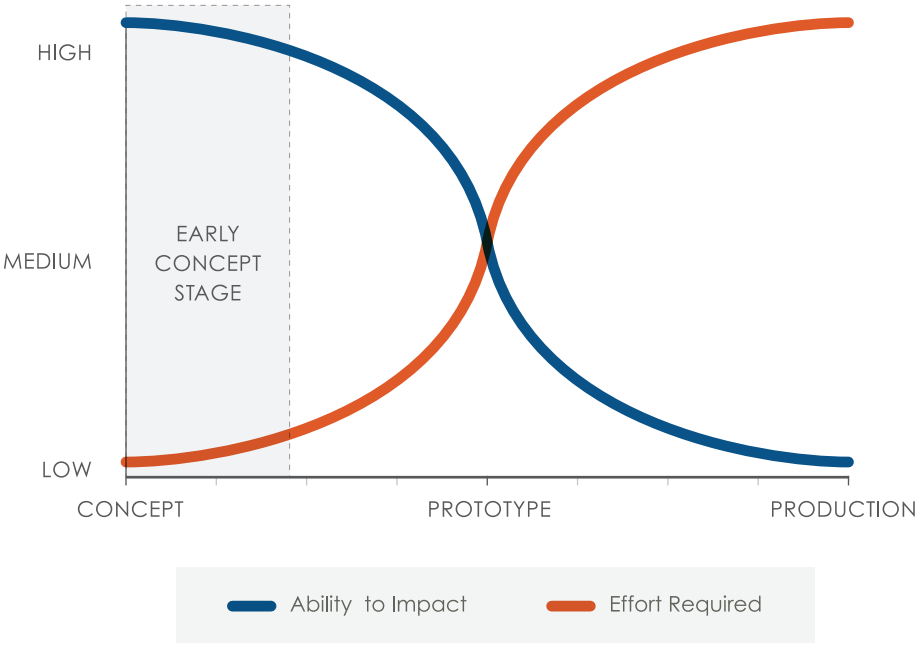

Figure 2: Device sustainability – ability to impact versus effort required.

STAGE 1: CONCEPT-SELECTION

At concept-selection stage, the opportunity to optimise a device design for sustainability is at its peak. Conversely, if you do not consider sustainability at this stage, your chance to consider it at later stages is much reduced, becomes more complicated and adds significant time and cost to the development lifecycle (Figure 2).

Design requirements are crucial input to the concept-selection stage, as all proposed concepts will ultimately be assessed against these. Therefore, establishing specific, measurable and attainable sustainability goals within the device requirements is a key contributor to success.

Jabil Healthcare uses a concept-selection matrix that accommodates a data-driven approach to assess each device against its design requirements. Applying a weight to each requirement and scoring each concept provides a holistic approach to assess the sustainability of a concept in the context of other requirements, such as functionality, manufacturability, usability and cost.

The three important sustainability factors to consider during the concept-selection stage include:

1. Modular Design

Modular design is particularly important for the more complex connected or electronic medical devices that are increasing in

the market today (Figure 3). It is crucial to consider how elements of the device that have specific medical waste disposal requirements (i.e. drug cartridges) can be separated from the overall device.

2. Component Reduction

A reduction of the component count or the amount of different material types in a device can have a large impact on how readily the device components can be introduced into the circular economy and the cost effectiveness of doing so. Reducing the size and amount of material in a device can have a positive impact on carbon emissions during transport, manufacture and assembly. With increased use of 3D-printed materials in medical devices, additive manufacturing can be assessed at the concept-selection stage to reduce component count and optimise material usage. This can be achieved through the use of lattice structures and organic features only possible in a 3D-printed design. Thus, the mechanical requirements of each component can be met with optimal material efficiency.

Figure 3: Jabil's Qfinity re-usable autoinjector employed sustainable design to reduce materials and provides over 100 injections per unit versus most injectors, which are single-use disposable.

3. Device Disassembly

Advancing concepts that optimise the device for disassembly should be a key sustainability requirement assessed at the concept-selection stage. An important factor to consider here is at what point does disassembly of the device to recover the constituent components for the circular economy become less sustainable than shredding the device and sorting the material via mechanical or chemical means. This assessment will have a big impact on the optimal design concept selected and should be determined at the design-requirements or concept-selection stage in consultation with subject matter experts in device recycling.

STAGE 2: DETAILED OPTIMISATION

Once a device concept is chosen, the next stage is a detailed optimisation of that design for the chosen manufacturing and assembly methods. For plastic medical devices that are produced at high volumes, a key area for improvement is the injection-moulding process for plastic components. Reducing the overall amount of material in the component by coring out features while maintaining part functionality is an important consideration. For manufacture of the moulded components, optimising runner systems to reduce material waste and selecting resins that have lower processing temperatures can also greatly enhance sustainability. Understanding the disassembly of the device is also key during this stage.

Design for Assembly

A standard approach to design for assembly (DfA) is to develop an assembly process flow and then optimise the part design to meet the assembly equipment, fixtures, feeding systems, vision systems and other interactions at each stage in the process flow. In the past, little consideration has been given to what happens to the assembled device after it is used.

When device sustainability is considered only after the device has entered production, it can bring many challenges. The device manufacturer is then swimming against the tide, attempting to separate out materials from a device that is not designed to be disassembled.

The sustainable approach is to understand the post-use economy for the device and design it so that materials can be easily separated and recovered for the chosen recycling method. This might necessitate a move away from assembly processes that chemically bond the materials together, such as ultrasonic welding or laser welding. These processes also have high energy requirements that can contribute to a larger manufacturing carbon footprint.

Jabil Healthcare recommends the following:

- Avoid the use of lubricants or solvents that can contaminate waste streams and reduce the value of the device as a circular asset.
- Reduce the use of screws or bolts that will make disassembly more time-consuming. If screws are required, ferrous materials are optimal so they can be magnetically separated during recycling.
- Avoid the use of inks or painting of parts that can contaminate whole plastic batches. Consider processes such as in-moulded marking or laser marking as alternatives.

- Consider the use of shape memory resins in device clipping mechanisms. These can be designed in such a way as to secure the device enclosure during use but also facilitate easy disassembly by heating the device post-use.

A "global returns" system is also key here, so that devices can be received back to the manufacturer after use and they can then become a circular asset that can be re-used, recycled or refurbished. Of course, there is a point reached where the time, effort and energy required to disassemble a device become too high and focus should be diverted to optimal design for a device that will be recycled via shredding and separation. In this instance, material selection during the detailed simulation stage will be the higher priority.

STAGE 3: DETAILED SIMULATION

Material Selection

Optimising component material selection is valuable to achieve a sustainable design. But understanding the most sustainable material to progress forward at the early design stage can be difficult. Jabil Healthcare worked with partners to develop a database that compares different material options and helps with the selection of the most sustainable material for each component in the early design stage. This assessment includes:

- Recycling method
- Environmental impact of the material production
- Carbon footprint of the supply chain for the material
- The material supplier's sustainability credentials
- The predicted outcome for the material post-use (i.e. landfill, waste-to-energy, circular economy).

Figure 4 shows the step-by-step process in action:

1. The component requirements are compiled
2. A list of materials that meet all component requirements is generated
3. Datasheets from these materials are uploaded to the sustainability database
4. This information is disseminated to network partners in the circular economy
5. The sustainability credentials of material production and material suppliers are assessed
6. Feedback from network partners and material suppliers is reviewed and the most sustainable material choice for the component is approved to move forward.

For single-use plastic devices, understanding the environmental impact of the resin production is also important. Use of recycled material continues to be challenging due to the risks of contamination and material traceability. Companies such as Borealis (Vienna, Austria) are working on operations in advanced recycling to return plastics back to their basic monomers, which would be suitable for medical device manufacture. But there are economies of scale required that make this challenging in the short term.[4]

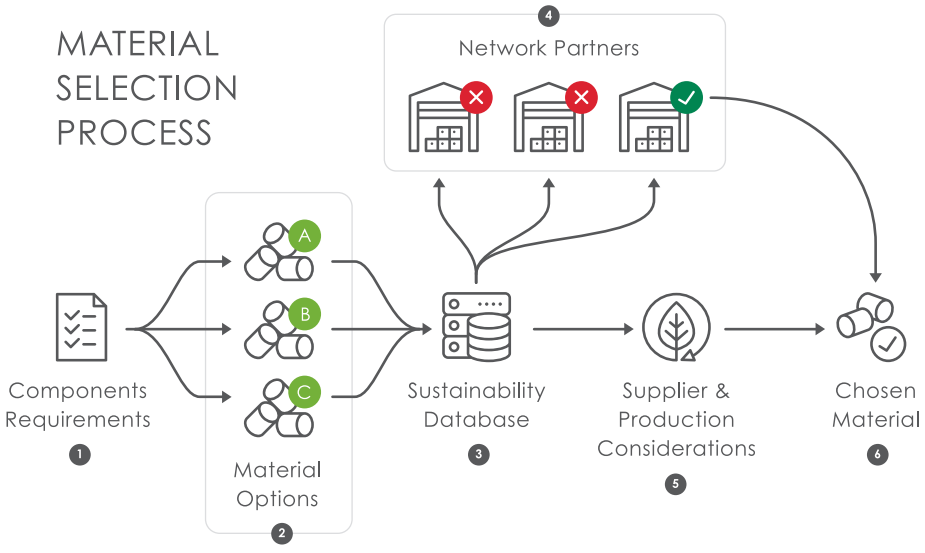

Figure 4: Jabil Healthcare's material selection process.

For resins, in particular, the feedstock used is critical. One way of transitioning away from fossil fuel feedstocks is to use a mass-balance approach. The mass-balance approach is a method of linking sustainable feedstocks to end products.[5] It enables a shift away from fossil fuel feedstocks to a more sustainable circular economy. This system requires resin manufacturers to gradually use more and more bio-based or circular feedstocks in products. It is a similar process to how "green energy" initiatives work, with some of the electricity in the grid coming from renewable sources and some from fossil fuels. For example, there are now sustainably produced medical-grade materials, almost identical to the existing product but made up of 95–100% biocontent (biogas). These materials have typically less than 50% of the carbon footprint of the original materials produced from fossil fuels. This gives the medical device designer the option to select more sustainable materials that meet the same performance criteria.

CONCLUSION

Producing a sustainable medical device is not without its challenges. By tackling this problem at the early design stage, there is maximum flexibility to optimise device sustainability with minimal impact on project timelines and cost. To do this effectively, Jabil Healthcare recommends integrating sustainability into all aspects of the early-stage design process, starting at the concept-selection process, by only progressing the most sustainable concepts. By following a DfA process, where the device is optimised for disassembly and component segregation after use and through a materials selection process that preferentially selects sustainably produced and recyclable materials for each component.

By implementing a thoughtful design-for-sustainability process, product developers can ensure that future medical devices not only improve patients' lives but are also kinder to the environment.

ABOUT THE COMPANY

Jabil Healthcare (formerly Nypro) is one of the industry's largest, most comprehensive healthcare manufacturing solutions and capabilities providers. Its customers have access to an array of engineering,

design and manufacturing solutions across multiple sectors in the healthcare industry. The Pharmaceutical Delivery Systems business within Jabil continues to accelerate leadership within the industry, with disciplined and innovative execution on design, engineering, product development and manufacture across multiple platforms including autoinjectors, inhalers and dosing.

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ABOUT THE AUTHORS

Michael Kiely is Principal Device Development Engineer at Jabil Healthcare. Since joining the company in 2013, he has been involved in the development of a diverse range of medical devices across diagnostics, pharmaceutical delivery systems, surgical devices and medical packaging. He was a finalist in the Jabil Deliver Best Practice competition in 2018 for his project on optimisation of the theoretical design stage. Mr Kiely is a graduate in applied physics from Dublin City University (Ireland).

Gerard Linnane is Engineering Services Director at Jabil Healthcare, where he leads the device development team in meeting the complex demands of the diagnostic, medical device and pharmaceutical markets, enabling the world's leading brands to fulfil their market potential. He has over 20 years' experience in medical device and combination product development, having held different R&D roles at Mallinckrodt, Novartis, Sandoz, Chiesi and Sanofi-Aventis.

Justin Carroll is a graduate in Biomedical Engineering from University College Dublin, where he is currently undertaking a two-year master's degree. As part of his master's programme, Mr Carroll undertook a six-month work placement at Jabil Healthcare, where he completed extensive research on optimisation of design for sustainability, particularly in relation to sustainable production methods for resin materials.

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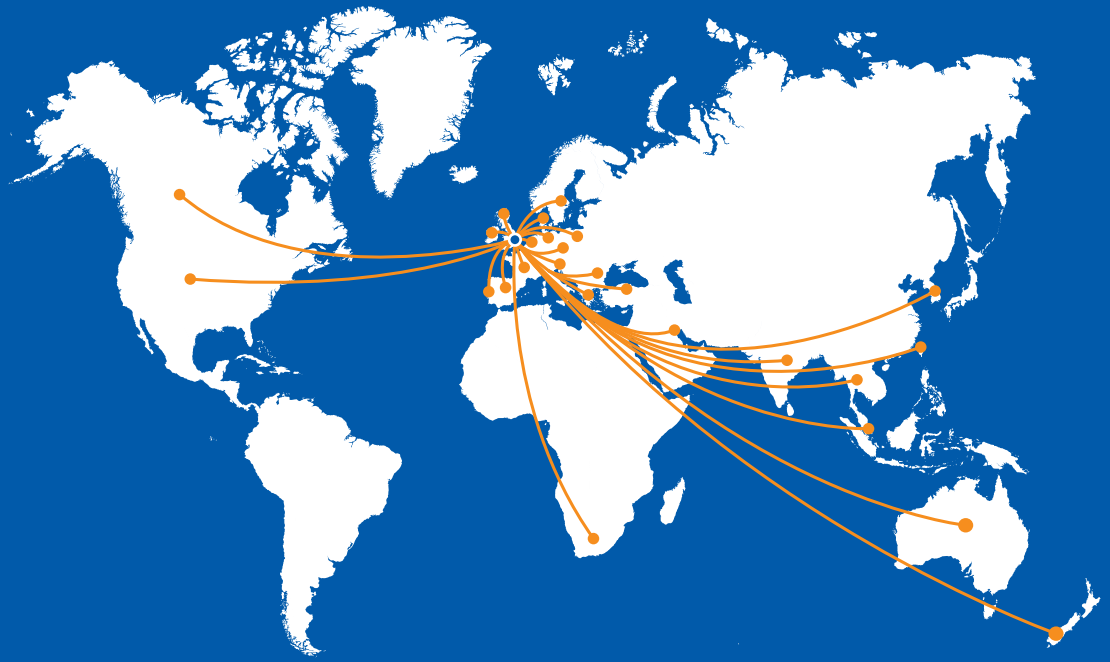

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