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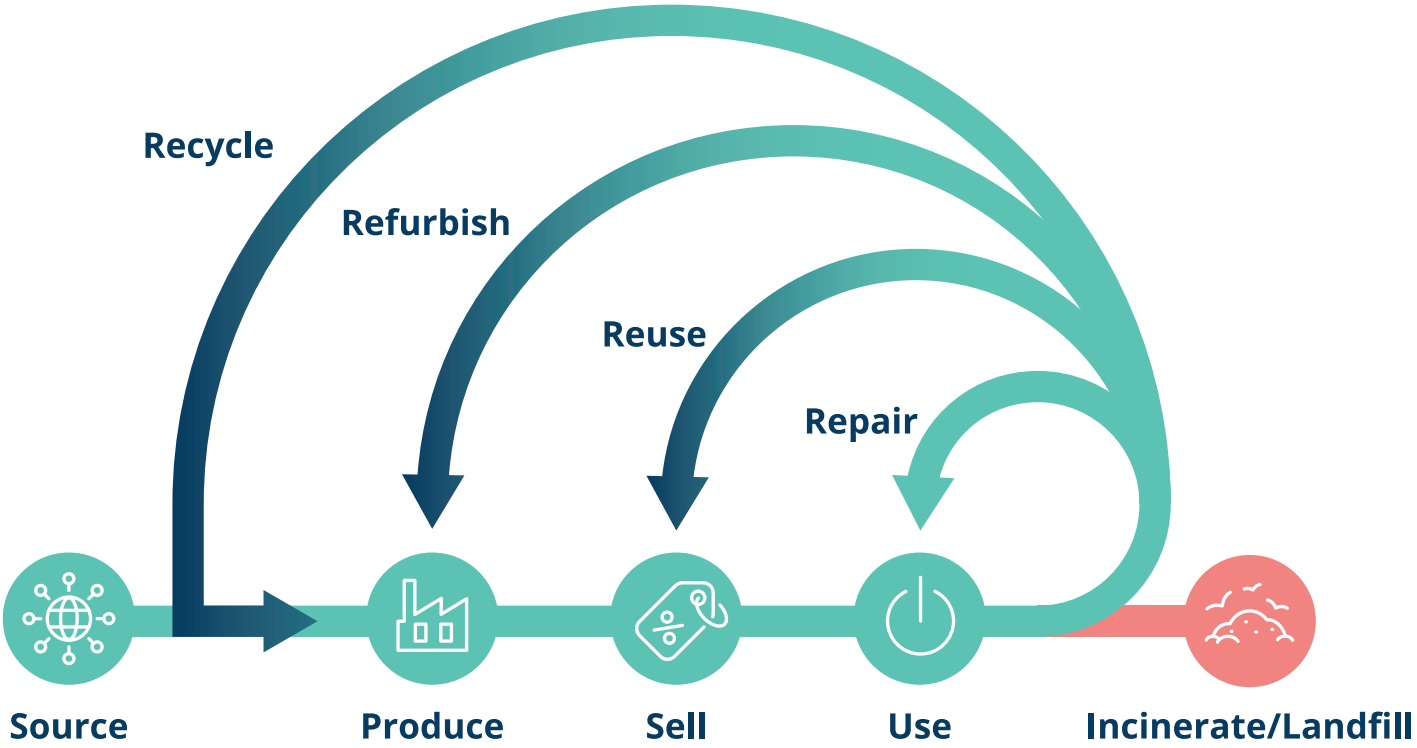

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DRUG DELIVERY & ENVIRONMENTAL SUSTAINABILITY

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May 2022	Injectable Drug Delivery: Formulations & Devices
Jun	Connecting Drug Delivery
Jul	Novel Oral Delivery Systems
Aug	Industrialising Drug Delivery
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Oct/Nov	Drug Delivery & Environmental Sustainability
Nov	Pulmonary & Nasal Drug Delivery
Dec	Connecting Drug Delivery
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SUSTAINABILITY: WHAT CAN THE HEALTHCARE SECTOR LEARN FROM CONSUMER DESIGN?

In this article, Fran Penrose, Mechanical Engineer at Cambridge Design Partnership, considers the lessons the healthcare sector can draw from the fast-moving consumer sector when designing for sustainability and asks, "Can we go even further?"

Environmental responsibility has been climbing the agenda for the pharmaceutical sector, as shown by a surge of net-zero pledges from some of the world's largest drugmakers.[1] As a result, healthcare innovators must add sustainability to their list of essential design requirements.

The consumer sector faces different design challenges to the healthcare market. Compared with healthcare, fewer regulations and the influence of ever-changing consumer tastes result in an environment that supports rapid innovation. When combined with a lower cost-to-market, the consumer sector can take more risks and respond quickly to demand for sustainable products.

This means that the consumer sector can provide healthcare product innovators with a large pool of virtual "test data", which – with careful interpretation – can be applied to its own design cycles. This article looks at three key areas where the healthcare sector can learn from the experiences of its faster-moving counterpart:

- Materials selection
- Electronics
- End-of-life management.

MATERIALS SELECTION

Increasingly, consumers are choosing sustainable brands. Those that produce less waste, incorporate sustainable packaging or have a reduced carbon footprint are most likely to affect purchasing behaviour. Rejecting single-use plastics was the most common way consumers engaged in sustainable behaviour in 2021.[2] In response, the consumer sector continues to develop an array of sustainability-focused strategies for material use, product design and business model adaptation – many of which are candidates for use in the healthcare industry.

> "Healthcare product designers can use this principle of minimising the number of different materials in a product to increase the likelihood of compatibility with existing recycling schemes and infrastructure."

Also of note is the fact that, contrary to the historical strategy of differentiation to create a competitive advantage, the consumer packaging industry is now coalescing around a small number of polymers. This convergence of material usage allows for more economic recovery and recycling, a move supported by consumers.

Healthcare product designers can use this principle of minimising the number of different materials in a product to increase

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Figure 1: Reusable electronics strategies.

the likelihood of compatibility with existing recycling schemes and infrastructure. Devices may also be designed to have easily separable components to reduce the effort required to reclaim their materials for recycling.

The use of mechanically recycled plastics (in which waste material is ground and remoulded) is an increasingly common materials strategy in the consumer world. Previously, post-consumer recycled (PCR) plastics have been unlikely to feature in medical device developments due to a lack of control over the composition of the final plastic. Food-grade PCR polyethylene terephthalate (PET) is now commercially available through a US FDA-recognised approval process, showing a potential route for healthcare applications as material recovery and verification systems improve. Strategies such as lamination of virgin and PCR plastics (used in the cosmetic and consumer health industries) can also be used to ensure that virgin materials are used in all regions of the device in contact with either the drug or the user.

Chemical recycling (where plastic waste is converted to base chemicals and chemical feedstocks) is an example of how recycling can produce a tightly controlled product; although current volume, price and lifecycle performance considerations limit the commercial attractiveness of this option. However, there are high levels of investment in this space, suggesting that chemically recycled polymers may be a candidate for use in future sustainable healthcare products.

Bio-based materials might offer a sustainable alternative to single-use plastics for medical components that cannot be recycled, such as those that risk biohazard contamination. Bio-based feedstocks for polymers and natural fibre-reinforced plastics are examples of material development that aim to replace traditional plastics directly.

Consumer products also use a wide variety of organic materials, with paper pulp-based materials making headlines in the consumer packaging space.[3] The potential to apply such materials to medical devices and their packaging is vast and largely untapped. First movers include Ypsomed (Burgdorf, Switzerland), which has developed a net-zero carbon emission prefilled autoinjector,[4] using advances in biopolymer development from Celanese (TX, US).[5]

Whether sustainable materials are employed or not, significant reductions in environmental impact can be made by reducing the material mass in a device or incorporating reusable elements. Changing consumer preferences have enabled this in the packaged goods sector – what once would have been derided as cheap or flimsy is now lauded as efficient and sustainable. This is an essential short-term improvement measure with relatively little risk but is insufficient to meet medium- and long-term sustainability goals.

ELECTRONICS

Electronic devices pose an increasing environmental challenge due to their growing ubiquity. Material extraction, the complexity of subsystems and the inability to separate components easily into their base materials for recycling are significant barriers to sustainable design for electronics. However, various strategies have been developed to overcome the challenges electronics present (Figure 1).

> "Where complex electronic functionality must be incorporated in the device, there is great benefit in isolating the electronics from biohazard contamination, allowing the device's most environmentally impactful elements to be reused."

The consumer sector has been at the forefront of reducing such waste by removing complex electronics from electromechanical devices and transferring their "smart" components to smartphones. This can be fulfilled through a QR code to provide information or interactivity, or by using near-field communication tag functionality to allow each device to store unique information.

In addition to smartphones, other connected durables, such as a home-based hub or waste bin, can capture data, reducing the need for complex electronics inside the consumable device itself. Applications in the consumer sector include a smart public nappy-recycling bin, opened using an app that also issues vouchers as a reward for use.[6] Potentially, the healthcare sector could use such technology to track patient adherence or alert the user when it is time to restock.

Where complex electronic functionality must be incorporated in the device, there is great benefit in isolating the electronics from biohazard contamination, allowing the device's most environmentally impactful elements to be reused. Medical technologies commonly make use of this strategy already, one example being tethered insulin pumps, where a reusable electronic drive unit is combined with a disposable drug or human-contact component. Another example is Phillips-Medisize's (WI, US) recently unveiled Aria autoinjector, which has a reusable handset and disposable cassettes, designed to help pharmaceutical companies meet sustainability mandates.[7]

The design of modular devices provides an interesting opportunity for user customisation. It can also create easily repairable devices to facilitate an extended product lifetime. In the consumer sector, Fairphone (Amsterdam, Netherlands) has created a modular smartphone for which consumers can buy replacement modules rather than replacing the whole device. This approach allows for easy replacement of components with short lifetimes, potentially extending the overall lifetime of the device.

> "A key lesson from the consumer packaging sector is that designing a recyclable product is not the same as ensuring the product forms part of a functioning recycling system."

Where functionality demands that electronics must remain in a disposable product, the consequences of this can be mitigated in several ways. These include using low-impact manufacturing techniques (for example, substituting basic integrated circuits for innovative printed electronics) and designing devices to help the process of recovering electronic components. Creation of such modular or easy-to-disassemble products can reduce the amount of electronic waste sent to landfill.

END OF LIFE

Sustainable design considers what happens at the end of a product's use-life and aims to establish a closed-loop system or "circular economy". Wherever possible, the materials and energy put into the device will be reclaimed through reuse, remanufacture or recycling (Figure 2). Disposal should be considered a last resort and carefully managed to minimise the impact of any waste.

The consumer space has many examples of these strategies in action. The clothing company Patagonia (CA, US), for instance, encourages reuse through "second lives" for unwanted clothes and provides repair services to extend a product's use-life.

Remanufacture is the process of returning a device to the manufacturer for functional restoration to create a second life. It is commonly used for high-value consumer electronics, with several companies, such as Fonebank (London, UK), selling refurbished second-hand devices. Using modular design principles could greatly simplify remanufacture by enabling each module to be tested and replaced independently. This could minimise the time and effort required to restore the functionality of a device.

A key lesson from the consumer packaging sector is that designing a recyclable product is not the same as ensuring the product forms part of a functioning recycling system. While the former can be a relatively straightforward design exercise, the latter involves complex system design, requiring companies to reach beyond the borders of their traditional value chain.

The consumer sector has a head start in developing strategies to address this, displayed by Colgate-Palmolive's (NY, US) mono-material toothpaste tube. While developing the tube may directly affect only a small portion of the market, the company has allowed others to access their design and supplier to encourage them to adopt the same design and increase economies of scale.[8] Such collaboration is likely to benefit the efficacy of recycling infrastructure, providing economic benefits for all sectors involved in product design.

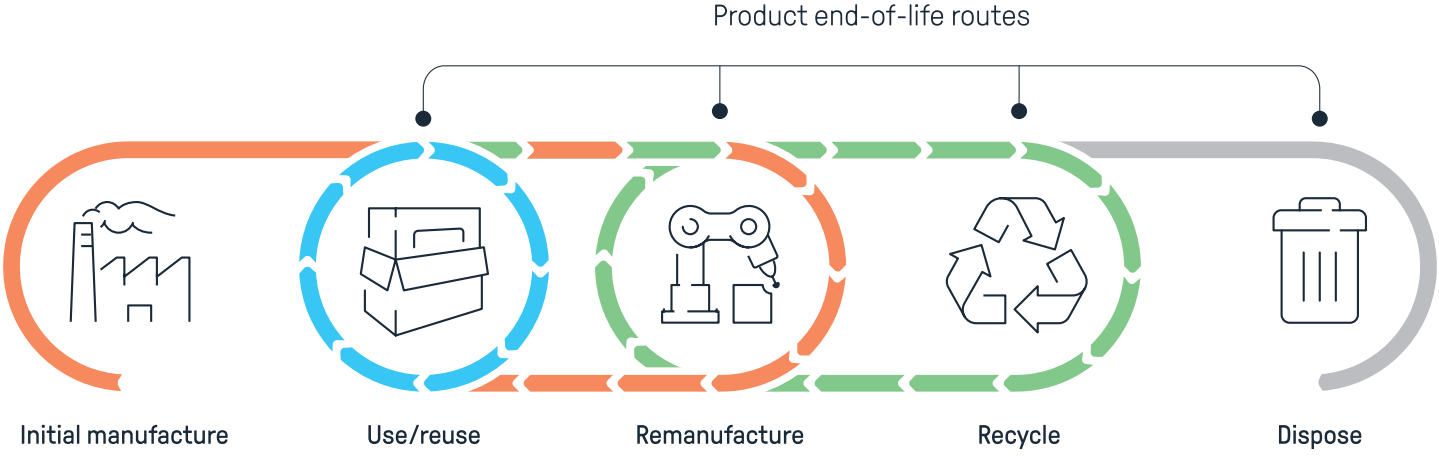

Figure 2: Product end-of-life routes.

"Sustainable design is no longer a luxury, and the affordances previously made for healthcare markets are no longer satisfying user consciences."

Reuse and remanufacture present different challenges in the healthcare sector due to product validation and sterility questions. There are, however, opportunities to explore how careful system design and management of end-of-life processes can increase sustainability. For example, the UK NHS uses remanufactured products across multiple therapy areas, suggesting that controlled processes can enable successful second lives for healthcare devices.[9]

EMBRACING CONSUMER-LED HEALTHCARE DESIGN

While the consumer sector is making advances in sustainable design, it is accountable to consumer perception. This means it may favour more visible changes rather than those that are not so apparent with the end product in hand. In healthcare developments, however, there is an opportunity to embrace the most impactful sustainability strategies while working towards the primary goal of improving patient outcomes.

Sustainable design is no longer a luxury, and the affordances previously made for healthcare markets are no longer satisfying user consciences. The ability to innovate quickly in the consumer sector has led to the development of a wide variety of strategies for sustainable design. Knowledge of these, alongside an awareness of consumer preferences, can be combined with expertise in the drug delivery sector to create the next generation of sustainable drug delivery devices.

Healthcare innovators are well placed to capitalise on the consumer-led climate of sustainability awareness and create devices and products that improve outcomes for both the patient and the environment.

ABOUT THE COMPANY

Cambridge Design Partnership is an end-to-end innovation partner, propelling global brands and ambitious start-ups to success. The company builds breakthrough products and services – from insight to ideas, prototypes to production – bringing innovation to life. Its teams are multidisciplinary, uniting scientific rigour, design ingenuity and engineering excellence for consumer, healthcare and industrial clients.

People-centred, deeply collaborative and, above all, expert, Cambridge Design Partnership is uniquely positioned to shape the future for consumers, patients and industry. Even the company's ownership model is innovative – the company is 100% owned by employees, ensuring an open culture and a total commitment to each project's success.

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ABOUT THE AUTHOR

Fran Penrose is a mechanical engineer, specialising in the early-stage design of medical devices. She has experience in device design from concept generation to design verification testing and manufacturing scale-up spanning many medical devices, including variable dose injector pens. She has a keen interest in the intersection between sustainability and medical device design. Ms Penrose forms part of Cambridge Design Partnership's core sustainability group, where she is responsible for identifying opportunities for sustainable innovation within the drug delivery sector. She has an MEng in Mechanical and Biomedical Engineering from the University of Cambridge (UK).

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SUSTAINABILITY IN MEDTECH DEVELOPMENT: AN ITERATIVE APPROACH BASED ON ECODESIGN AND LIFE CYCLE SCREENINGS

Life Cycle Assessments are a valuable but time-consuming and, ultimately, retrospective method for assessing MedTech product sustainability. In this article, Christoffer Thomsen, Development Engineer, and Peter Werner Hansen, Partner and Head of Business Development, both at Technolution, dive into an iterative and data-driven approach to more sustainable MedTech development based on Ecodesign and Life Cycle Screenings.

WHY SUSTAINABILITY IN MEDTECH?

Sustainability demands have become ubiquitous in today's MedTech industry. Regulatory requirements for sustainability are increasing. Moreover, sustainability criteria are becoming commonplace in tender processes within the healthcare sector. Also, patients want to understand the environmental impact of the MedTech products used to improve their everyday lives.

These are just a few examples in the range of sustainability demands currently facing the MedTech industry, as experienced by a number of Technolution's clients (Figure 1).

However, making products more sustainable is no simple task for MedTech companies. Development cycles lasting several years and strict regulatory requirements on products and safety, for example, make it challenging to incorporate sustainability in an already complex development process. Furthermore, gaining data about the sustainability performance of a medical device through Life Cycle Assessments (LCAs) is a costly and resource-consuming affair.

Technolution has developed an approach to more sustainable medical device development based on ecodesign principles and life cycle screenings. The approach is firmly based on industry standards and can be applied from the beginning of the development process in a more timely and agile way than LCAs. Rather than being retrospective in character, this approach is useful during all stages of product development. The goal is to bring a proactive approach to more sustainable product development by gaining fast access to dependable sustainability data throughout the development process.

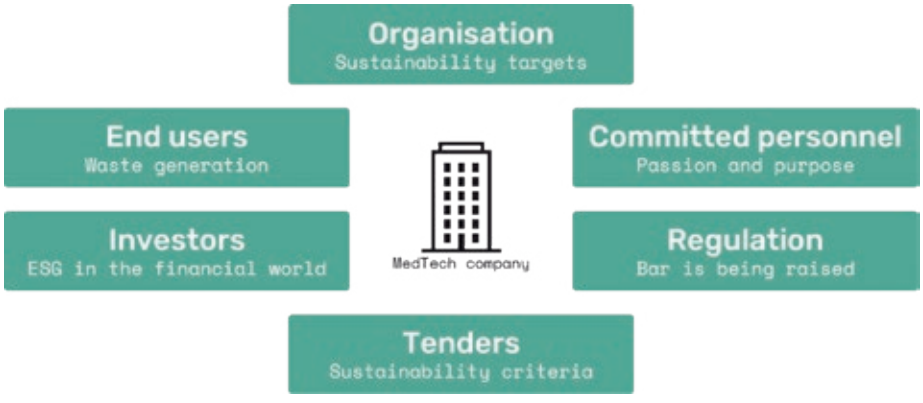

Figure 1: The MedTech industry is faced with a broad range of sustainability demands.

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GOING GREEN THROUGH ECODESIGN AND LIFE CYCLE SCREENINGS

When developing medical devices with a smaller environmental footprint over the entire life cycle of a product, Technolution uses a combination of qualitative and quantitative methods.

Technolution's ecodesign principles are based on industry best practices as a fundamental and systematic part of the company's development to analyse and choose the most appropriate ways of achieving more environmentally sustainable medical devices. This is the qualitative approach.

Technolution also uses life cycle screenings based on the LCA methodology in ISO 14040/44 to measure environmental impacts, thereby enabling data-driven decision making throughout the development process. This quantitative approach is key to ensure that sustainability improvements are made to the product with data to support the decisions.

Sustainability engineering should become a "swimlane" of its own during the development process, not just an add-on to existing areas, such as mechanical engineering. This is where ecodesign and life cycle screenings become a key tool for improving and assessing product sustainability during development in a manner that facilitates fast decision making while being based on data all the way. The goal is to enable MedTech product developers to bring more sustainability into the development process easily, from the very beginning, and keep a laser-sharp focus on making green improvements throughout.

Figure 2: The six Ecodesign principles of Technolution.

ECODESIGN – THE QUALITATIVE APPROACH

Applying ecodesign principles is a systematic approach that considers environmental aspects in design and development with the aim of reducing adverse environmental impacts throughout the life cycle of a product. The approach strives to achieve products with the lowest possible environmental impact throughout the product life cycle without compromising performance, patient safety, functionality, aesthetics, quality or cost.

Technolution uses six ecodesign principles (Figure 2) as a foundation for improving various aspects of sustainability during the development process. The principles align with the sustainability guidelines of the company's customers, which makes the principles firmly grounded in industry best practices. The principles are also based on established theory from the ecodesign research community.

It is important to note that the six ecodesign principles are not necessarily weighted equally and should not be seen as a checklist where every principle must be addressed. Their priority highly depends on project context – some principles may not be prioritised at all, while others may influence or be in conflict with each other.

However, all ecodesign principles use the same taxonomy based on guidelines. For instance, the ecodesign principle *minimise material consumption* uses the four guidelines in Figure 3 to specify the areas of focus when attempting to make sustainability improvements in the medical device.

As can be seen from the guidelines, the goal of the *minimise material consumption* ecodesign principle is to reduce material consumption as much as possible in relevant stages of the product life cycle. This is not only beneficial from an environmental viewpoint but can also lead to cost savings and support a lean production mindset through, for example, light-weighting or miniaturisation. While reducing material consumption is not new to the industry in general, quantifying the environmental benefits often has not been a priority so far.

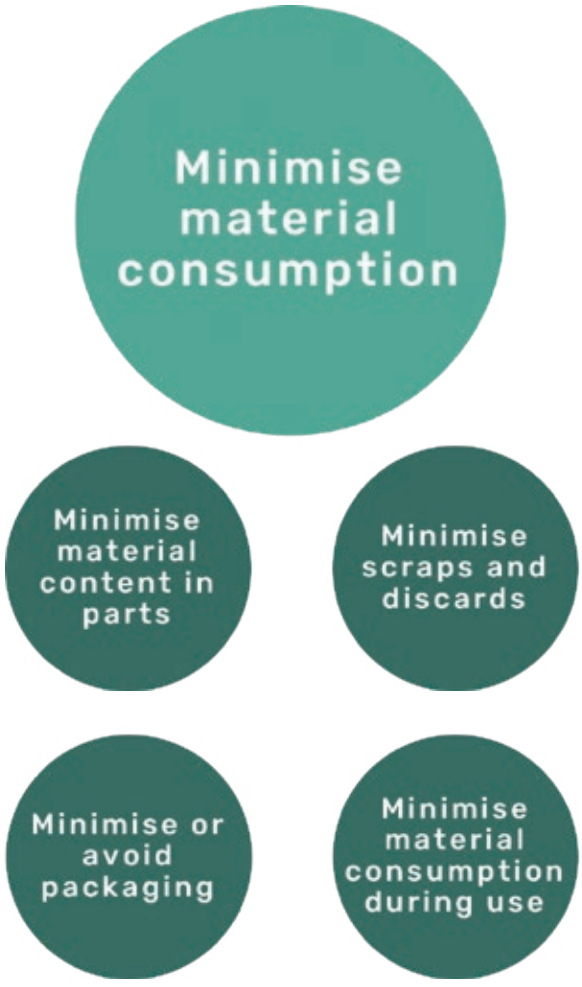

Figure 3: The four guidelines for the Ecodesign principle minimise material consumption.

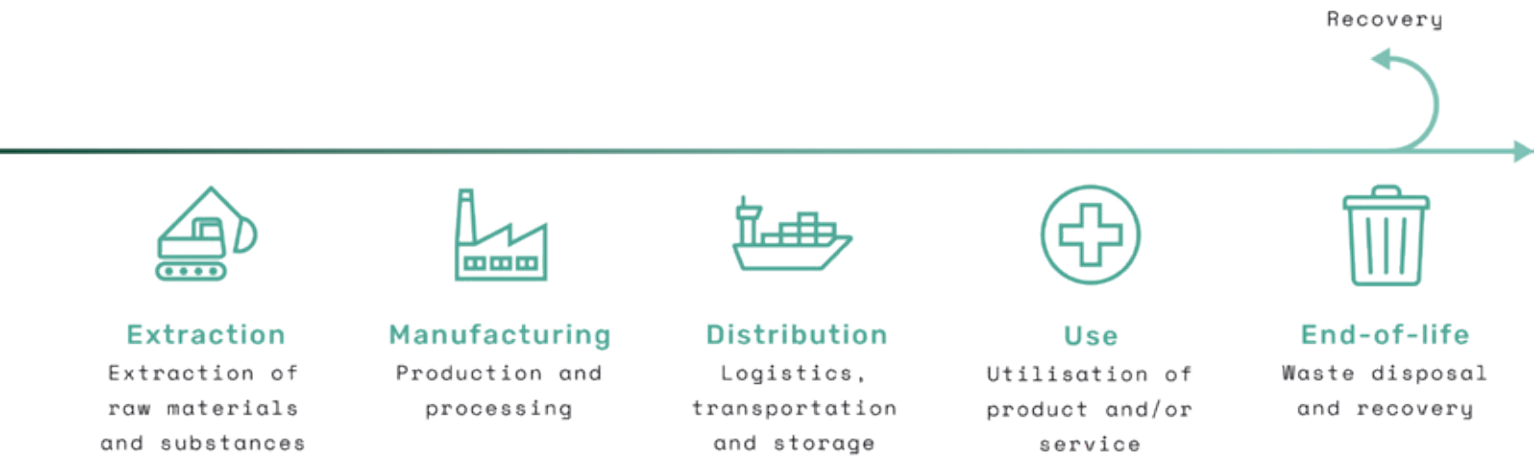

Figure 4: The five generic life cycle stages of a product from extraction of materials to end-of-life.

Another important aspect of the ecodesign principles is the alignment of circular economy concepts. The *facilitate disassembly* ecodesign principle is a great example, as this principle ensures that a medical device is designed with the purpose of separating the parts or materials at end-of-life. By using reversible joining systems or only permanently joining parts made from the same material, for example, the materials used for manufacturing can be "resynthesised" and used again as part of recovery at the end-of-life stage (Figure 4).

Picking the right subset of ecodesign principles to focus on during medical device development cannot be done without the proper data acting as support and validation for the sustainability choices being made – this calls for a quantitative approach.

LIFE CYCLE SCREENINGS – THE QUANTITATIVE APPROACH

Making continuous sustainability improvements to a medical device during product development requires specific knowledge about its environmental impact. It is well known in the industry that LCAs are of a retrospective nature and therefore not well-suited for use during product development.

> "Bridging the gap between complete sustainability knowledge about a MedTech product throughout its life cycle and, on the other hand, being able to use sustainability knowledge actively during development is key to success when making greener medical devices."

Bridging the gap between complete sustainability knowledge about a MedTech product throughout its life cycle and, on the other hand, being able to use sustainability knowledge actively during development is key to success when making greener medical devices.

Technolution's life cycle screenings are based on the LCA methodology in ISO 14040/44 and aim to provide the same information as an LCA but in less detail, based on more generic data and assumptions. This makes it applicable during a product development process, providing invaluable feedback to the ecodesign process in an iterative way, as shown in Figure 5.

The framework for making life cycle screenings contains the same four key steps as an LCA (Figure 6). Initially, Technolution sets a goal and a scope for the screening, such as a hot-spot analysis of the biggest environmental impacts of a product or concept. The next step is to create an inventory for the product, such as the parts in an autoinjector, including, among other things, information about manufacturing processes, packaging and data related to transportation. At this point, the level of detail is not as fine-grained as an LCA but still high enough to produce useful sustainability data. Then an impact assessment can be made by quantifying impacts, followed by a data interpretation step. This is the last step in which assumptions can be revisited and challenged if necessary.

If the data interpretation shows that materials are responsible for the biggest environmental impact, for example, it aligns with the ecodesign principles related to improving sustainability based on materials. This creates a foundation for making improvements to the medical device design, assessing the sustainability impacts with another life cycle screening and so forth.

Figure 5: The iterative relationship between Ecodesign principles and life cycle screenings. The earlier a focus on sustainability is implemented in development, the more environmental benefits can be obtained.

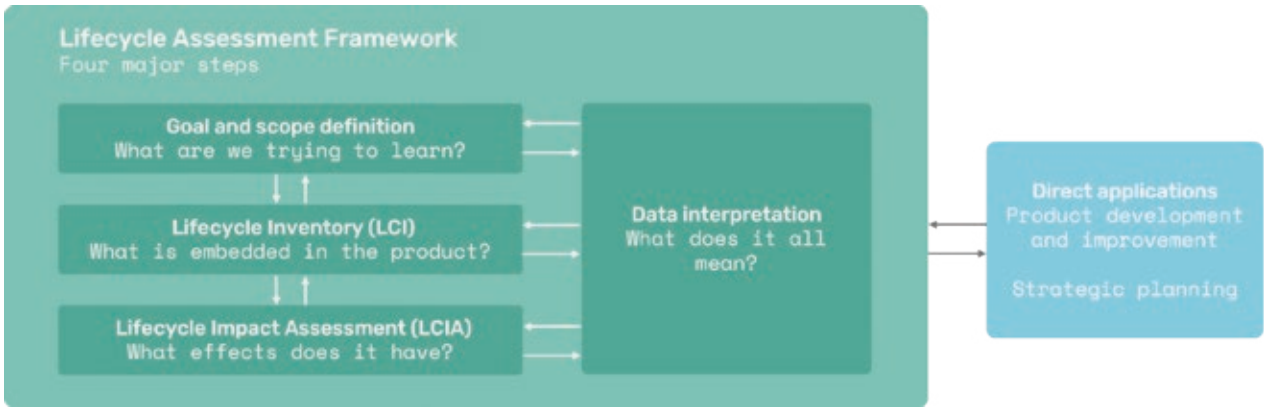

Figure 6: The framework for conducting life cycle screenings is derived from the LCA framework as outlined in ISO 14040. Results are used with Ecodesign principles to improve sustainability performance. (Source: ISO 14040)

One major pitfall that can occur while making sustainability improvements to a product is to focus too narrowly on climate change. While greenhouse gas emissions are certainly one of the most significant concerns regarding the global ecosystem, many other environmental parameters should also be considered during medical device development. This includes, but is not limited to, freshwater eutrophication, human toxicity, mineral resource scarcity, water use and ozone depletion, as shown in Figure 7. The life cycle screening approach takes these parameters into consideration when doing the calculations for the life cycle impact assessment.

CONCLUSION

This article has discussed a two-pronged approach for making sustainability assessments and improvements during medical device development. The approach combines ecodesign principles with life cycle screenings and brings important aspects from LCAs into the core of the MedTech development process in a manner that is much faster and more agile than LCAs.

The iterative nature of this data-driven sustainability engineering process makes it possible to improve medical device sustainability at an early stage and throughout development. This is key to avoiding cost-intensive product changes at a late stage in the development process and to take the guesswork out of sustainability improvements.

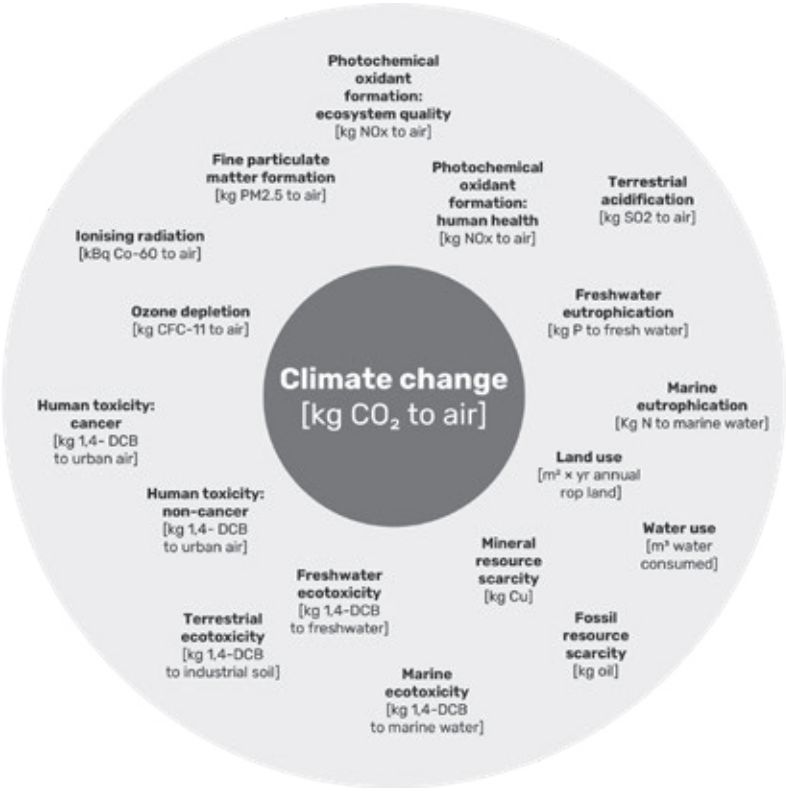

Figure 7: A narrow focus on greenhouse gas emissions and climate change leaves many important environmental issues out of sight, as shown with the ReCiPe 2016 midpoint categories.

ABOUT THE COMPANY

Technolution is a consultancy made by people driving innovation. Teaming up with Pharma and MedTech companies for ensuring high quality products and management, Technolution holds areas of expertise that enables the company to lead a full project from the very first ideation to finalised products. Where there is a need for a full project or a single competence, there is a team of specialists ready for onboarding. Established in 2003 and based in Denmark, the company was formed by experienced professionals and upcoming talents – true teamwork results in the company being trusted by some of the biggest players in the industry.

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ABOUT THE AUTHORS

Christoffer Thomsen is a Development Engineer at Technolution. Mr Thomsen's work is focused on incorporating sustainability in product development and engineering systems – a focus that interests him on a personal level as well as the professional challenge of creating more sustainable medical devices fit for the future. He holds both a Bachelor's and Master's degree in Design and Innovation from the Technical University of Denmark.

Peter Werner Hansen is a partner at Technolution where he leads the business development unit comprising project scoping, sustainability engineering and marketing. Mr Werner Hansen focuses on helping pharma and MedTech clients scope their projects enabling them to deliver above market value with their products, for example, by leading the product stream and design team at top tier pharma and MedTech companies. Mr Werner Hansen has previous experience from being Chief Technology Officer at an international consumer electronics company and project director at a product/marketing innovation consultancy serving the pharma and MedTech industries.

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SMART SOLUTIONS TO REDUCE CARBON FOOTPRINT

In this article, Rob Doorakkers, Chief Innovation Officer, and Geert van Amstel, Validation Team Lead, both at high-precision mould maker IGS GeboJagema, discuss why the company decided to become carbon neutral, how it is working to make injection moulding more sustainable and how the organisation is minimising its impact on the environment.

From Apple and Microsoft to IKEA and Unilever, the largest companies in the world have committed to becoming carbon neutral by 2030. The healthcare industry is no exception; all major players have made plans to make their operations planet-friendly. Those ambitions will have a large effect on the rest of the market too, as suppliers will be required to meet sustainability standards more and more often. IGS GeboJagema has been carbon neutral since 2019. Nonetheless, the company feels it still has plenty of work to do.

DECIDING TO BECOME CARBON NEUTRAL

There are many reasons to go carbon neutral. Of course, the overarching reason is climate change. The effects of the planet warming more than 1.5–2°C would be ruinous. IGS GeboJagema believes that companies need to take responsibility to reduce and offset their carbon footprint to the best of their ability.

But, to play devil's advocate for a moment, even companies that are less concerned with the effects of climate change would be wise to make plans to reduce their carbon footprint. An organisation's attitude and actions related to sustainability have a profound effect on its public perception, including that of suppliers, customers and employees. Companies that fail to move towards carbon neutrality will face increasing difficulties recruiting top talent and attracting new customers. Case in point: several clients have audited IGS GeboJagema through the Ecovadis sustainability assessment. By becoming a more sustainable company, IGS GeboJagema has been able to support its clients as they move towards a measurably and certifiably green supply chain.

In addition, the world is moving towards stricter CO_2 laws and regulations, such as carbon taxes. From this perspective, reducing carbon emissions today is nothing more than preparing for upcoming legislation. In short, IGS GeboJagema believes that any serious plan for the future should include a plan to minimise CO_2 emissions.

CARBON OFFSETTING

While IGS GeboJagema is carbon neutral, that does not mean the organisation does

> "With hundreds of moulds being produced at the IGS factory every year, the impact of more energy-efficient moulds could be highly significant."

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Figure 1: Land Life Company grows forests in plots of degraded land worldwide.

not emit any CO_2. It means that steps are being taken to reduce emissions as much as possible while offsetting the organisation's current carbon footprint. There are many ways to compensate for carbon emissions. IGS GeboJagema works with Land Life Company (Amsterdam, the Netherlands), which is arguably the fairest and most impactful way to offset emissions. Land Life grows forests in plots of degraded land all over the world, from Europe to Africa, and from Australia to North America. In addition to capturing CO_2 from the air, its reforestation efforts positively impact local communities by stimulating their economies, measurably decreasing the temperature and restoring flora and fauna (Figure 1).

ENERGY-EFFICIENT INJECTION MOULDING

Of course, CO_2 compensation is not a long-term solution. While reforestation can delay some of the harmful effects of climate change, it is critical for organisations to reduce their carbon footprint as much as possible. As a mould maker, IGS GeboJagema can make the biggest impact by helping its customers to do exactly that.

Injection moulding requires a lot of heat, making it an energy-intensive process. Depending on its type and size, an injection mould can use between 135,000 and 240,000 kWh per year (assuming an uptime of 95%). To put that into perspective, that is the same amount as 49–86 Dutch households.[1] It translates to 72–126 tonnes of CO_2 emissions a year.[2] With hundreds of moulds being produced at the IGS factory every year, the impact of more energy-efficient moulds could be highly significant.

Taking inspiration from that thought, IGS GeboJagema started a research project. The objective was to investigate whether energy consumption could be reduced by 20% while still retaining product quality and cycle time. A baseline test revealed that two factors made up over 80% of energy consumption:

1. Thermolater pump power
2. Thermolater heating.

With that in mind, the team investigated several optimisations. First, the team determined that the water flow rate could be reduced from 72 to 26.3 litres per minute, without affecting product quality or cycle time. This allowed for the installation of a less powerful thermolater pump. The amount of energy saved was quite dramatic: a reduction of 45%.

Second, to reduce the power used to heat the thermolater, the team wrapped isolating material around the moulds and placed isolation plates between the bed plates. This reduced energy usage by 24%.

Finally, the team found that further savings could be realised by lowering the mould temperature. Plastic suppliers provide a material data sheet that defines a temperature window for their product. Usually, this window is about 20°C. For the baseline test, the temperature was set in the middle of that window. But the team found that it could lower the temperature without affecting cycle time or product quality. This reduced energy consumption by another 8%.

> "In total, the difference between the baseline test and the optimised test was an impressive 77%."

In total, the difference between the baseline test and the optimised test was an impressive 77%. While such dramatic results cannot be expected on all moulds, this research shows that large reductions can be achieved.

IGS GeboJagema is already putting the results of this research into practice. For example, it has developed a method to minimise the energy consumption of its moulds, which will be a standard part of the validation stage going forward. Moreover, the first mould with isolation has already gone into production (Figure 2).

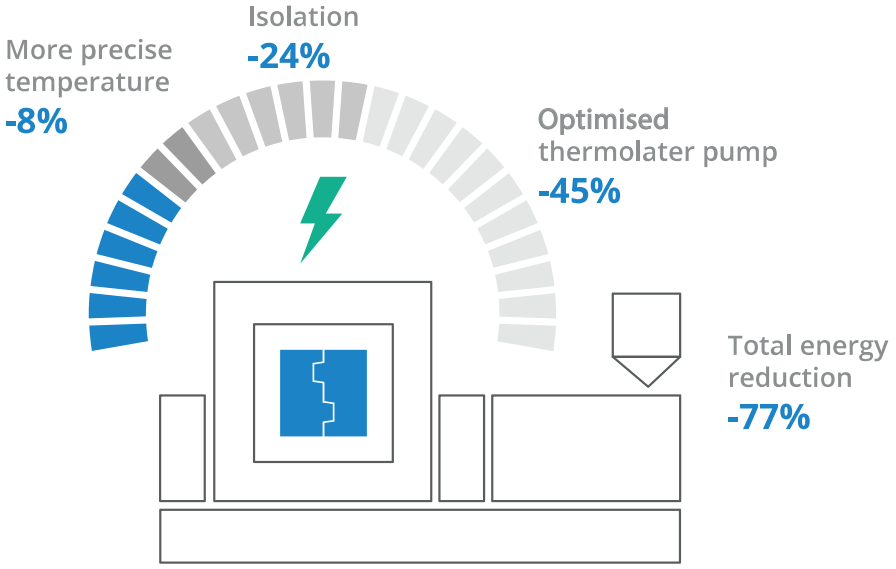

Figure 2: In the optimised test, an energy reduction of 77% was achieved.

STEPS TOWARDS MINIMAL EMISSIONS

While the move to "green moulds" can have the biggest overall impact, IGS GeboJagema is also taking action to minimise its own carbon footprint. Many of the measures taken might be common sense but are important nonetheless. LED lighting with motion sensors prevents unnecessary energy consumption. Lease vehicles will all be electric going forward. And, as with the rest of the world, since the pandemic the IGS team has started to work from home more.

Moreover, because of constant investments in state-of-the-art machinery, energy efficiency in the factory is high. Case in point: despite significant expansion of the factory and a drastic increase in output over the past 10 years, its energy consumption in 2020 was at the same level as in 2010 (Figure 3).

Technology Instead of Travel

It is well known that flying has a large impact on our carbon footprint but the numbers are still surprising. At IGS GeboJagema, air travel accounted for 51% of all travel-related emissions in 2019. Clearly, flying less is a very effective way to reduce carbon emissions. The pandemic has proved to the world that many in-person meetings can be conducted online. In fact, it saves hours of travel time. Of course, some in-person meetings are harder to replace with a standard video call, such as validation meetings or technical after-sales support.

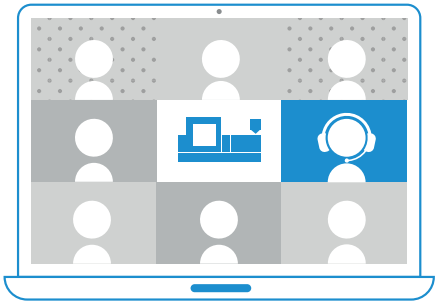

Figure 5: Remote validation was introduced by IGS GeboJagema in 2020.

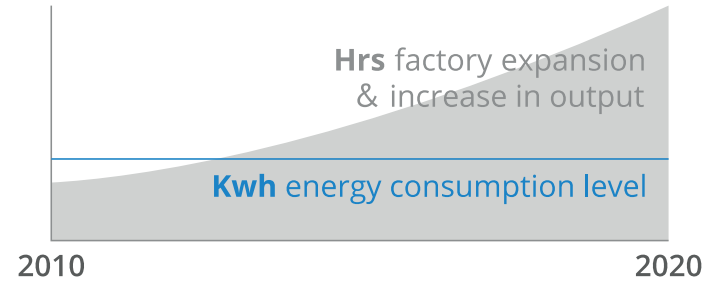

Figure 3: While output increased significantly, energy consumption remained at the same level in the IGS GeboJagema factory.

Figure 4: IGS GeboJagema provides factory tours through 360-degree images.

IGS GeboJagema has been working on several smart technical solutions to move these meetings online as well, whenever it is convenient for clients.

Virtual Factory Tour

IGS GeboJagema is proud of its state-of-the-art factory in Eindhoven, and regularly gives prospective clients a tour of the premises. The company now also offers a virtual tour of its headquarters. Through high-quality, 360-degree images, the virtual tour allows clients to see every part of the factory: the modern measuring tools, a newly expanded validation centre and the recently renovated offices (Figure 4).

Remote Validation

In 2020, IGS GeboJagema introduced remote validation (Figure 5). Remote validation makes it possible for clients to join the IGS team in the workshop from wherever they are in the world through a

Figure 6: The IGS operator communicates through a headset.

Figure 7: The HoloLens can project interactive holograms such as 3D-mould models, mould manuals and other files.

high-quality video stream and several smart technical solutions. Of course, a big reason to start offering this service was to speed up the validation process for customers. But it is also a great way to reduce CO_2 emissions (Figure 6).

Mixed Reality Support

IGS GeboJagema provides assistance on-site whenever necessary, such as during the site acceptance test or as part of its after-sales service. To make it faster and easier to assist when customers need help, the company also offers support through a Microsoft HoloLens 2. The HoloLens features a full-HD camera for crisp video footage and smart microphones that work even in noisy factories. It's as close as one can get to being physically present on-site.

A unique advantage of the HoloLens is that it can project interactive holograms such as 3D-mould models, mould manuals or other files. With all relevant information at one's fingertips and the IGS team providing live guidance, the experience of using the HoloLens for support is both surprisingly easy and highly intuitive (Figure 7).

TOWARDS A MORE SUSTAINABLE FUTURE

Urgent action is necessary to avoid the worst effects of climate change. Over the next decade, markets will continue to change and adapt around this reality. IGS GeboJagema expects that organisations that fail to significantly reduce their carbon emissions will find it challenging to retain clients, recruit new talent and keep their cost structure competitive. By contrast, there will be great opportunities for companies that are ahead of the curve. IGS GeboJagema will continue to develop innovative solutions with its partners to make the healthcare industry more sustainable together.

ABOUT THE COMPANY

IGS GeboJagema is a high-precision mould maker that designs, manufactures, validates and maintains moulds for products where extreme precision is vital, from glasses and contact lenses to asthma inhalers, insulin pens and blood diagnostic devices. IGS GeboJagema specialises in collaborating with medical original equipment manufacturers early in the product lifecycle, allowing its exceptional engineering team to develop innovative moulding solutions.

FOOTNOTES

1. *Assuming 0.53339 CO_2 per kWh. Greenhouse Gas Protocol, GHG Emissions Calculation Tool, accessed Mar 2022.*
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ABOUT THE AUTHORS

Rob Doorakkers is Chief Innovation Officer at IGS GeboJagema, where he focuses on optimising production processes, continuously improving product quality and finding innovative solutions to solve the most challenging technical challenges. Mr Doorakkers has over 30 years of experience in the injection moulding and manufacturing industry.

Geert van Amstel is a Team Lead in the IGS GeboJagema validation department. He is also currently completing his studies in Industrial Engineering and Management at Fontys University of Applied Sciences (Eindhoven the Netherlands).

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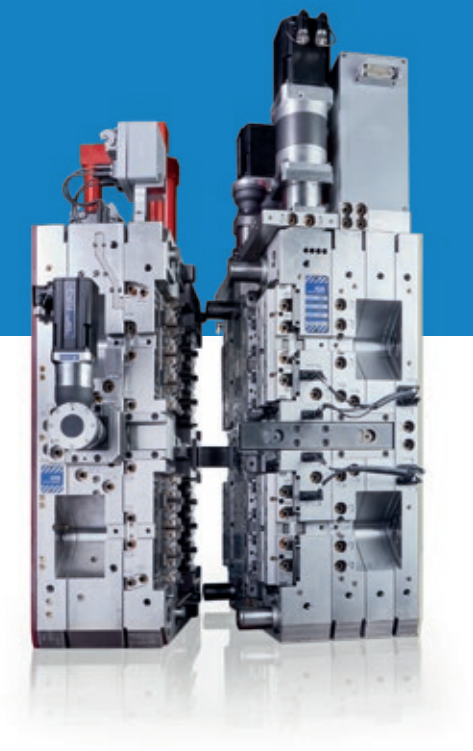

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DESIGNING DRUG DELIVERY DEVICES TO MEET EMERGING NEEDS AND SUSTAINABILITY GOALS

In this article, Pierre Moulinié, PhD, Head of Global Technical Marketing – Healthcare, Isaac Platte, Senior Application Development Engineer, and Lauren Zetts, Healthcare Marketing Manager, Americas, all at Covestro, discuss how polycarbonate-based materials deliver value to emerging drug delivery devices.

Innovation in autoinjector and pen injector platforms is increasingly oriented towards meeting sustainability-related requirements. The growing demand for materials with lower carbon footprints and the reduction of healthcare waste are among the drivers prompting designers to re-open the material choices for medical devices.

Polycarbonate, which offers an outstanding combination of engineering properties and high versatility for drug delivery devices, is available in various formulations that can help simplify designs for disassembly and sorting of reclaimed waste. With medical-grade polycarbonate availability in climate-neutral versions, drug delivery devices based on components made from polycarbonate can not only help with certain waste-related challenges but can also help the industry meet lower carbon dioxide footprint targets.

INNOVATIVE MATERIALS FOR NEXT-GENERATION DRUG DELIVERY DEVICES

The Trends

Drug delivery devices, such as inhalers, pens or autoinjectors, have seen strong growth over recent years. This growth is expected to continue, as they provide excellent solutions for both patients and healthcare providers for a variety of health issues. However, increased attention to end-of-life device disposal has opened up a debate on the materials selected. Where previously materials were chosen on the basis of the components' function and productivity, there is now a strong focus on eliminating waste within the next decade, which has caused companies in all industries, including healthcare,

> "Future drug delivery devices will not only be the target of innovation for increased technology and functionality but also for easier recovery and reuse of their materials."

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to reconsider design and material choices to facilitate recovery, reuse and lower the carbon footprint.

As a result of this new emphasis on lifecycle, materials that were once simply "good enough" now require better durability to withstand the added demands of a material's next application, while still providing functionality to lifesaving devices. Increased recycled content is well established in packaging and, in the past few years, emphasis has turned to drug delivery devices and their recovery, with a view to avoiding landfill or incineration through the reuse of the materials. Healthcare and pharmaceutical companies are among many that have mandated targets, such as zero-waste or climate-neutral operations, as part of their environmental, societal and governance goals. Hence, future drug delivery devices will not only be the target of innovation for increased technology and functionality but also for easier recovery and reuse of their materials.

With these emerging requirements in mind, and to make the designing of future devices easier, Covestro has expanded its portfolio of medical-grade polycarbonate materials. Like medical-grade Makrolon polycarbonate, these newly introduced products satisfy many elements for ISO 10993 biocompatibility and are available globally in customisable colours. In some cases, additional requirements (such as USP <661.1> or USP Class VI) are also met.

How Polycarbonate Materials Meet Technical Requirements

Polycarbonate is already well known as a material of choice for medical devices because of its outstanding combination of physical properties and amenability to high productivity with complex designs. To illustrate material innovations and benefits, Covestro developed a prototype (Figure 1) to demonstrate how newly developed, innovative materials function together and, ultimately, how a polycarbonate-based device can become more sustainable.

> "Plastics under long-term stress undergo creep, which is a permanent deformation related to their viscoelastic response to pressures."

Figure 1: Drug delivery device prototypes with all-polycarbonate components.

In many cases, these new polycarbonate-based materials have higher performance than more commonly used incumbent materials and can increase the capabilities of autoinjectors or pens. For example, parts that are under constant stress often require higher rigidity, creep-resistant materials, as provided by glass-reinforced plastics. Polycarbonate-based materials with superior mechanical performance are well suited for devices that deliver more viscous drugs, which may need higher forces and more creep resistance. Moreover, internal mechanisms with parts that slide together are made with low-friction materials to ensure consistent and smooth function. These materials are amenable to sterilisation methods not possible with many fluorinated plastics. In addition to illustrating the technical benefits of polycarbonate-based materials, the prototype in Figure 1 will also be discussed to highlight sustainability-related advantages.

Medical-Grade Polycarbonate-Improved Creep Resistance

Plastics under long-term stress undergo creep, which is a permanent deformation related to their viscoelastic response to pressures. This is particularly relevant for autoinjectors that contain spring-loaded mechanisms that remain ready to use for several years during the device's shelf life. In this case, a plastic remains under pressure and is subject to a slow deformation over this period. Creep resistance of glass-reinforced materials is known to be superior to unreinforced plastics, and such materials are often chosen for applications experiencing higher mechanical loads. Figure 2 compares the creep behaviour of several materials, including newly introduced medical-grade glass-reinforced Makrolon polycarbonates, ranging from 10% to 30% reinforcement.

Higher glass reinforcement generally improves creep resistance and, in all cases,

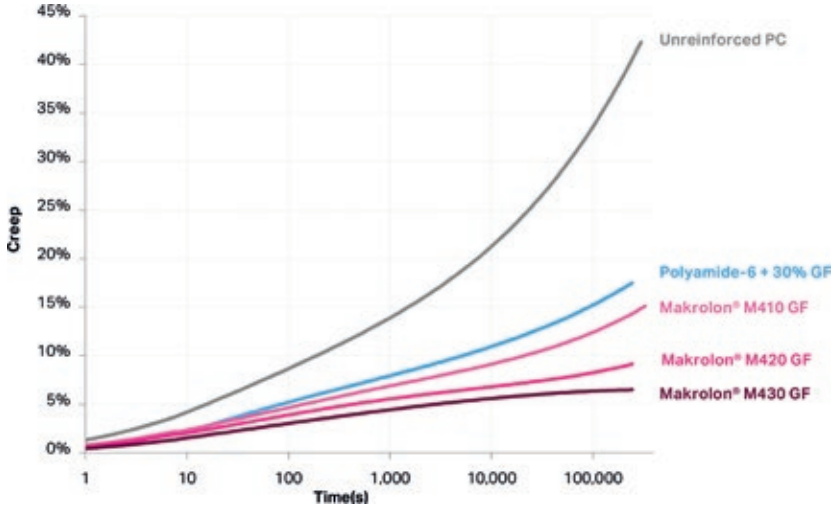

Figure 2: Tensile creep at 30 MPa stress shows low-creep medical-grade glass-filled Makrolon.

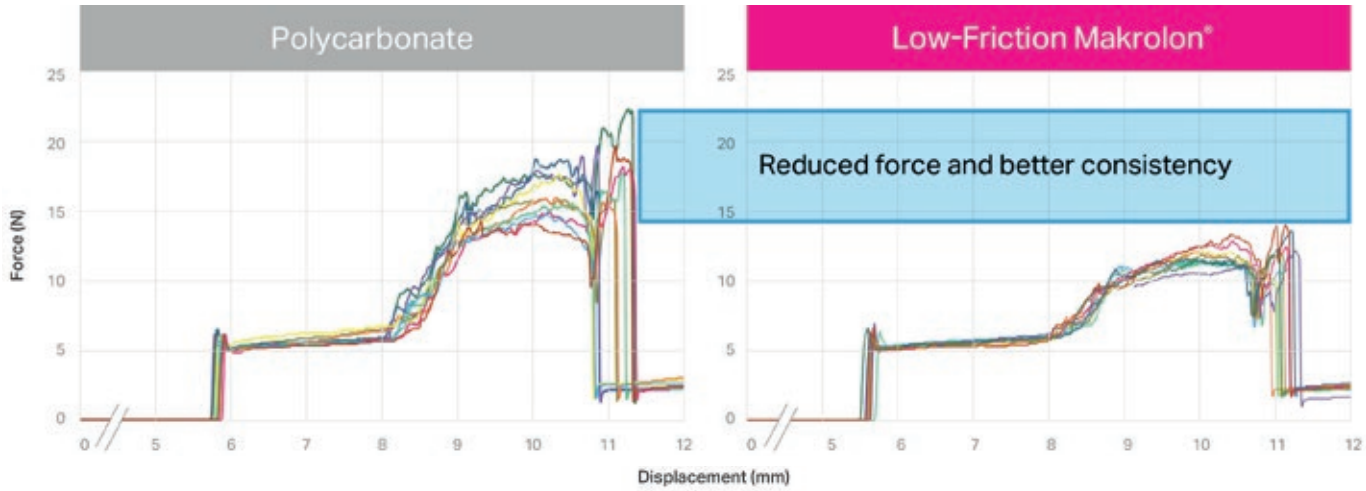

Figure 3: Forces versus displacement for button fire with polycarbonate (left) and medical-grade low-friction Makrolon (right).

reinforced resins offer superior performance to unreinforced plastics. Glass-filled (GF) polyamide, a commonly chosen material for reinforced plastics, may offer high rigidity but suffers from more significant creep compared with polycarbonate. Furthermore, polyamides are also well known for high absorbance of ambient moisture and for properties that change with humidity (e.g. modulus and dimensions). As with low-friction polycarbonate, GF polycarbonate is part of innovative designs that are oriented to easier recovery and reuse of materials.

Medical-Grade Low-Friction Polycarbonate

Achieving low-friction surfaces has traditionally been achieved with materials such as polytetrafluoroethylene or polyoxymethylene. Recent innovations in materials and processing have enabled the introduction of medical-grade low-friction Makrolon, where a coefficient of friction (COF) that is competitive with traditional low-friction materials has been observed.[1] Furthermore, low-COF polycarbonate materials have also shown significantly decreased mould-ejection forces to help increase manufacturing productivity.[2]

Low-friction polycarbonate can be an excellent choice in autoinjectors to improve the consistency of deployment forces. Figure 3 illustrates the button-release force measured on the Covestro prototype devices (Figure 1) with polycarbonate-based components. Low-friction Makrolon in Figure 3 shows reduced force in activation of the prototype, as well as improved consistency in the force required. Makrolon polycarbonate-based solutions for low friction in medical applications offer higher versatility in terms of sterilisability (e.g. by radiation) and overall stability. Low-friction Makrolon also offers a solution for new designs oriented to recovery and reuse of materials and reduced waste.

> "Low-friction polycarbonate can be an excellent choice in autoinjectors to improve the consistency of deployment forces."

PC/ABS and PC+ Polyesters for Medical Applications

Polycarbonate blends – for example, polycarbonate/acrylonitrile butadiene styrene (PC/ABS) – have been materials of choice for electrical and electronic equipment for decades, as they provide the right balance of performance and productivity. As such, medical-grade Bayblend PC/ABS has also been an important solution for drug delivery devices. As these devices become connected and require power sources, medical grades with various Underwriters Laboratories certifications for flame retardancy are expected to become popular choices. Higher-performance medical-grade Makroblend PC+ polyesters have also been solutions for applications with higher requirements, such as wearables that need better resistance to skin lotions.

The portfolio of blends for housings continues to be expanded with new flame-retardant polycarbonates designed for superior resistance to disinfectants or sterilisation methods, as new cleaners or sterilisation methods (such as UVC) are introduced.[3,4]

MAKING DRUG DELIVERY DEVICES MORE SUSTAINABLE

Climate-Neutral Materials

Previous work has shown that polycarbonates' combination of properties, especially rigidity and high heat resistance, can be leveraged to increase productivity and even lower electricity consumption during the injection-moulding process.[5,6] In addition to this important value proposition, recent developments in the processes used to make basic chemical building blocks have facilitated the replacement of traditional petrochemical feedstocks with renewably sourced raw materials. Production of engineering thermoplastics via non-petrochemical raw materials has paved the way to the manufacture of resins, like polycarbonate, with a lower carbon dioxide footprint.

The concept of mass-balance allocation further recognises the benefits of substituting fossil-based chemicals over a specified period of time and has become an established method to account for decreased carbon dioxide emissions during the production of polymers.[7] Covestro's recent introduction of climate-neutral polycarbonate, an industry first announced in 2021, relies on combining the benefits of mass balance with further advantages offered by operations relying on electric power from renewable sources.[8]

Enabling Unsorted Mixtures and Closed Loops

Drug delivery devices today are made of a variety of plastics. With plastics' widely differing chemistries, recycling and recovery of materials becomes challenging through the lens of today's sustainability goals, particularly in cases where incompatible materials may very likely become mixed together and, therefore, not

Figure 4: Simplified sorting with all-polycarbonate components in drug delivery devices.

recyclable. With the device prototype shown in Figure 1, various functional materials are brought together into a device capable of delivering consistent performance in an attractive design using materials that avoid complicated choices when planning for recycling.[9] While there are alternative plastics to polycarbonate that may offer similar functionality, the value proposition of using polycarbonate-based materials for all components is not just limited to expanded possibilities offered by the elimination of constraints (e.g. GF polyamide and humidity effects described previously).

In this section, we discuss how using all-polycarbonate components can significantly simplify material sorting after disassembly by offering a solution for "unsorted" scenarios. In the more realistic unsorted scenario, all plastic materials from a drug delivery device are mechanically mixed and remoulded. Regardless of whether manufacturers consider so-called closed-loop recycling (i.e. recovering one's own products and using them to make new ones) or open-loop recycling (i.e. recovering one's own products and using them to make something else), a significant challenge is to avoid inadvertent mixing of incompatible plastics. Figure 4 illustrates the replacement of traditional plastics with polycarbonate-based materials that can serve the same functionality.

Covestro set out to investigate the effect of cross mixing the materials from the different components in the prototype. Through simple experiments, the company studied the physical properties obtained when polycarbonate (50%), low-friction polycarbonate (20%), GF polycarbonate (10%) and PC/ABS (20%) were mixed to simulate an instance where unsorted plastics from the prototype in Figure 1 are recycled. To further simulate closed-loop manufacturing, a 100% regrind study was carried out, where the mixed material was subsequently reground, remoulded into standard test specimens (i.e. American Society for Testing and Materials D638 tensile bars and D256 impact bars) and then tested. A total of nine test/regrind/remould loops were completed.

An important advantage offered by designing a device with a uniform material suite (in this case all-polycarbonate materials) is the inherent compatibility of each material from a chemistry perspective. This can offer significantly easier paths to the reuse of the plastics after recovery and disassembly of the device. Many other materials require significant measures and efforts to avoid cross-contamination to avoid auto-catalytic – hazard generating – degradation reactions.[10] Figure 5 summarises important physical properties from the unsorted/mixed material. As shown, the all-polycarbonate mixture provided consistent properties, owing to the inherent compatibility of all the materials.

> "Innovative polycarbonate-based materials can replace traditional materials in drug delivery devices."

For many designs, tensile properties and impact strength are the principal choice drivers to ensure the plastic can perform for the intended application. The tensile properties and impact strength for the mixed materials showed excellent consistency across the regrind cycles and were better than those typically observed for polycarbonate blends with 10% glass-fibre reinforcement. This simple experiment suggests that simply mixing all-polycarbonate components from a recovered drug delivery device could still deliver consistent properties for other applications.

CONCLUSION

Innovative polycarbonate-based materials can replace traditional materials in drug delivery devices. Working together in a drug delivery device, Makrolon, Bayblend and Makroblend products can not only help to solve certain waste-related challenges but also help the industry meet lower carbon dioxide footprint targets, all while providing functionality to lifesaving medical devices.

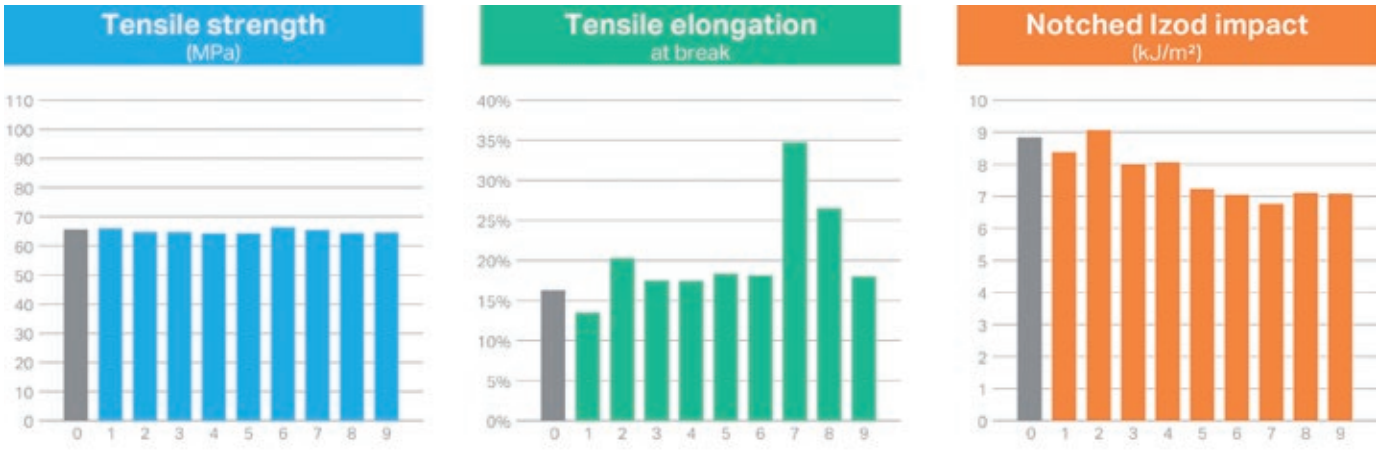

Figure 5: Physical properties of unsorted polycarbonate-based materials after multiple 100% regrind recycle loops.

ABOUT THE COMPANY

Covestro LLC is part of the global Covestro business, which is among the world's leading manufacturers of high-quality polymer materials and their components. With its innovative products, processes and methods, the company helps enhance sustainability and quality of life in many areas. Covestro supplies customers around the world in key industries such as mobility, building and living, as well as the electrical and electronics sector. In addition, polymers from Covestro are used in sectors such as sports and leisure, cosmetics and health, as well as in the chemical industry itself.

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Pierre Moulinié, PhD, leads Global Technical Marketing for Healthcare at Covestro's Engineering Plastics Business. He has a PhD in Chemistry from Carleton University in Ottawa (Canada) and has been a regular contributor to technical conferences, journal articles, patent applications and book chapters for the past 25 years.

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Lauren Zetts is the Healthcare Marketing Manager for the Americas region at Covestro. She is responsible for strategy development within Engineering Plastics, including product and technology launches. Ms Zetts graduated with a BSc in Chemical Engineering and a master's degree in Biomedical Engineering from the University of Michigan (MI, US).

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ARE GOVERNMENTS BANNING THE MOST ENVIRONMENTALLY FRIENDLY INHALER?

Here, Rob Udale, Principal Engineer, Catriona Eldridge, Materials Scientist, and Omar Shah, Materials Engineer, all of Springboard, assess the assertion that pMDIs are the most environmentally damaging of the available pulmonary drug delivery device archetypes, and explore some of the intricacies not accounted for in the public discourse surrounding pMDIs.

INTRODUCTION

At COP26, countries committed to bold action to reduce their climate impact and achieve net zero emissions by 2050. These commitments are now percolating into the private sector, as FTSE100 companies, including AstraZeneca and GSK, announce plans to eliminate their contribution to climate change by 2050.[1]

Within the public sector, the UK NHS has stated its aim to be the world's first net zero emission national health service for the emissions it controls directly by 2040 and reach an 80% reduction at some point between 2028 and 2032.[2] Within this context, pressurised metered dose inhalers (pMDIs) have come under scrutiny, due to the high global warming potential of their propellants, as illustrated in a recent BBC news article.[3]

Some people may question the significance of asthma medication on global emissions, but data suggests that around 4% of the NHS's entire carbon footprint comes from asthma drugs,[3] and pMDIs account for 0.1% of the UK's national carbon footprint.[4] This number has been deemed too large to ignore and some parts of the NHS are looking to phase out pMDIs.[5] But are dry powder inhalers (DPIs) and soft mist inhalers (SMIs) really better for the environment – and for patients – than pMDIs?

IT IS ALWAYS MORE COMPLICATED THAN THAT

Appealing though this bold conclusion is, it is over-simplistic. Firstly, it focuses only on the use phase of the device, neglecting the carbon embodied in manufacture and disposal. It also considers only the device's CO_2 equivalent (CO_2e), which, although perhaps the most important, is only one of a suite of metrics used to quantify environmental impact.

> "An LCA is a methodical framework for assessing the environmental impacts associated with a product system, from the extraction of raw materials through to its end of life."

To make an informed decision, a complete lifecycle assessment is required. Additionally, not all patients can safely use alternative devices (Table 1); for instance, DPIs require a sharp intake of breath that isn't possible for some patients, particularly those with the sorts of chronic lung conditions often treated with inhaled medications.

LIFECYCLE ASSESSMENT

A lifecycle assessment (LCA) is a methodical framework for assessing the environmental impacts associated with a product system, from the extraction of raw materials through to its end of life. Firstly, an LCA must define the scope of the assessment: Where should it start and end the "lifecycle" in question? Is it considering the recycling and waste streams of the product?

The assessment also needs to define the functional unit. When comparing two products, it is important to make sure that the units are functionally equivalent – you can't compare apples and oranges, but you can compare 50 g portions of different types of dried fruit. In this case, a suitable unit is one therapeutic dose from a pulmonary drug delivery system.

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	pMDIs	DPIs	SMIs
Shake device before use?	Yes	No	No
Typical recommended intake profile	Gentle, deep intake of air to reduce impaction of drug in the throat ▼ Hold breath for a few seconds ▼ Exhale	Rapid deep intake of air in order to aerosolise the dose to the requisite fine particle sizes ▼ Hold breath for a few seconds ▼ Exhale	Gentle, deep intake of air ▼ Hold breath for a few seconds ▼ Exhale
Typical flow resistance of device	Low	High	Medium

Table 1: Typical use steps and required intake profile for the three inhalation device types under discussion.

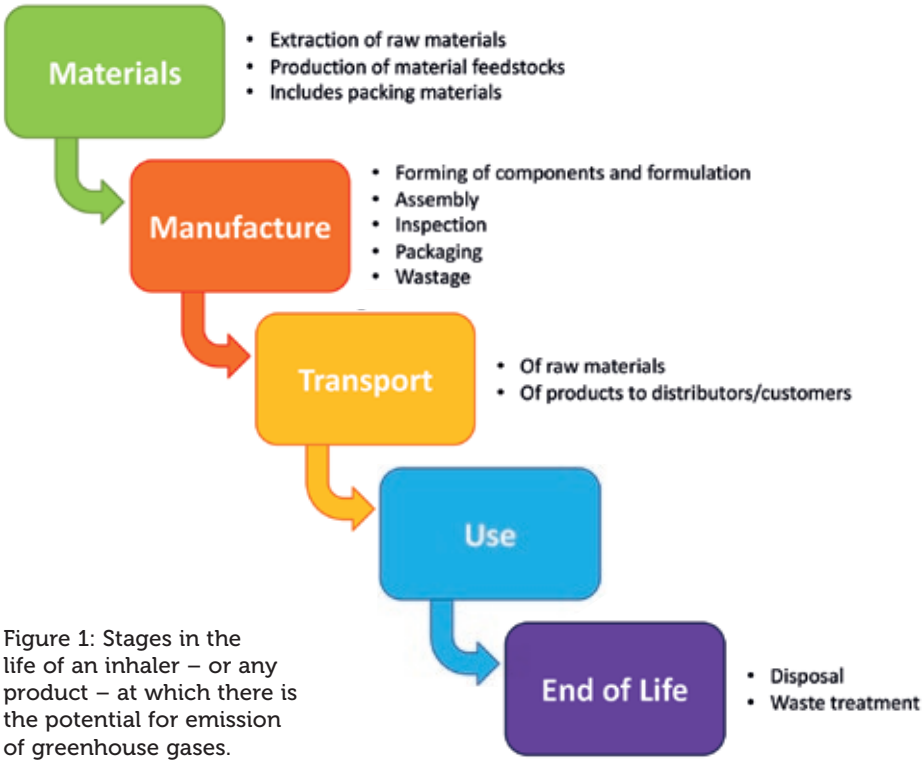

Figure 1: Stages in the life of an inhaler – or any product – at which there is the potential for emission of greenhouse gases.

Material	pMDIs	DPIs	SMIs
Polymers (g)	15	65	45
Steel (g)	1	1	20
Aluminium (g)	6	8	2
Total g CO_2e per device	95	285	210
Number of doses	200	30	150*
Total g CO_2e per dose	**0.5**	**9.5**	**1.5**

Table 2: Typical masses of materials in different inhaler types. Typical embodied carbon for materials: Steel: 1.9 g CO_2 g^{-1}, Polymers: 3.5 g CO_2 g^{-1}, Aluminium: 7 g CO_2 g^{-1} (values from references 6–8). *SMIs currently on the market are refillable a limited number of times. This figure is an estimate.

LCAs come in many varieties, from quick, back-of-the-envelope calculations at the concept and feasibility stage, to detailed comparative LCAs after product launch. LCAs are most valuable in the early development stages, where corrective action can be taken with relative ease, rather than waiting until a device is finished to discover its problems. LCAs can inform choices of concept, materials and even design, such as designing for disassembly.

A MORE REPRESENTATIVE ANALYSIS

To develop a more accurate picture of the environmental impact of pMDIs, they can be compared with the two currently available alternatives – DPIs and SMIs – with the functional unit as one therapeutic dose. Currently, medical devices are not widely recycled (although this is improving). To illustrate this concept, let's perform a crude hypothetical cradle-to-grave LCA, with a "cut-off" approach (i.e. assuming no waste is recycled). For simplicity, this assessment will only consider the contribution to global warming.

The lifecycle of a device can be broken into the following stages (Figure 1):

1. Materials (extraction and production)
2. Manufacture (materials processing and assembly)
3. Transport
4. Use
5. End of life.

Materials

Table 2 lists typical values of embodied carbon for different materials used in inhalers. Using such values, it is possible to estimate the CO_2e engendered in the materials of these devices.

Manufacturing

Without primary data on the manufacturing processes, estimating manufacturing energy cost or wastage is difficult. Additionally, these values can vary substantially by manufacturing location due to differences in the local grid energy mix. For this reason, this back-of-the-envelope LCA will neglect this phase.

Use

While DPIs and SMIs produce relatively few emissions in use, pMDIs use a hydrofluoroalkane (HFA) propellant that is released with every dose. These compounds have extremely high global warming

"Although DPIs and SMIs embody more carbon and send more waste to landfill, these factors are outweighed by the GWP of the propellant in pMDIs by an order of magnitude."

potential (GWP) – a measure that describes how potent a greenhouse gas the compound is over a set time period, relative to CO_2.

HFA-134a is the most common propellant and has a GWP of 1,300 g g^{-1}. With a typical loading of 15 g giving 200 doses, each dose has a CO_2e of 100 g. Another commonly used propellant, HFA 227ea, has a GWP of 3,350 g g^{-1}, which is even worse.[9]

End of Life

Because this rough assessment is employing a cut-off approach, it assumes none of the materials are recycled; therefore, the only salient figure of merit is the mass of material sent to landfill, shown in Table 3.

Summary

What this assessment shows is that, although DPIs and SMIs embody more carbon and send more waste to landfill, these factors are outweighed by the GWP of the propellant in pMDIs by an order of magnitude (Table 4). This highlights the need for improvement in this area, which could potentially make pMDIs the green choice compared with the competition.

Another factor to consider is the relative complexity of DPIs and SMIs. pMDIs are much simpler, which not only makes them cheaper to produce, but also easier to design for recyclability, giving them greater potential for improvement.

DESIGNING BETTER DEVICES

This simplistic LCA shows that the propellant is the root cause of the majority of a pMDI's carbon footprint – a conclusion with which the Carbon Trust's (London, UK) analysis of GSK's inhalers agrees. Approximately 75% of GSK's Seretide MDI's carbon footprint comes from the HFC-134a propellant.[10] To combat this, the inhalation sector and pMDIs are moving rapidly towards lower impact propellants

Inhaler type	pMDIs	DPIs	SMIs
Typical total mass (g)	22	75	65
Mass per dose (g)	**0.1**	**2.5**	**0.4**

Table 3: Typical masses of different inhaler types.

Inhaler type	HFA-134a pMDI	DPI	SMI
CO_2e per dose engendered in the materials (g)	0.5	9.5	1.5
CO_2e per dose emitted during use (g)	100	0	0
Total CO_2e per dose (g)	**100**	**9.5**	**1.5**

Table 4: Total equivalent CO_2 per dose, including materials and usage.

with isobutane, HFA-152-a from Koura[11] (MA, US) and Honeywell's (NC, US) HFO-1234-ze(E)[12] currently leading the race to replace existing propellants.

Adopting these replacements will require a significant redesign of the standard pMDI canister and valve components, as well as adapting the filling process, due to 1234ze and 152a's flammability. However, this change will reduce the GWP of pMDIs by an order of magnitude.[9] This could bring pMDIs into line with, or even ahead of, the competition. But what other changes can improve a product's sustainability? And when can they be made?

At Product Launch

Once a product reaches the market, the possible reductions are limited. Recycling schemes, like Chiesi's TakeAIR[13] or GSK's Complete The Cycle (now defunct),[14] do exist, and a good understanding of an inhaler's sustainability should include recyclability. An estimated 0.5 million tonnes of CO_2e would be saved annually if every inhaler in the UK was recycled.[15]

Recycling does some good – for example, unused propellant can be used in air conditioning units and aluminium cans can be reclaimed – but it is limited. Without infrastructure for separate waste collection, there will be no recycling at all; GSK's recycling scheme achieved a <1% collection rate. Even with collection schemes in place, most of the plastic components will still go to landfill or energy-from-waste schemes.[14] Furthermore, recycling cannot reverse environmental impacts that have already occurred; it cannot recapture propellant which has already been released during use, or un-spend the energy used to make the device. However, better design can reduce or remove these impacts before they occur. In comparison, recycling is, at best, only mitigation, not a cure.

Designing for Manufacture

Larger reductions are possible earlier in product development. Stepping back just to selecting manufacturers, careful choices can reduce environmental impact. Selecting manufacturers with more renewable energy supplies reduces CO_2e emissions, and reducing the distance between manufacturer and customer reduces transport emissions. An inhaler manufactured in Germany would be produced using approximately 50% renewable energy,[16] but then would have to travel a significant distance to reach a customer in the US, and it would cost considerably more than a product manufactured in China (Figure 2).

Additionally, manufacturing methods will affect the device's environmental impact – for example, efficient manufacturing equipment, such as electric rather than hydraulic plastic injection moulding machines, could reduce energy costs by over 30%,[17] and vacuum-crimping the canister rather than purging with propellant could also make significant reductions. All these considerations should be taken into account when assessing sustainability; LCA is a useful framework for balancing these trade-offs.

During the Design Phase

To achieve more fundamental improvements, it is prudent to consider the design itself. Here, material choices and more efficient design can reduce the environmental impact of a device; for example, selecting and

Figure 2: Illustration of the trade-offs manufacturers face when choosing the manufacturing location.

designing for a lower-impact propellant, choosing steel over aluminium or titanium, or designing for efficient manufacturing methods, such as injection moulding, rather than more wasteful ones, such as milling.

Recyclability can also be designed in at this stage, such as designing for a more easily disassembled device and implementing single-polymer components. With ease-of-separation designed in, more of the device can actually be recycled at end of life, rather than going into landfill or energy-from-waste schemes. There are now collection-for-recycling schemes for items ranging from lithium batteries[18] to injector pens,[19] as well as material-specific schemes, including medical PVC pilot schemes.[20] Medical-grade materials have great recycling potential, due to their high quality and traceability. However, if components cannot be separated into different materials, they often cannot be usefully recycled.[21] Without designing-in recyclability, this high-value waste is lost to landfill.

Counterintuitively, designing away from recyclability can reduce overall environmental impact; a less recyclable device with a longer working lifetime may have a lower impact overall than a fully recyclable but shorter-lived alternative. For example, a reusable core with disposable sub-systems could minimise both environmental impact and cost. This approach is extremely pertinent in the development of connected devices, where the material and environmental costs of the electronics sub-system are large compared with the rest of the device. LCA provides a framework for comparing the impact of a product's embodied energy, lifetime, function and end of life.

"Such assessments demonstrate that the environmental impact of current pMDIs is not significantly different from that of their competitors and, with the development and introduction of new, lower-GWP propellants on the horizon, they have the potential to become better."

The Concept Stage

The biggest reductions are possible at the concept stage. Most pMDI emissions are from the propellant. At the concept stage, a design can switch between propellants, or from a single use to a partially reusable device, with relative ease, potentially significantly lowering the device's overall environmental impact. Such changes would be significantly harder later in the design process.

A simple, small-scale LCA in the early design stages can help companies identify their most (and least) sustainable options and avoid locking in an inherently unsustainable design. If sustainability is ignored until the product launches, it will be too late to improve a product's fundamental sustainability without expensive redesigns and manufacturing adjustments.

Designing for sustainability can be counterintuitive; direct comparisons of products in use can miss the wider picture and can artificially inflate or obscure the impact of various design choices. A full-lifecycle approach to assessing sustainability is vital for good design and is most effective when it is part of the design process from the start.

CONCLUSION

The NHS and other payers should not only look at emissions during use, but rather assess the full lifecycle before deciding to switch from one type of device to another. Such assessments demonstrate that the environmental impact of current pMDIs is not significantly different from that of their competitors and, with the development and introduction of new, lower-GWP propellants on the horizon, they have the potential to become better.

However, this drive for reduced environmental footprint must be balanced with the needs of the other stakeholders – principally, cost to the payer and outcomes for both payer and patient – and balanced against the strengths and weaknesses of alternative devices (Table 5). Historically, the key advantages of pMDIs have been their suitability for children and patients with breathing limitations, and their low cost – will that remain the case with the new propellants?

By employing good design principles and LCAs throughout the design process, it is possible to meet the requirements of both the end user and the wider stakeholders. Watch this space – pMDIs may well be the green option in 10 years and should not be banned!

	pMDIs		DPIs	SMIs
	Simple device (no breath actuation)	Breath-actuated device		
Example	GSK Ventolin, Kindeva Sirdupla	Kindeva Autohaler, Mundipharma K-haler, Teva Easi-breath	GSK Elipta, Novartis Breezhaler, Chiesi NEXThaler	Boehringer Ingelheim's Respimat
Environmental impact	↑↑	↑↑↑	↑	↑
Cost per dose	$	$$	$$	$$$
Delivery efficiency	**Low to Moderate** Require co-ordination between inhalation and actuation, leading to variable delivery efficiency drug delivery	**Moderate** Inhalation and activation controlled so more consistent delivery efficiency	**Moderate**	**Best in class**[22] Excellent fine particle fraction (FPF) and easy to co-ordinate, hence high delivered dose
Advantages	Small and discreet Commonly hold a large number of delivered doses Total isolation of the drug from the external environment		Highest mass of drug per dose of all the inhaler forms Dose counters included	Small and portable Require less breath co-ordination than pMDIs, due to low soft mist velocity, and less of a sharp breath than DPIs
Disadvantages	Require shaking and priming – which is often forgotten about, leading to variable dose efficiency Developing physically and chemically stable formulations compatible with HFA propellants is challenging		The sharp intake of breath that is commonly required isn't possible for all patients Difficulty in developing a stable powder formulation that meets the challenging requirements for good aerosol performance	Relatively low number of doses per device Not yet suitable for all drug formulations and drug needs to be resistant to high shear forces in nozzle

Table 5: Illustration of the typical strengths and weaknesses of the three main inhaler types.[22]

ABOUT THE COMPANY

Springboard specialises in developing devices from concept to manufacture for regulated markets. The company is expert at creating innovative yet robust designs and solving difficult technical problems quickly. Springboard does not have internal projects so it is as fast and cost effective as possible, and the intellectual property belongs to its clients.

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Rob Udale is a Principal Engineer at Springboard, where he leads engineering and scientific teams developing new medical devices, including surgical tools, injectors and inhalers. He has been the named inventor on multiple patents and is a Chartered Engineer. He read Engineering at the University of Cambridge (UK), where he developed his background in both fluids and mechanics at the prestigious Whittle Laboratory. In developing devices, Mr Udale seeks to balance technical, user and commercial requirements to produce simple and robust solutions.

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HOW CAN THE PHARMA INDUSTRY PREPARE FOR NEW pMDI PROPELLANTS?

In this article, Nick Atkinson, Strategic Engineering Programme Manager at Recipharm, looks at the changes that are set to hit pressurised metered dose inhaler manufacturing as new propellants are introduced and how pharma companies can prepare for the switch.

Pressurised metered dose inhalers (pMDIs) are the most frequently prescribed inhaler devices worldwide (Figure 1), enabling patients to manage respiratory conditions such as asthma and chronic obstructive pulmonary disease (COPD).

However, pharmaceutical companies must prepare for new changes that are set to impact the industry as legislation governing the use of pMDI propellants is tightened. Many pMDIs use hydrofluoroalkanes (HFAs) – specifically HFA-134a and HFA-227ea – as propellants, which are set to be phased out across other industries due to their high global warming potential (GWP) to pave the way for lower-GWP alternatives.

Although the pharmaceutical industry is currently exempt from the HFA phasedown, their industrial use across other sectors is already on the decline. As a result, these propellants will become more difficult and costly to acquire.

This transition is likely to present challenges to pharmaceutical companies, as next-generation low-GWP propellants can potentially impact formulation

Figure 1: A selection of pMDI actuators and valves.

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"Pharmaceutical companies must assess the potential risks of new propellants to determine how to safely handle, transport and contain them."

requirements, valve design and manufacturing equipment. As such, companies must prepare their manufacturing environments and processes for the introduction of new low-GWP propellants for pMDIs in the near future.

Pharmaceutical companies must assess the potential risks of new propellants to determine how to safely handle, transport and contain them. This leads to one of the main challenges that manufacturers must overcome with the introduction of new propellants: working with flammable gases. This article will explore flammability challenges and how pharma companies can prepare their pMDI manufacturing environments to safely handle new propellants.

TACKLING FLAMMABILITY CONCERNS

There are two potentially sustainable propellant candidates currently under consideration with lower GWP levels than HFA-134a (which has a GWP of 1,430) and HFA-227ea (which has a GWP of 3,220):

- 1,1-difluoroethane (HFA-152a): GWP of 124
- 1,3,3,3-tetrafluoropropene (HFO-1234ze(E)): GWP of less than 1.

Under certain conditions, HFA-152a and HFO-1234ze(E) have been classified as flammable and mildly flammable, respectively, which means that production of pMDIs using them will require pharmaceutical companies to develop a deep understanding of the safety controls that must be implemented across their processes.

When working with flammable aerosol propellants, fire or explosion risks must be carefully considered. At a basic level, there must be fuel, oxygen and an ignition source present for a fire to occur. Regardless of the propellant that is used, it is imperative that pharmaceutical companies assess the risk and prepare their processes and environments to prevent scenarios where a fire or explosion could occur.

WHAT ARE THE RISKS ASSOCIATED WITH FLAMMABLE PROPELLANTS?

There are a number of potential risks related to the handling, storage and transportation of pMDI propellants. Typically, a mixing vessel containing the propellant, API and any excipients is required to manufacture a given pMDI formulation. Before pMDIs can be filled, mixing must take place within a sealed manufacturing system.

"Reducing the risk of working with flammable propellants requires manufacturers to carefully consider their cleanroom environments."

It is crucial that steps are taken to prevent the propellant escaping the vessels and pipework. However, if this does happen, under the right conditions there is an increased risk of propellant (fuel), oxygen and an ignition source coming together to create a fire or explosion. The risk of an undetected leak taking place must be mitigated against, as this could result in a catastrophic event, given the potential volume of propellant in the manufacturing system.

Propellants must also be properly stored in an area where they cannot come into contact with a heat source, as the overheating of storage vessels could cause aerosol expansion and possibly result in a boiling liquid expanding vapour explosion (BLEVE). Controls must be implemented that aim to prevent overheating of flammable aerosols during storage and bulk transport.

REDUCING RISK IN A GMP MANUFACTURING ENVIRONMENT

GMP manufacturing requires rigorous cleaning and inspection measures across each process, which can heighten the risk of a leak occurring. High levels of intervention across cleaning, inspections, product changeovers, connections with mobile equipment (e.g. drug addition vessels) and filter changes will, in turn, heighten the risk of a leak.

There are a number of measures that can be taken to reduce this risk in a GMP manufacturing environment. As set out in Regulation 6 of the Dangerous Substances and Explosive Atmospheres Regulations (DSEAR) – the UK implementation of the EU ATEX Workplace Directive – the steps that should be taken to minimise risk include the following:

Reduce Quantity – Compartmentalising

Manufacturers can take steps to segregate and isolate parts of their manufacturing system to minimise the quantity of the dangerous substance in one place, with isolation valves being an effective method.

Preventing Releases – Gas Detection Systems

Equipment must be appropriately designed and engineered to prevent leaks. Integrity of the manufacturing system can be confirmed following intervention by pressure testing. If a leak were to occur, gas detection systems can be used to monitor the concentration of a flammable substance in the atmosphere, and can be linked to isolation valves to minimise further leakage.

Control Ignition Sources – Classification

Manufacturers must also ensure that any hazardous areas are classified, and that all equipment is rated appropriately to minimise the risk of ignition.

Mitigation – Damage-Limiting Construction

Damage-limiting construction (DLC) can be used to mitigate the detrimental effects of a vapour cloud explosion (deflagration) and limit its impact to within the enclosure.

Instruction – Ensuring User Competence

Accurate instruction is necessary to ensure that any risk is safely contained, removed to a safe place or otherwise rendered safe. Operators must also possess the skills, knowledge, training and ability to safely conduct their operations.

> "Preparing manufacturing environments as soon as possible for the changes that new, more sustainable propellants will bring is key to ensuring the safe development and delivery of inhalable drugs."

Determining Necessary Levels of Hazard Control

If the hazardous substances cannot be eliminated, there must be measures in place to minimise risk. This typically requires several independent "layers" of protection, and the potential shortcomings of each layer of protection must be carefully evaluated.

CLEANROOM CONSIDERATIONS

Reducing the risk of working with flammable propellants requires manufacturers to carefully consider their cleanroom environments. The formulation, mixing and filling activities required for pMDI projects should be performed in an ISO 8-grade cleanroom (Grade D). This environment must be designed for accessible and easy cleaning, with no crevices or surfaces for dust and debris to settle.

Spaces should also be fitted with air exhaust systems to prevent the formation of a flammable atmosphere when hazardous substances are being handled. The air-change rate must be confirmed as adequate and would typically be higher than that needed to maintain GMP conditions. For areas classed as highly hazardous, manufacturers must ensure that extracted air cannot be recirculated back into the system to avoid redistributing the flammable vapour into other uncontrolled areas.

LOOKING AHEAD

Preparing manufacturing environments as soon as possible for the changes that new, more sustainable propellants will bring is key to ensuring the safe development and delivery of inhalable drugs. While HFA-152a and HFO-1234ze(E) are currently the most promising contenders to replace existing propellants, there is still work to be done to fully assess their flammability risks and implement appropriate engineering controls.

Future-proofing drug supply will require pharmaceutical companies to seek support from a dedicated partner specialising in pMDIs. Choosing a partner, such as Recipharm, that can help them through these changes will allow companies to better understand and adapt faster to the requirements of these new propellants.

ABOUT THE COMPANY

Recipharm is a leading CDMO headquartered in Stockholm, Sweden. The company operates development and manufacturing facilities in France, Germany, India, Israel, Italy, Portugal, Spain, Sweden, the UK and the US and is continuing to grow and expand its offering for its customers. Employing around 9,000 people, Recipharm is focused on supporting pharmaceutical companies with its full-service offering, taking products from early development through to commercial production. For over 25 years, Recipharm has been there for its clients throughout the entire product lifecycle, providing pharmaceutical expertise and managing complexity, time and time again. Despite its growing global footprint, Recipharm conducts its business as it always has and continues to deliver value for money with each customer's needs firmly at the heart of all that it does. That's the Recipharm way.

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Nick Atkinson is Strategic Engineering Programme Manager at Recipharm. He has extensive knowledge of the design and implementation of manufacturing systems for orally inhaled and nasal drug products, across all manufacturing scales. Mr Atkinson has led the implementation of new – and adaptation of existing – manufacturing processes at clinical and commercial scales. Prior to his current role, he led the engineering project delivery team at Recipharm's Holmes Chapel site in the UK.

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CAPSULES: CLASSIC DRUG DELIVERY FORM HOLDS POTENTIAL FOR SUSTAINABLE DELIVERY

In this article, Jnanadeva Bhat, PhD, Vice-President – Formulation R&D, and Anita Solanki, Lead – White Papers & Publications, both of ACG's Pharma & Nutra division, discuss the role that hard capsules are able to play in delivering a more sustainable pharmaceutical industry, both as an oral solid dosage form and in dry powder inhalers.

Humanity's wellbeing is not only associated with our own health but closely related to the condition of our surrounding environment. As such, environmental sustainability and protection are crucial, and it is our responsibility to safeguard environmental resources and ecosystems to ensure wellbeing both now and in the future. The pharmaceutical industry has a significant global environmental impact, from excessive waste creation to greenhouse gas emissions and the use of non-renewable energy. To move forwards, environmental sustainability needs to be considered across all activities and processes, from manufacturing to design and development.

The pharmaceutical industry must acknowledge this and face up to the challenge of improving the way it operates to create a sustainable future, whilst maintaining access to good quality medicines for all. Environmentally accountable pharmaceutical firms should develop practices for manufacturing their products in a more efficient and sustainable manner. Companies should have self-imposed targets and initiatives to reduce the impact of their activities on the environment, while also keeping the patient in mind and product efficacy intact. Strategies that can foster environmental sustainability within the pharmaceutical sector are those that promote the efficient development and production of sustainable products.

Accounting for around 60% of drug products,[1] oral solid dosage forms are some of the most widely manufactured drug delivery systems, and advancements in oral drug delivery are contributing to the growing variety of products on the market. It is therefore imperative to take measures and adopt more sustainable practices, particularly within this drug delivery sector.

> "Sustainability is not a trend but a prerequisite for the pharmaceutical industry to safeguard its future."

Capsules are one of the most established and flexible solid oral dosage forms and can play an important role in the journey towards accessible, sustainable drug delivery systems. This article will examine how capsules can become an environmentally friendly and sustainable dosage form, including:

- Capsule formulation development
- Capsule manufacturing
- Sustainable clean label and vegetarian options for capsules
- Capsules for inhaled drug delivery.

HARD CAPSULE FORMULATION DEVELOPMENT

Sustainability is not a trend but a prerequisite for the pharmaceutical industry to safeguard its future. This may mean product development using either direct ingredients or minimally processed excipients or may even refer to products being developed using fewer ingredients.

The very first step in formulation development and design is evaluating the compatibility of various ingredients. The key is to assess crucial attributes, such as the physico-chemical properties of the drug and formulation compatibility. Hard capsules are ideal for this process of dosage form development, as they provide the flexibility of filling the desired dose from large-scale, fully automated filling machines, intermediate-scale semi-automatic filling or very small-scale manual filling operations.

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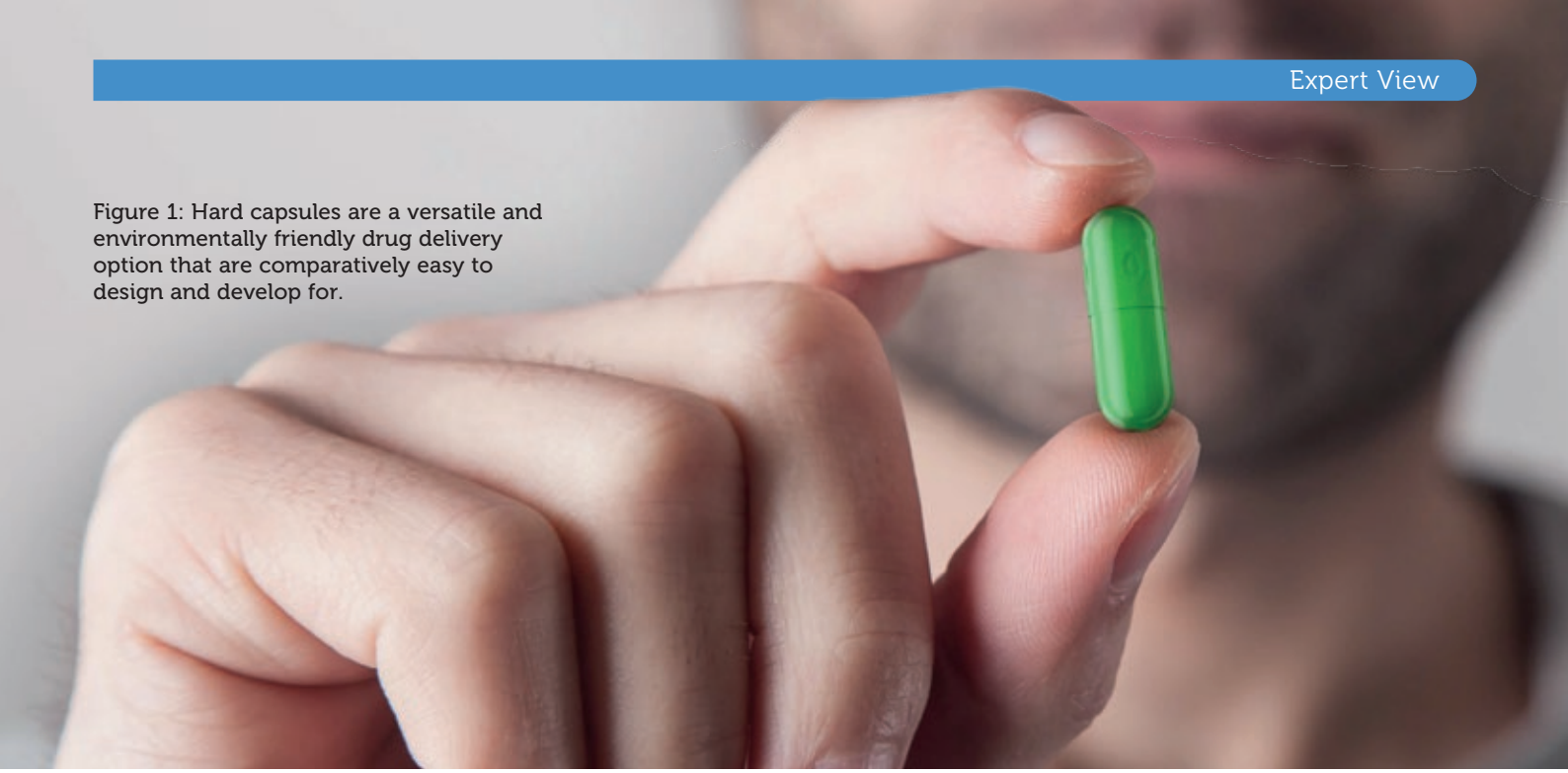

Figure 1: Hard capsules are a versatile and environmentally friendly drug delivery option that are comparatively easy to design and develop for.

Capsules as a dosage form are relatively easy to design and develop (Figure 1). Complex machines are not required, as capsule formulation development can be achieved in laboratories using either a manual or small-scale capsule filling machine. Hard capsules eliminate the need to make complex formulations compared with other dosage forms. This means a reduction in the use of excipients or additives, which corresponds to using fewer ingredients during large-scale manufacturing.

Improvements in capsule technologies mean that two different dosage forms can now be combined into a single hard capsule. This eliminates the need to develop separate formulations or dosage forms. The additional savings that can be made by combining two dosage forms not only include the reduction in required human and manufacturing resources but also reductions of material usage in the wider supply chain, including resources for packaging, storage, transportation and further storage before final distribution. A wide variety of multi-release, multi-phasic and multiple dosage forms can be developed in a hard capsule. A combined formulation of pellets or multi-tablets inside a capsule, or capsule inside a capsule, enables formulation scientists to achieve the desired therapeutic action in a more effective manner.

HARD CAPSULE MANUFACTURING

Hard capsules generally require a lower number of excipients and fewer processes and analytical tests, which accelerates validation and speeds up manufacturing. Unlike tablets, the manufacture of hard capsules does not require granulation, drying, compression, coating or printing.[2] As such, the required machinery has fewer components, is more energy efficient and the process is faster.

Compared with soft gel, hard capsules require fewer manufacturing steps and have reduced production timelines, waste production and other operational costs. By comparison, the volume of gelatine offcuts, known as "nets", generated after soft gel manufacturing can be very high and represents a serious waste of raw materials. Therefore, attempts have been made to recycle discarded gelatine nets but, as gelatine contains a wide variety of additives used in the manufacture of gelatine ribbons, it is a difficult process to recycle gelatine. Due to the presence of plasticisers, water and other preservatives, colourants, opacifier, etc,[3] several processes to remove the additives are required. Recycling methods continue to be explored.

"Compared with soft gel, hard capsules require fewer manufacturing steps and have reduced production timelines, waste production and other operational costs."

Various sustainable processes, such as zero liquid discharge and wastewater management, are being implemented in the manufacture of hard capsules. Zero liquid discharge is a strategic wastewater management system that eliminates the discharge of industrial wastewater into the environment. This is achieved by treating wastewater, adopting a "recycle, recover and reuse" approach for other industrial purposes and reducing the intake of fresh water. Another sustainable strategy is the use of solar energy which helps to reduce non-renewable energy consumption and its associated carbon footprint.

SUSTAINABLE, CLEAN LABEL AND VEGETARIAN OPTIONS IN CAPSULES

Gelatine Capsules – Sustainable Option

Gelatine is a sustainable and versatile polymer, contributing to its place as the main polymer for producing capsules. Unlike many other ingredients, it is derived from animals, being extracted from bone collagen and cattle hides. Gelatine aids in the complete usage of materials that are by-products of the meat industry, contributing to a zero-waste of materials.

HPMC – Clean Label and Vegetarian Option

In recent years, there has been a shift towards hydroxypropyl methylcellulose (HPMC) as the material of choice for capsules in both the pharmaceutical and dietary supplement industries (Figure 2). HPMC offers myriad advantages on top of being a vegetarian polymer. These capsules are widely used by many pharmaceutical companies for new molecules and products. From conventional capsules filled with powder, pellets or liquids intended for oral administration to those intended for dry powder inhalation applications, HPMC capsules are used in a range of

Figure 2: The pharmaceutical industry is seeing a shift towards HMPC as the material of choice for hard capsules.

> "Capsule-based dry powder inhalers are sustainable in large part because the capsules are developed from biodegradable polymers, such as gelatine and HPMC."

therapeutic areas. Capsules come with certifications from the Vegan Society (Birmingham, UK) and Clean Label Project (CO, US), assuring that HPMC capsules are clean, safe and sustainable.

CAPSULES FOR INHALATION APPLICATIONS

Asthma and chronic obstructive pulmonary disease (COPD) are among the most common chronic respiratory diseases worldwide. One way these conditions are treated is by delivering medication as an aerosol using a metered dose inhaler (MDI). However, MDIs use hydrofluorocarbon (HFC) propellants – powerful greenhouse gases that excessively contribute to the climate temperature crunch.[4]

Previously, MDIs used chlorofluorocarbons (CFCs) as a propellant but, due to the damage CFCs cause to the ozone layer, MDIs transitioned to using HFCs, which do not deplete the ozone layer but are more potent greenhouse gases than CO_2. Modern MDIs depend on hydrofluoroalkanes (HFAs) that have a carbon footprint equivalent to more than 500 g of CO_2 per dose – more than 25 times that of dry powder inhalers (DPIs).[5] In a case study, it was reported that MDIs using HFAs as a propellant gas can have, on average, a carbon footprint up to 50 times higher than that of a capsule-based DPI.[6]

The more sustainable and environmentally friendly alternative is capsule-based DPIs, which are widely accepted by healthcare professionals and patients. Capsule-based DPIs are sustainable in large part because the capsules are developed from biodegradable polymers, such as gelatine and HPMC. DPIs do not require propellants and their effectiveness depends solely on the capsule, the device, the powder formulation and the patient's inhalation. They are easy to use and control, as well as being cost effective, painless, portable and, most importantly, patient friendly.

In the meantime, steps should be taken to develop all inhalers in a more sustainable way, keeping in mind the "recycle, recover and reuse" approach. Such a move may require higher investment when establishing a product, verifying the efficacy and dose control of a device over many years of repeated use. The device components need to be made from robust materials that are compatible and can be recycled. Furthermore, it is anticipated that such use of sustainable materials and reduction of waste and carbon emissions will be enforced by future regulation.

CONCLUSION

Owing to urgent ecological demands, an emphasis on protecting the natural environment for coming generations is crucial. With a shift to more reliable use and product development, pharmaceutical companies are willing to adopt more eco-friendly approaches. Sustainability and environmentally friendly practices should be a priority for the pharmaceutical industry. Reducing the industry's carbon footprint and developing sustainable products are of key importance.

Hard capsules, being an oral solid dosage form, play an important role in sustainability. Gelatine and HPMC hard capsules are environmentally friendly and biodegradable, while being capable of delivering accurate doses. Hard capsule formulation development and manufacturing both hold potential for sustainable drug delivery. Furthermore, dry powder formulations are one of the most

sustainable ways to deliver drugs via the inhalation route. The pharmaceutical industry must live up to the responsibility of sustainability for the benefit of the natural environment – even the smallest contribution will be one step closer to achieving a better future.

ABOUT THE COMPANY

ACG has been delivering solutions to the global pharmaceutical and nutraceutical industry for more than 60 years, across six continents and in 100 countries. ACG is the world's only integrated pharma manufacturing solutions company with products ranging from capsules to films and foils, engineering equipment and inspection systems, all meeting international regulatory requirements. Collaboration is at the core of ACG's ethos of finding innovative solutions to the world's greatest health challenges.

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SUSTAINABILITY WITH THE ARIA AUTOINJECTOR: THE ROUTE TO FURTHER IMPROVEMENTS

Here, Emil Fraenkel, Sustainability Engineer, and Bjarne Sørensen, Director, Front-End Innovation, both at Phillips-Medisize, investigate the route to further sustainability improvements for the Aria autoinjector. This article is a sequel to a benchmark study on the environmental impact of Aria presented by Phillips-Medisize in *ONdrugDelivery Issue 126 (Oct/Nov 2021)*.

Though growing rapidly, the practice of developing and implementing circular products and business models is in an early stage. As a result, little research has been done on the application of circular design principles to specific industries and how the needs of those industries might affect circular design frameworks for their products. From an environmental perspective, studies have indicated that the healthcare sector accounts for 4.4% of global emissions.[1] This needs to change, as has been clearly recognised by key stakeholders, including pharma and device companies as well as healthcare providers and patients. The business incentive for reducing emissions is less clear in some markets – Europe is starting to experience a real demand for more sustainable devices, while other markets are showing less concern.

This article considers the role of circular design in sustainable product development and its application to one such field: the medical device (MD) industry. In particular, it outlines the role that the remanufacturing of MDs can play in lowering the environmental impact of MDs. Using this principle and other aspects of circular design thinking, the article provides projections on how to further reduce the impact of the Aria autoinjector.

APPROACHES TO IMPROVE PRODUCT SUSTAINABILITY

How can products be designed to be inherently good for both the future of the planet and the users that they are made for? This is a question increasingly being asked by product designers as more and more is understood about the environmental threats we face.

Traditional "design for sustainability" has attempted to minimise the pollution and carbon footprint caused by products. Today, we also recognise the importance of the raw material value that is lost and the environmental damage that occurs when products are manufactured from extracted materials, used and then disposed of in a single cycle.

In response to this, the idea of the circular economy[2] has been developed, in which the reuse of products, or their component materials or subsystems, is considered. This is an idea which, starting from the 1970s, grew out of various schools of thought within economics, environmental science, engineering and design, and has been developed further by academic researchers and industry organisations ever since.

Despite all the efforts the health sector may make to decarbonise, some obstinate

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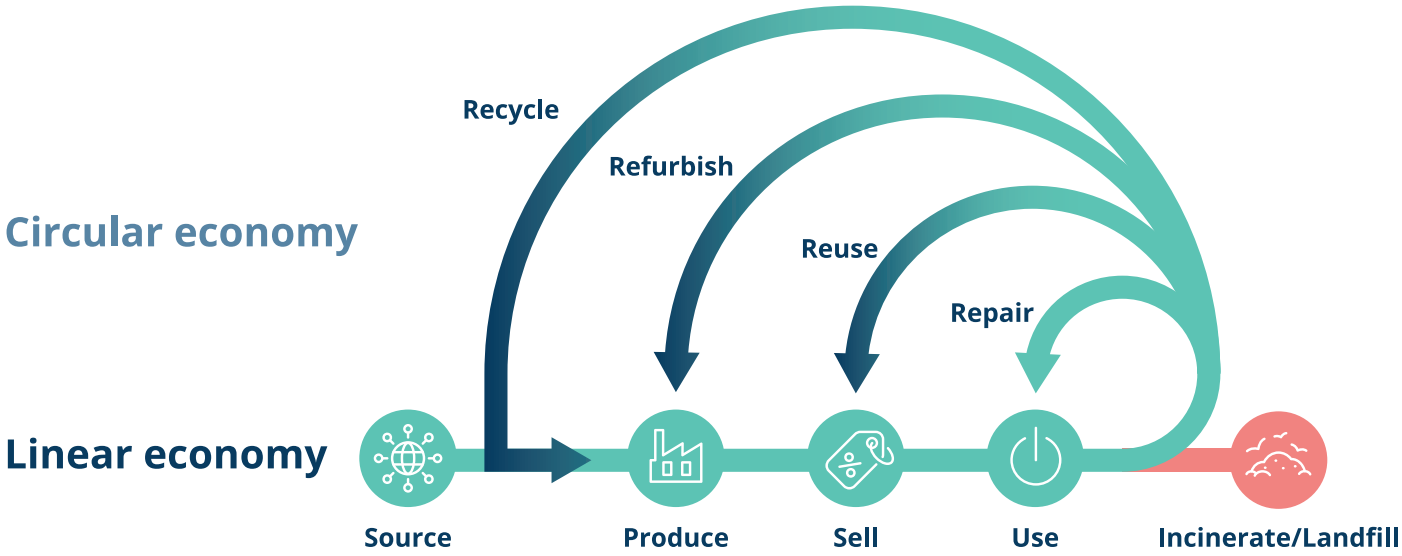


Figure 1: Linear and circular economy illustration – we should strive for tighter loops as repair is more advantageous than recycling.[2]

emissions will remain, even though they may get smaller over time. The industry must strive to ensure that these residual emissions are managed in a way that will support a healthier and more sustainable future.

The MD industry needs to be at the forefront of developing an approach to address these emissions by establishing bespoke health-based solutions that focus on reducing emissions at the source as a means of decarbonising.

Reduction of Emissions at the Source as an Alternative to Carbon Offsets

Lately, we have seen the development of carbon-neutral devices leveraging the sustainability megatrend and developed to achieve a zero-emissions position.[3] The increased focus and awareness in the industry is positive but one should be careful with claiming absolute sustainability for devices as there is no such thing as an emission-free product. However, some products are less impactful than others and we should strive to minimise their environmental impact wherever possible.

Carbon-neutral products must rely fully or partially on compensating for their carbon footprint using CO_2 certificates – often through third parties (e.g. reforestation programmes or investments in renewable energy) – a method that is heavily debated as to whether or not it has any significant positive impact on the environment. Typical offsets, like nature-based solutions (carbon sink enhancement), will not provide sufficient compensation for the level of residual management that is needed in the world and are often not considered sufficiently permanent or equitable.[4]

This is clearly a complex area of uncharted territory, with many ethical and practical pitfalls. The next step is for robust research into how such health-based solutions and interventions might support permanent emissions reductions that can meet the strictest criteria of standard offsets while avoiding their drawbacks.

> "Reusable autoinjectors, such as Phillips-Medisize's Aria, consist of a disposable cassette, designed with recycling in mind, and a durable device, designed for longer use and suitable for refurbishment."

Phillips-Medisize believes that designing for reduction, reuse and recycling will enable a more circular system where pharma companies, device developers and sub-suppliers must ultimately co-operate in taking back products for optimal repair, reuse, refurbishment and recycling (Figure 1).

A transition to a circular economy is needed to reduce the overall impact of the industry. Reusable autoinjectors, such as Phillips-Medisize's Aria, consist of a disposable cassette, designed with recycling in mind, and a durable device, designed for longer use and suitable for refurbishment.

OVERVIEW OF THE ARIA AUTOINJECTOR PLATFORM

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 is currently in development and not yet cleared by the US FDA and other medical device regulators. It consists of a reusable electronic power unit, which replaces the spring-powered drive in a mechanical device, coupled with a disposable cassette, which contains the prefilled syringe and provides needle safety, using a moveable shield, like most disposable devices. The cassette can accommodate both 1.00 mL and 2.25 mL prefilled syringes. There are two main models:

1. Aria – which has a simple user interface
2. Aria+ – which offers several advanced features, including a graphical user interface.

Both models include Bluetooth connectivity. Figure 2 shows the Aria device and cassette.

Figure 2: The Aria device and cassette.

WE BELIEVE THERE IS POTENTIAL TO REDUCE THE CARBON FOOTPRINT OF THE ARIA AUTOINJECTOR BY 48%

In Phillips-Medisize's previous ONdrugDelivery article on this topic,[5] validated lifecycle assessment (LCA) data was presented, highlighting the Aria autoinjector's potential CO_2 footprint of 0.2 kg CO_2 equivalent (eq) per injection. This figure was based on the scenario of a weekly injection over a device lifetime of three years, equivalent to a total of 156 injections.

The scope of the calculations and the assumptions here are the same as the calculations presented in the previous article and in Phillips-Medisize's full LCA report, which is available upon request.

Phillips-Medisize's projections show that refurbishment – a process in which devices are taken back, renovated, repackaged and then sent out for another lifecycle – will lower the environmental impact of the durable device. Changing the plastic material of the cassette to a bioplastic-based one will reduce the carbon footprint of the cassette significantly. Finally, incorporating the cassette into a recycling scheme will avoid emissions from new plastic being produced. Combined, these initiatives will potentially reduce the carbon footprint per injection by 48% (Figure 3).

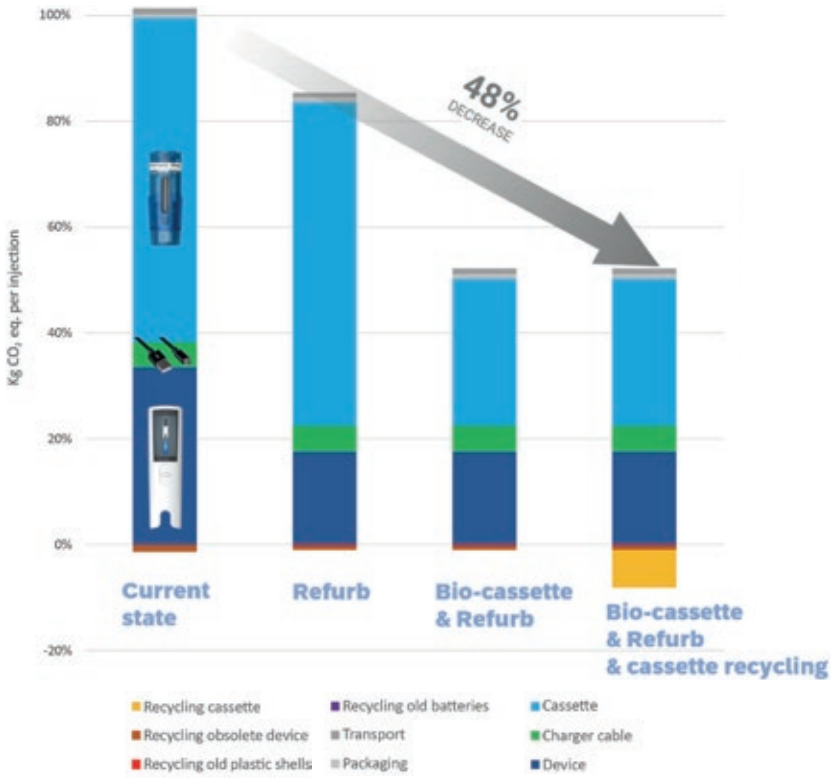


Figure 3: Overview of the impact of the current Aria autoinjector and the potential influence from different improvements.

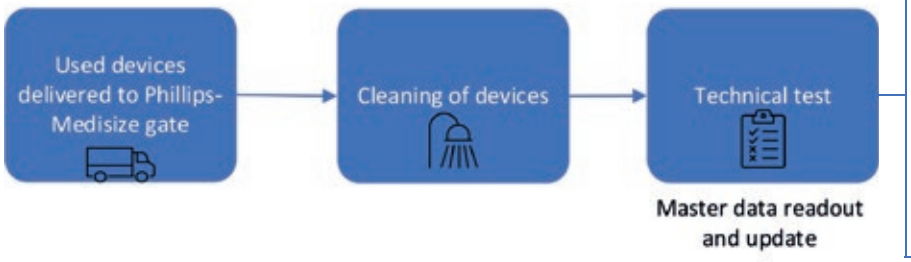


Figure 4: The refurbishment flow starts with devices being cleaned and tested. The device master data supplies information about the use cycle and can help determine if the device should be recycled due to high wear and tear or if there is a case for refurbishment, changing out worn parts like the plastic outer shell or the battery.

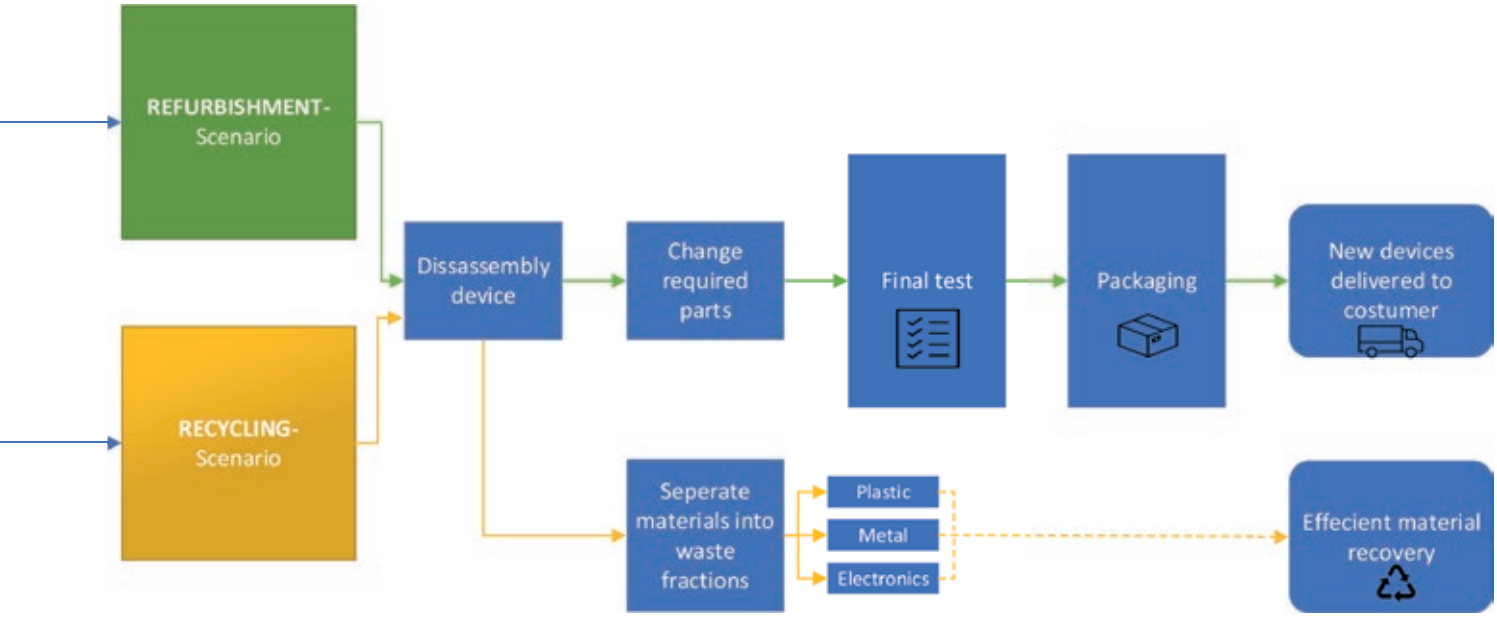
REFURBISHMENT OF DEVICE

Manufacturers typically do not feel responsible for what happens with their products after customer use. Most products are designed in such a way that, while materials, assembly and distribution costs are minimised, their repair, reuse and disposal requirements are not considered. Manufacturers generally believe that the costs of incorporating these requirements would outweigh the benefits. Historically, most customers were not prepared to pay an additional fee for a "green" product[6] – but the situation is changing.

Products that are obsolete or near obsolescence, such as through wear and tear, can be retrieved by manufacturers at the end of their lifecycle and put back into service by the replacement of crucial parts, a process known as refurbishing or remanufacturing.[6] Figure 4 illustrates a process overview of what a refurbishment process could look like for the Aria autoinjector.

Phillips-Medisize can read out the device data containing key information about the actual use cycle and the number of injections the device has delivered, which is key for the refurbishment process. Based on the number of injections and state of the device, a decision procedure leads to either a "refurbishment scenario" or a "recycling scenario" determining the following process path:

- **Refurbishment scenario** – a technical test, including data readout, will determine which parts need to be replaced. The outer casing of the reusable drive unit is likely to need replacement every time for visual appearance and hygiene reasons. The battery is another component likely to require replacement due to its limited lifespan. Any harvested components will be sorted into specific waste fractions for the best possible material recovery.
- **Recycling scenario** – even durable devices will reach a point where the producer cannot guarantee the function of the product due to wear and tear. However, the device still needs proper handling. Durable components, such as the electric motor, can be harvested for reuse in new autoinjectors or in other products. Hereafter, the device is dismantled and sorted into specific waste fractions for efficient recycling.



The final testing and packaging process is thought to be identical to the original process for a "virgin" device. Logistics scenarios and business aspects of the overall process will be determined in co-operation with the customer. With a refurbishment scheme as described, it is expected that the environmental impact of the Aria autoinjector will be reduced and that the device will sustain its useful life for a longer period of time.

In Phillips-Medisize's own reduction projections regarding refurbishment of the Aria, the company bases the scenario on the device being refurbished once (exchanging shells and batteries), extending the lifetime from 156 injections to 312 injections, but further cycles of refurbishment are a possibility. The outer casing and battery are assumed to be recycled, and the obsolete device is assumed to be recycled by the consumer.

BIOPLASTIC CASSETTE

A substitution from a fossil-based plastic to bioplastic alternatives can be a relevant approach to lowering the carbon footprint of a product. However, while many things have been said about bioplastics, they certainly are no silver bullet to our plastic problem.

The first-generation bioplastic was based on feedstock from crops and plants, which is then removed from the food supply chain. Second-generation feedstock refers to crops and plants not suitable for human or animal consumption (food and feed). Second-generation feedstock can be either non-food crops (cellulosic feedstock) or waste materials from first-generation feedstock (e.g. waste vegetable oil).

Polyolefins can be made from bio-based feedstock, resulting in significantly lower greenhouse gas emissions compared with polyolefins made from fossil-based feedstock. The bio-based feedstock is often a waste material or residue from vegetable oils (second-generation bioplastics). The advantages of these bio-based polyolefins are that they have identical physical, mechanical and chemical properties, regardless of which feedstock was used in the production process – fossil- or renewable-based. This makes them suitable for medical appliances and can avoid expensive testing and documentation associated with new material selection.

As an example of such a bio-based material, Figure 5 illustrates the lower footprint of bio-based polypropylene (PP) (-0.5 kg CO_2 eq / kg PP) compared with traditional, fossil-based PP (1.6 kg CO_2 eq / kg PP) – a decrease of >120% in carbon footprint. The reduced footprint is due to the stored carbon in a plant's biomass, which it takes from the atmosphere during the plant's growth phase. Calculations are based on the mass balance approach and is a cradle-to-gate consideration.

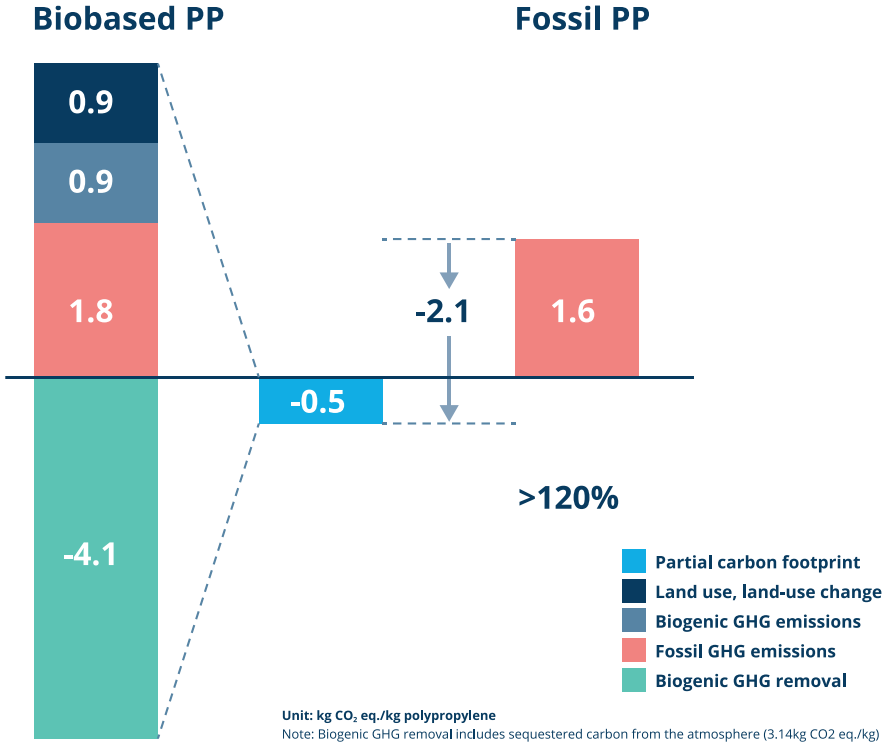


Figure 5: LCA data on the carbon footprint of biobased PP. (Data derived from a study carried out by the Institute for Energy and Environmental Research on Bornewables PP produced at Borealis's sites using steam cracker or propane dehydrogenation – highlighting that the bio-based PP is a lower-emission alternative to fossil-based PP.[7])

"From an environmental perspective, products should be designed for reuse as we ultimately want to keep products in the loop for as long as possible."

The emission data highlighted in Figure 5 serves as rationale for Phillips-Medisize's reduction projections regarding bioplastic cassettes. Phillips-Medisize is currently investigating the possibility of supplying both bio- and fossil-based PP cassettes.

CASSETTE RECYCLING

The sustainability of a product can be increased by designing for its end of life. In design for recycling, products are designed for easy disassembly and make use of recycling-compatible resins in material selection, allowing for easier material separation. Problems of plastic waste generation were taken into consideration at the design stage of the development of the Aria cassette. It is technically feasible to recycle the cassette, but there are some barriers that need to be addressed.

Figure 6: Aria cassette without syringe inserted, ready for recycling.

Barriers

From an environmental perspective, products should be designed for reuse as, ultimately, we want to keep products in the loop for as long as possible. However, in specific cases, other aspects can be of higher priority, such as safety in the case of a medical device. Potentially biohazardous waste products, such as autoinjectors, are likely to be classified as "hazardous waste", which means that they must follow a strict disposal procedure, often being disposed of in sharps bins and then incinerated at special treatment plants.

The Aria cassette contains a prefilled syringe and needle, which is in contact with the patient and therefore assumed to be hazardous waste after use. From a regulatory point of view, there are restrictions on the transfer of this special type of waste, which can complicate recycling processes. The cassette (Figure 6) is needle-safe, which could potentially allow it to come under a different classification of waste, thus allowing the possibility of recycling, either locally or as part of a take-back system that aims to reuse the material in new cassette production.

Carriers

The cassette is a mono-material design using PP for all components, reducing the number of different materials used from eight to just one (excepting the prefilled syringe), compared with typical disposable autoinjectors. While the syringe complicates the case for recycling disposable autoinjectors, the Aria cassette is designed with separation in mind. A locking mechanism keeps the syringe in place during use but can be unlocked in the disassembly process, allowing the syringe to be removed and the cassette body, a clean PP fraction, to be recycled into plastic granulate – preferably going back into the production of new cassettes to ensure circularity.

Assuming the cassettes are collected, an automated process for removing the syringe is perfectly feasible. The syringes can be recycled in a glass/plastic fraction. The syringe supplier, as an expert in its own product, could take back the syringe to ensure optimal recycling and potentially feed back the materials into its own production. Or, if this is not feasible with current designs, the material could be used for other applications.

Due to the versatility of PP, it is the most widely used type of plastic in disposable devices. This is an enabler for recycling – both in terms of recycling in local waste management systems and in potential take-back systems. If the material is not considered suitable for looping into the production of new cassettes, the PP fraction will still be a valuable fraction for products in other industries.

In Phillips-Medisize's projections for improved sustainability through recycling, the company bases the scenario on the cassette being efficiently recycled into new granulate, thereby avoiding emissions associated with the production of new virgin granulate.

DESIGN STRATEGIES FOR IMPROVED MATERIAL CIRCULATION

Separation of recyclable waste and circularity of home healthcare MDs are new fields that are still being explored. The unexplored opportunities observed in this sector show the need for design strategies to expand the circularity of MDs. Recovery opportunities in the medical sector have been shown primarily to depend on the criticality of hygiene, product value and the environmental

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support structure, which affect infection control requirements on the one hand and the resources required for repair, refurbishment and recycling on the other. Figure 7 illustrates a matrix highlighting different design strategies, depending on product value/hygiene criticality.

Refurbishment of complex and expensive equipment, such as MRI and X-ray equipment, is already performed in practice,[9] with well-documented design guidelines. In contrast, widespread hygienic recovery of high-criticality, medium-to-high-value devices is often performed poorly, with the design of such devices rarely accounting for such recovery and many of them unnecessarily being sold as "single use".

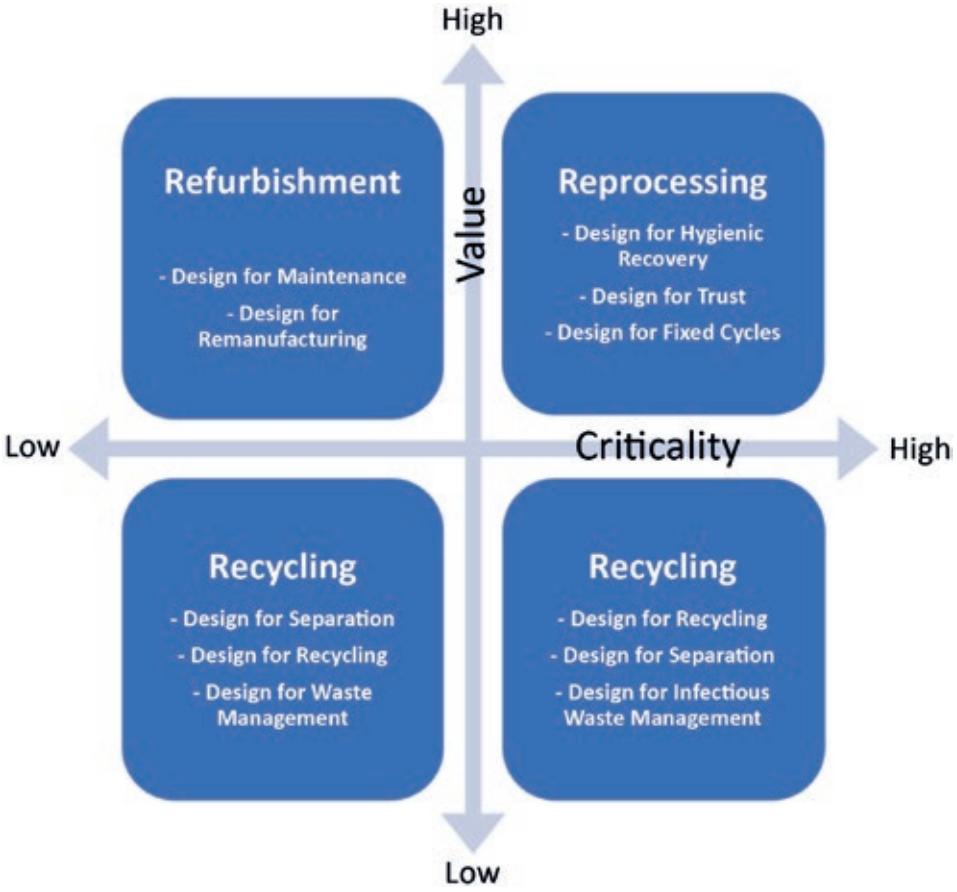

Figure 7: Design strategies for recovery of circular medical products in relation to product value and criticality – based on the work of Kane GM *et al*.[8]

Low-value, high-criticality products, such as disposable autoinjectors and the Aria cassette, are perhaps the most difficult subclass to develop a circular design strategy for, as they combine a high cost of recovery with a low product value and low cost of disposal and replacement. Design innovations for this group of products may be best targeted not at the products themselves but at the equipment and infrastructure required for their recovery. The Aria cassette is designed with recycling, separation and infectious waste management in mind. As with all high-criticality devices, extreme care must be taken when following this design strategy to ensure that patient safety is ensured.

High-value, non-critical products are those which can be reused without the necessity for hygienic recovery through aggressive sterilisation. These products are generally complex, durable pieces of equipment, such as Aria's reusable electronic drive unit, and their designers can follow well-established principles for the design of long-life equipment and its refurbishment and maintenance. This means that products should be designed to facilitate the remanufacturing process, including component durability, design for disassembly and reassembly, accessibility, cleaning, reverse logistics and marketing.

Hatcher GD *et al*[10] put together an overview of design concepts that are useful in design for remanufacturing: modularisation, platform design, active disassembly and failure mode. Design for refurbishment involves decisions related to the standardisation of parts, selection of durable materials and reversible fasteners.

CONCLUSION

By differentiating between the design strategy required for a reusable device and a disposable cassette, it is possible to optimise the sustainability aspects of the device and cassette even further to go beyond the benefits already attained though reuse of the device and minimisation of the materials used in the cassette. With a refurbishment scheme for the reusable device, it is possible to maximise the functional lifetime of the device's constituent parts – and, when they reach the end of their lifecycles, the material recovery can be executed as efficiently as possible. From a commercial and sustainability perspective, this also means that the reusable approach is suitable for most injection frequency and stay-time scenarios.

From the outset, the Aria cassette's size and weight have been minimised and further improvements to its sustainability profile are clearly possible, such as by manufacturing the cassette from bioplastic. Recycling scenarios for hazardous waste are more complicated, however it is technically easy to separate the syringe from the cassette in an automated process and harvest the glass and plastic material for reuse.

Generally, refurbishment and recycling are an area where global, as well as local, regulatory aspects can introduce challenges and obstacles that still need to be identified and further investigated. There are already options for servicing medical devices but, in the interest of broader sustainability improvements, regulatory hurdles could be challenged and potentially revised. Clearly, separating Aria's drive unit from the disposable cassette, Phillips-Medisize has made it possible to pursue both optimum performance and connectivity options, while simultaneously minimising waste and carbon footprint per injection.

By making a full consideration of the principles of the circular economy, reusable devices like Aria can offer significant sustainability benefits compared with disposable devices.

ABOUT THE COMPANY

Phillips-Medisize, a Molex company, brings decades of innovation to leading healthcare and life science companies to develop groundbreaking solutions that help people live healthier, more productive lives.

On average, the company commercialises 50 new products a year for customers, including the first-to-market US FDA-registered drug-delivery device using a connected health system. Molex brings decades of experience in advanced electronics, connectivity and sensor technologies to help transform medical and pharmaceutical solutions.

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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.

SUSTAINABILITY CONSIDERATIONS FOR END-TO-END DRUG DELIVERY DEVICE SOLUTIONS

In this article, Barbara Lead, Chief Executive Officer of Cambridge Pharma and Oval Medical Technologies, outlines the sustainability efforts undertaken by SMC Group associated companies, including facilitating the transition from hospital to at-home treatment and investment in greener facilities.

At the 2021 COP26 summit in Glasgow, further cuts to carbon dioxide emissions were agreed to accelerate action on climate change over the course of this decade. The aim is to keep the average global temperature increase to less than 1.5°C, as recommended by scientists to prevent a climate catastrophe. Beyond legislative requirements, businesses must innovate and act smartly to support this objective.

The SMC Group, comprised of Oval Medical Technologies, SMC Ltd and Cambridge Pharma, is mindful of this. SMC Group provides an end-to-end solution for sterile injection devices, including autoinjectors. This end-to-end solution includes customisation of the appropriate device platform to meet the specific user requirements, component manufacture, filling of the primary drug container, and assembly and integration to produce the final device. In addition, process development from laboratory scale to clinical scale can be provided, as well as quality control and stability testing. Further process development, scale up and technology transfer to commercial quantities can be provided for product launches.

In the provision of this end-to-end solution, the Group's sustainability strategy has four key components:

1. Replace high carbon footprint plastics with lower carbon footprint alternatives
2. Develop autoinjectors that facilitate at-home treatments that reduce the need for patient travel and day care hospital beds
3. Cambridge Pharma uses dynamic heating, ventilation and air conditioning (HVAC) systems, which reduce energy usage, and green energy suppliers
4. Cambridge Pharma offers pharmaceutical development services in the UK, enabling customers to reduce transport miles in their supply chains.

The aim of SMC Group's strategy to minimise the carbon footprint of its facilities and products is to, in turn, reduce the carbon footprint associated with drug delivery. SMC Group seeks to achieve this not only through device manufacture but also by delivering innovations that enable the reduction of the carbon footprint associated with patients' treatments. To realise the goal of providing an end-to-end solution while minimising the carbon footprint of the final drug-device combination, it is necessary to perform an analysis of the value chain and trends in patient treatments.

> "The aim of SMC Group's strategy to minimise the carbon footprint of its facilities and products is to, in turn, reduce the carbon footprint associated with drug delivery."

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DEVICE DESIGN AND MANUFACTURE

There are several ways of minimising the carbon footprint of a drug delivery device. Oval's devices use a novel primary drug container made of cyclic olefin polymer instead of glass. Plastics are better for the environment as the manufacture and shipping of glass uses more energy. Oval also aims to use grades of plastic that have low carbon footprints.

SMC Ltd manufactures the plastic components for all its drug delivery devices and has attained a bronze award from EcoVadis for its environmentally friendly manufacturing processes and energy minimisation strategies. Oval is following SMC Ltd's lead on this front and aims to achieve an EcoVadis award with the next year.

While biodegradable materials are becoming available, they are not yet suitable for medical devices. However, Oval does use these materials for rapid prototyping during the development process as part of its environmental policies.

Furthermore, Oval is now following SMC Ltd's example with respect to energy use minimisation. The company's electricity provider uses clean energy, lighting is controlled by movement sensors and the company uses local UK suppliers wherever possible.

MOVING FROM HOSPITAL TO HOME AND EXTENDING TIME BETWEEN TREATMENTS

The carbon footprint of a drug delivery device can be dwarfed by that of the patient journey involved in providing treatment. Many drug treatments, such as chemotherapy, are provided in a hospital, either as an outpatient treatment or, on occasion, requiring an overnight stay.

The covid-19 pandemic led to healthcare providers (HCPs) visiting patients in their homes. Additionally, many clinical trials were taken out of the clinic and moved into patients' homes. This change in treatment provision during the pandemic has led to a change in HCPs' perspectives on at-home treatment, with many seeking to move more treatments from hospital to home.

The movement of treatment from hospital to home frequently involves a change in a drug's route of administration from intravenous to subcutaneous. Many pharma companies are reformulating existing products and formulating new products to allow for subcutaneous or intramuscular administration for use by outreach HCPs or patients themselves. As a result, there is increasing demand for autoinjectors that can deliver 5–20 mL of drug formulation, some of increasingly high viscosity. There is also a trend towards extending the time between treatments using long-acting injectables. These formulations are often gel-like suspensions or ultra-high viscosity, which are challenging to deliver.

Oval has platforms that can deliver large volume, ultra-high viscosity formulations, including gels and suspensions. These formulations are delivered by devices containing powerful springs and Oval's propriety cyclic olefin primary drug containers, which have been designed with high burst strength to facilitate such deliveries. These devices are designed to be intuitive to use, and studies have shown very low levels of user errors even without training, ensuring treatment efficacy. For frequent administration or multiple injections in a home setting, reusable devices can reduce a treatment's carbon footprint even further.

By facilitating self-administration, Oval's autoinjectors reduce the travel required to and from the hospital and reduce the need for beds for day patients and overnight stays. The ability to deliver long-acting injectables reduces the number of devices required per year to treat a patient, greatly reducing the consumption of materials in manufacturing and the impact of their supply chain on the environment.

"The ability to deliver long-acting injectables reduces the number of devices required per year to treat a patient, greatly reducing the consumption of materials in manufacturing and the impact of their supply chain on the environment."

SUSTAINABILITY AT CAMBRIDGE PHARMA

Cambridge Pharma is a new pharmaceutical services business, specialising in process development, sterile fill-finish, quality control and stability testing of small-batch sterile products for clinical trials and launch volumes. The process development team has experience with fill-finish of difficult-to-fill formulations and has the capability to fill vials, syringes and cartridges, as well as custom primary drug containers.

The company's new fill-finish facility has two cleanrooms equipped with isolators for aseptic fill-finish. Each filling suite has independent HVAC systems that use dynamic air control to maintain room classifications and reduce air flow when the room is not in use overnight and at weekends. This intelligent cleanroom control system delivers a demonstrable change in energy consumption – a reduction in excess of 60% in previous projects when compared with static systems. This is extremely important when cleanroom energy consumption accounts for 65–70% of cleanroom costs. The facility uses green energy and lighting is controlled by movement sensors.

Based in Cambridge (UK), this new business offers UK customers an opportunity to reduce their carbon footprint still further by reducing transport. The ability to fill ultra-high-viscosity formulations, gels and suspensions in the UK has the potential to reduce product transport requirements by miles, as well as reducing travel distance for customers working with Cambridge Pharma's teams.

SUSTAINABILITY AT SMC LTD

SMC Ltd has its headquarters in Somerset (WI, US) and six manufacturing locations, four in the US, one in Costa Rica and one in India. The company provides contract manufacturing services to three primary market sectors, medical devices, diagnostics and pharma in drug delivery. Sustainability has been an SMC Ltd focus for many years, primarily in the tracking and reporting of greenhouse gas emissions. Improvements have been driven in all facilities across various areas:

1. Installing LED lighting and motion sensors
2. Installing more efficient air compressors
3. Switching to servo-driven moulding machines versus hydraulic-driven, which require up to 70% less energy
4. Use of solar panels in select locations
5. Using variable frequency drives on water chillers (based on building demand).

For the past four years SMC Ltd has been a part of the EcoVadis programme. EcoVadis is a third-party company that provides holistic

sustainability ratings for companies to incorporate and use as part of their sustainability programmes, focusing on four key areas:

- Environmental
- Labour and human rights
- Ethics
- Sustainable procurement impacts.

SMC Ltd achieved an EcoVadis "Bronze Sustainability Rating" for 2021, which places it among the top 50% of all companies assessed by EcoVadis.

ABOUT THE COMPANIES

Oval Medical Technologies specialises in the development of patient-centric autoinjectors that meet the most challenging requirements arising from diverse patient groups and novel drug formulations. Oval's technology platforms can be customised to deliver a wide range of drug formulations, including fragile molecules, biologics for both subcutaneous and intramuscular injection with high viscosities and large volumes. Oval's patented primary drug container technology provides the design freedom to create truly optimised devices for patient benefit.

SMC Ltd, with more than 33 years of experience, provides product services from initial concept to the final packaged device, including programme management, design and development, product manufacturing, clinical/commercial manufacturing, electronics integration and global supply chain management. SMC Ltd has global GMP manufacturing sites in the US, the UK, Costa Rica and India.

Cambridge Pharma specialises in pharmaceutical services, sterile fill-finish batches of 100–10,000 units for a range of presentations including its own primary containers, as well as syringes, cartridges and vials. The company works with a wide variety of formulations including small molecules, proteins, peptides and biologics. Its flexible, broad service offering includes development and scale-up of the fill-finish process, including development of container closure integrity test methodology, analytical method development for QC release, and stability testing.

ABOUT THE AUTHOR

Barbara Lead is the Chief Executive Officer of Cambridge Pharma and Oval Medical Technologies. Ms Lead has held senior positions in three pharma companies and has experience in R&D and industrialisation. Working in the field of asthma and allergy, she has experience working with a variety of drug-device combination products and in solving manufacturing and design issues with drug delivery devices. Over many years, Ms Lead has come to realise the importance of good device design, risk assessment and human factors in the development of delivery devices to ensure effective drug delivery and correct use by patients.


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