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ONdrugDelivery Issue N° 139, November 10th, 2022

DRUG DELIVERY & ENVIRONMENTAL SUSTAINABILITY

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

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Dec	Connecting Drug Delivery
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Oct	Prefilled Syringes & Injection Devices
Oct/Nov	Drug Delivery & Environmental Sustainability

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SUSTAINABLE DESIGN AND MANUFACTURE IN MEDICAL DEVICES: WHERE TO START

In this article, Cormac O'Prey, Principal at Kestrel Technology Consulting, discusses the challenges and advantages of implementing circular economy principles in the medical device sector, with a particular consideration of the difficulty of making remanufacturing work for high-volume, low-value devices.

INTRODUCTION

Last year, Kestrel Technology Consulting wrote a piece for ONdrugDelivery Magazine on the drivers for sustainability in medical device design and manufacture, and an overview of some of the options available.[1] Since then, in a flurry of post-pandemic activity, the medical industry has woken up to the urgent need to do something about sustainability. Some might say this is due to the sudden realisation that the UK NHS really means it when it says it will not use suppliers who do not comply with its supplier sustainability requirements. The question now being asked by drug delivery device, critical care equipment, personal protective equipment and wound care manufacturers is how to meet those requirements. Medical equipment manufacturers need to know where to start, how to measure improvements so compliance can be demonstrated, what needs to be done to the design and manufacture of devices and, most importantly, how to manage risk so that patient safety is not compromised.

In response to customer, clinician, user and regulatory demands, many medical device manufacturers are increasingly being held accountable for their plastic waste and carbon equivalent (CO_2e) emissions. Many look to circular economy models for recovery and processing of used devices, but the challenge is how to make these commercially sustainable, and where to start – you start with what you can get back.

Although environmental impact has been an area of concern in business sectors, such as electronics and automotive, for many years, the medical device industry has largely been considered exempt until relatively recently. With the priority being patient safety, designers and manufacturers of medical devices have historically considered the environmental impact of their operations to be of secondary or little concern. This has changed. But how can manufacturers respond to the need to reduce the environmental impact of their products without damaging their businesses?

In a June 2022 update on a 2015 study, The Lancet found that pollution remains responsible for approximately nine million deaths per year globally.[2] This makes pollution the world's largest environmental risk factor for disease and premature death, corresponding to one in six deaths worldwide. We now know that the medical and healthcare industry is responsible for a significant part of this pollution and is directly contributing to environmental damage that results in increased human mortality rates.

If ranked alongside countries, the healthcare industry would be the fifth-largest emitter of CO_2 on the planet.[3] Healthcare contributes 4–5% of all global greenhouse gas emissions, with inhalers comprising a significant portion of that; in the UK, inhalers account for 3–3.5% of the NHS's carbon footprint.[4] Amanda Pritchard, Chief Executive of NHS England stated on September 30, 2021, on the NHS Public Board that, "The effects of poor air quality and climate change are already being seen in our GP practices and in our hospitals, and it is absolutely right that we are part of the solution. But we can't do this alone. It is so important that we throw down the gauntlet today to our suppliers too." If the fundamental mission of healthcare professionals and those in the medical industry who support them is to extend life and prevent suffering, we are getting it wrong. We need to change.

WHAT IS SUSTAINABILITY – DEFINITIONS AND INDUSTRY FOCUS

In 1987 The United Nations World Commission on Sustainability appointed the Brundtland Commission to create

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"Efforts to reduce high GWP gas emissions will do little to address the issue of plastic waste from used devices, packaging and manufacturing by-products."

what has now become widely accepted as the standard definition of sustainability – "Sustainable development seeks to meet the needs and aspirations of the present without compromising those of the future".[5] Improving sustainability and reducing the environmental impact of the medical and healthcare industry covers many approaches including, for example, improving energy efficiency and water usage. Sustainability in the context of drug delivery devices has broadly focused on two disciplines – sustainable product design and sustainable manufacture – where CO_2, CO_2e gas emissions and environmentally damaging material waste are minimised.

With global warming and climate change identified as the top environmental priority, the focus has been on reducing the emissions of high global warming potential (GWP) gasses. As an example, 28% of GSK's CO_2e emissions (amounting to 8.4 million tonnes) come from pressurised metered dose inhaler (pMDI) cannister propellants alone, and this is where efforts to reduce environmental impact in the inhaled medicine sector have been concentrated. However, medical device manufacturing also plays a part in reducing greenhouse gas emissions. In the US, manufacturing accounts for almost a quarter (23%) of direct carbon emissions overall, according to the US Environmental Protection Agency.[6] In Europe, the situation is equally dire; the industry emits an annual total of 880 million tonnes of CO_2e making it one of the largest emitters of greenhouse gases on the continent.

That said, there are options for improvement. According to the United Nations, an 80% reduction in CO_2e emissions is achievable by adopting sustainable manufacturing.[7] However, while embracing more circular manufacturing methods can help achieve reductions in GWP gasses, as well as reducing plastic waste, efforts to reduce high GWP gas emissions will do little to address the issue of plastic waste from used devices, packaging and manufacturing by-products. We need to take care of our rubbish as well.

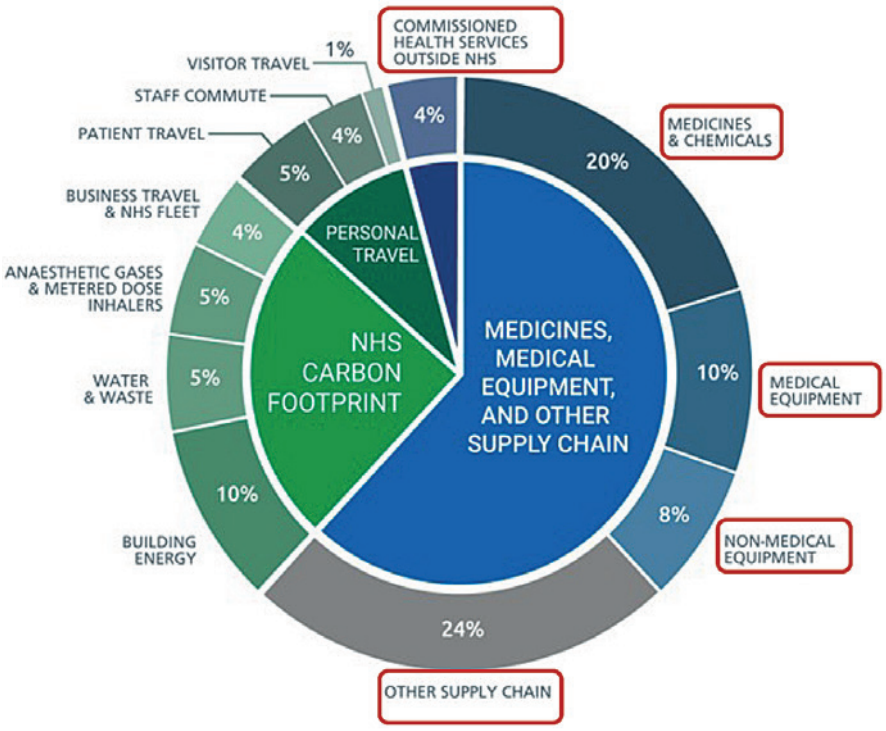

Figure 1: Breakdown of the NHS's carbon emissions.

DRIVERS BEHIND SUSTAINABILITY – WHY SHOULD WE CARE AND WHY DOES IT MATTER TO MEDICAL?

As well as the direct impact on human health, global warming and pollution from waste plastic, other factors are now driving device designers and manufacturers to take sustainability seriously, including clear messages from high-profile customers, regulatory authorities, healthcare professional groups, patients, the general public and their own staff. According to research by Oliver Healthcare Packaging, sustainability is now a strategic priority for the top 20 medical device manufacturers.

NHS England has now identified that 62% of its carbon emissions come from the supply chain (Figure 1). As a consequence, NHS procurement practice will include net-zero carbon and social value principles in all purchasing decisions. This has now been embodied in the NHS "Delivering a 'Net Zero' National Health Service – July 2022" report,[8] which states that "all suppliers will be required to demonstrate progress in-line with the NHS's net zero targets, through published progress reports and continued carbon emissions reporting" by 2030, as part of a structured supplier roadmap up to 2045. NHS spokespersons have further made it clear that carbon offsetting, greenwashing and commercial difficulties in meeting the requirements related to company size will not be considered valid excuses for non-compliance.

Furthermore, in the EU (and possibly in the UK), the EU Plastic Packaging Waste Directive (PPWD) will charge manufacturers of medical plastic waste at a rate of €0.8 (£0.7) per kg of non-recycled plastic packaging. This will affect high-volume, low-value medical device manufacturers and may well require decisions about the value of used device and packaging recovery schemes to be re-evaluated.

In the US, Extended Producer Responsibility (EPR), which "places the financial or physical responsibility of packaging and products' end-of-life on manufacturers",[9] was started in 2021 and is being rolled out across multiple states. The focus is on plastic packaging, with up to nine states expected to pass state bills in 2022 outlining EPR regulations for packaging, including Washington, California, Colorado, Minnesota, Illinois, Maryland, New York, Connecticut, Vermont and Massachusetts.[10] As the legislation will affect the business case for group purchasing organisations, which collectively provide 70% of all healthcare funding in the US, and many drug delivery devices are identified as "secondary packaging", it remains to be seen how this legislation will be applied in the global medical device industry.

"Many of the techniques and strategies required to move towards more sustainable manufacturing have already been developed in other industries or have been used in medical applications previously."

In conclusion, the need for medical device manufacturers – including drug delivery device and single-use device (SUD) manufacturers – to engage with sustainability in reducing their plastic waste, as well as their CO_2 emissions, is compelling and urgent. The question is – what to do about it?

SUSTAINABLE DESIGN AND MANUFACTURE IN MEDICAL – WHAT TO DO AND WHERE TO START

The good news for medical device manufacturers, as indicated earlier, is that many of the techniques and strategies required to move towards more sustainable manufacturing have already been developed in other industries or have been used in medical applications previously. Indeed, many procedures for reusing surgical instruments were made standard practice decades ago, and some medical device manufacturers have been using circular manufacturing practices for economic reasons for many years.

The medical device industry is, by nature and for good reason, intrinsically risk averse. Adopting and adapting proven models from other sectors and from old medical device management procedures therefore offers advantages in reduced risk, lower costs and shorter adoption timeframes. The NHS has released "How-to Guides" for trusts to help identify improvement strategies, including the "5Rs" (Figure 2).

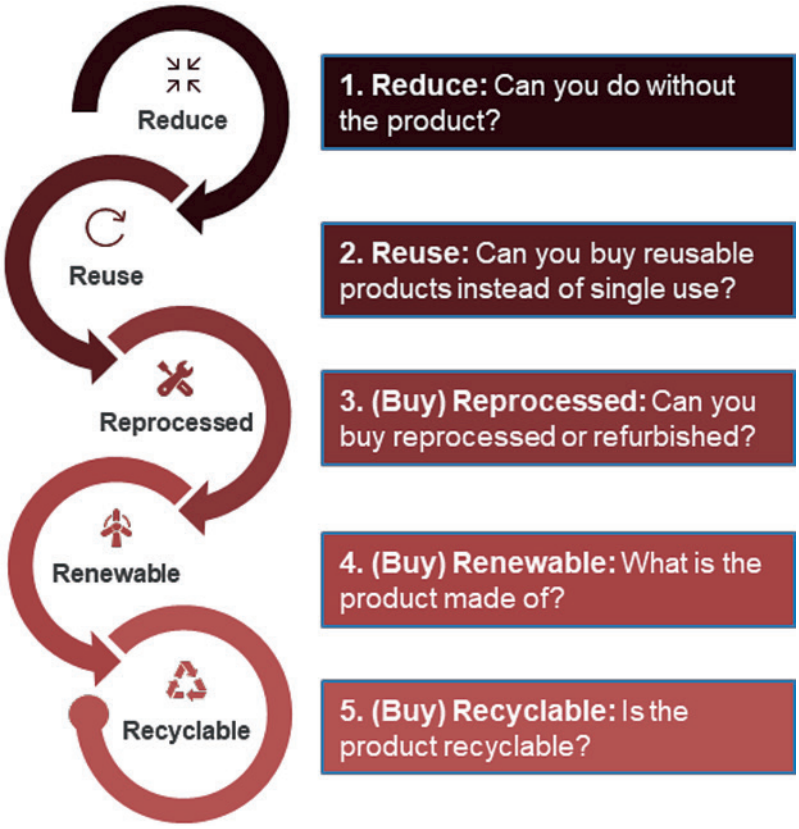

Figure 2: The 5Rs approach for reducing carbon emissions.

Sustainable manufacturing models such as the "Circular Economy" model promoted by the Ellen Macarthur Foundation and the "Design for Manufacture, Assembly, Disassembly and End of Life Processing (MADE)" model described in BS 8887-1:2006, provide a range of options for reducing the environmental impact of manufacturing operations.[11,12] The BS 8887 TPR1/7/5 subcommittee created in 2021 now specifically looks at standards and best practice for medical devices, supported by medical device manufacturers, designers, researchers and, crucially, regulatory authorities, as well as customer organisations.

In both these models, businesses are encouraged to move from traditional "linear" manufacturing (Figure 3) to a more "circular" model (Figure 4). In traditional linear manufacturing, products are manufactured, shipped, distributed to users (patients) and disposed of. No used products are recovered and what happens to the used products and packaging is not considered to be the concern of the manufacturer.

In a circular model, used devices are recovered and processed in various ways that reduce their environmental impact. So far, these have tended to be material recycling schemes to keep devices out of landfill, such as the GSK and Novo Nordisk recycling schemes,[13] but can also include secondary use in other applications, refurbishment and resale, life extension

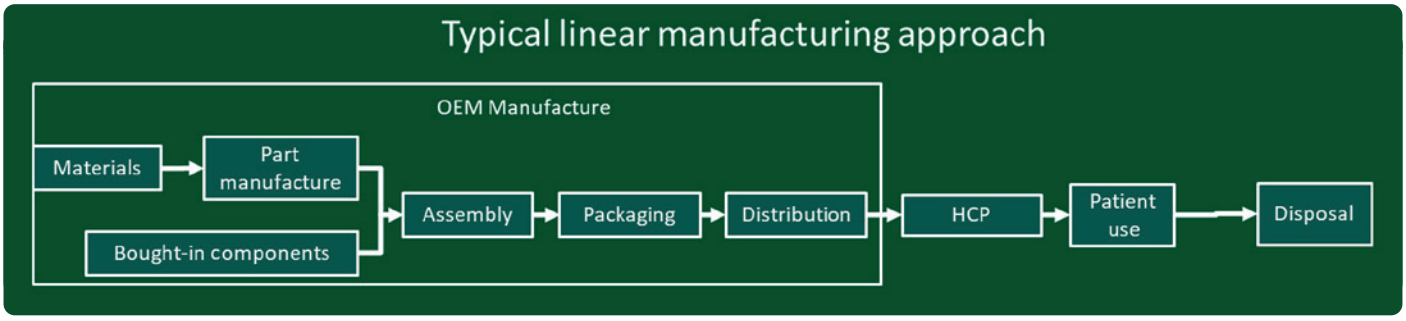

Figure 3: Diagram of a linear manufacturing model.

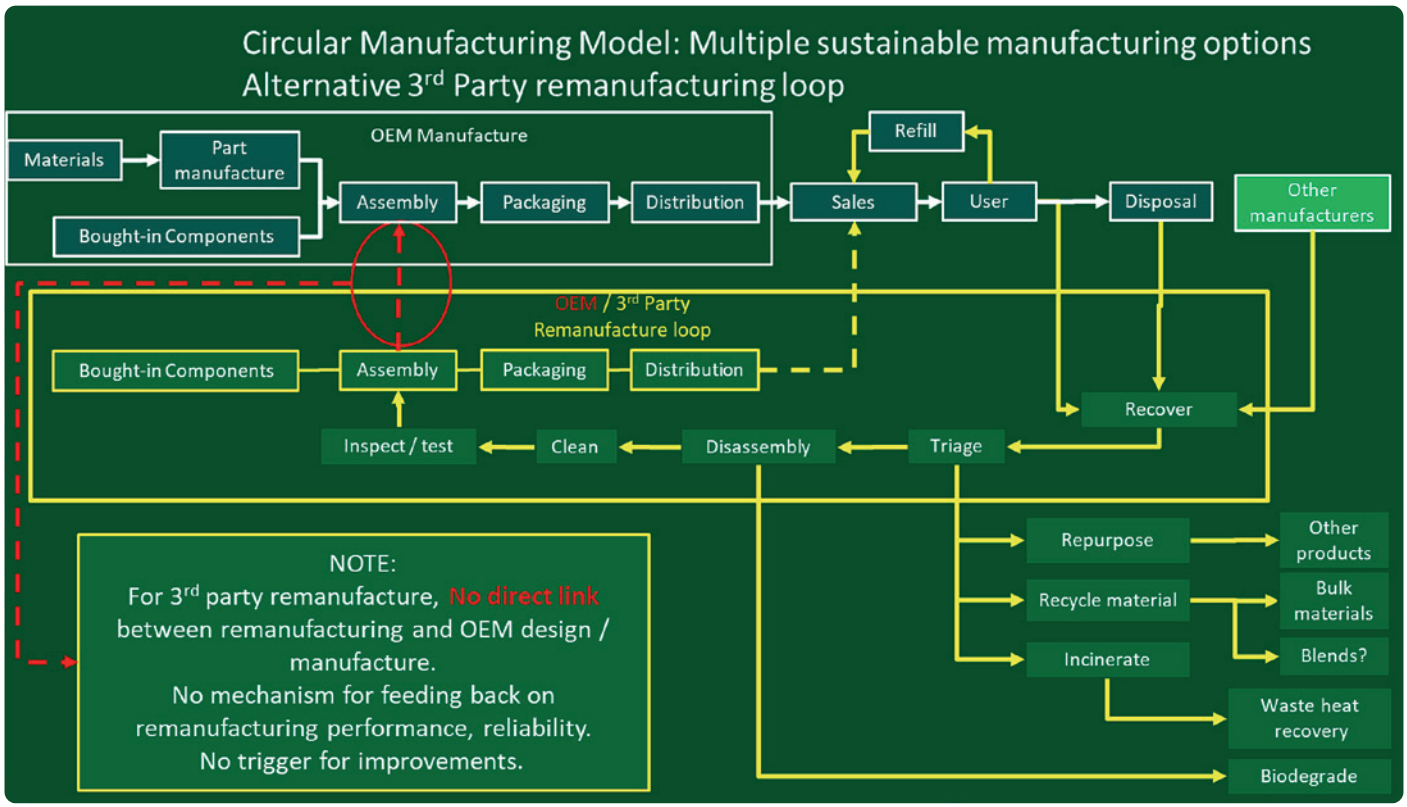

Figure 4: Diagram of a circular manufacturing model.

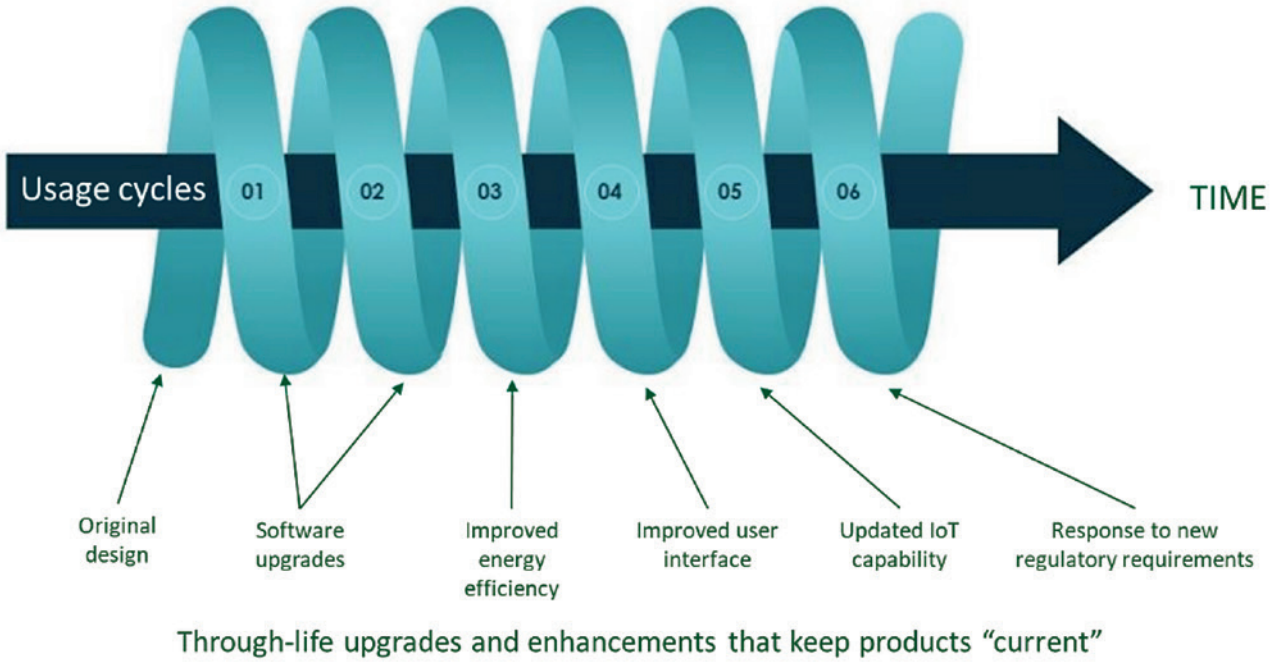

Figure 5: Some medical device developers may prefer a spiral economy approach to a circular one.

and even composting components made from biopolymers. It is a more complex model with multiple options and routes to consider, which can be off-putting for some manufacturers.

The preferred route, however, is remanufacturing. Indeed, the NHS's "Device Remanufacture 'How To' Guide: Medical Devices" focuses on remanufacturing as one implementation approach of the circular model, and the Ellen Macarthur Foundation recommends remanufacturing as the least environmentally impactful, but most commercially viable, route for used devices.[11] Remanufacturing returns used or partially used devices to the market in "at least as good as new" condition with accompanying warranties and at the equivalent price of a new device. The classic circular economy model describes used devices returned to an "as-new" condition. However, an alternative "spiral" implementation of the circular model recognises the need for manufacturers to keep their recovered products current (Figure 5).

During remanufacturing, devices must be cleaned and repaired to an as-new condition, but as-new may not be what the market needs if sufficient time has passed to render the product old-fashioned or

"Remanufacturing can look attractive for manufacturers in principle because, unlike recycling schemes where any value embedded in used devices is largely written off, significant "residual value" can be recovered from some used devices."

obsolete. Designers must leave room for new technology or changes in aesthetics to be accommodated in future cycles. Nokia has successfully followed this approach in the telecommunications industry for many years.[14]

Remanufacturing can look attractive for manufacturers in principle because, unlike recycling schemes where any value embedded in used devices is largely written off, significant "residual value" can be recovered from some used devices. This can offset new product manufacture costs by reducing the number of new components that must be supplied and assembled. Reductions in transportation and disposal costs, as well as the aforementioned 80% reduction in CO_2e emissions, can be achieved, removing a sales barrier to some customers. The key to the commercial viability of this process, however, is for the residual value recovered to be worth more than the cost to recover it. This is where many manufacturers of low-cost or low-residual-value devices are currently stuck.

Lifecycle analyses and sales incentivisation programmes based on existing linear economy models typically only look at provision of new products to the market. Circular/spiral models require a more complex understanding, often going back further to include assessment of the environmental impact of extraction and material refining operations, as well as looking ahead at post-use impact. Furthermore, the implementation and integration of complex and unknown recovery, processing and re-introduction schemes to allow recovered components to be used in remanufactured products would affect businesses, suppliers and customers, as well as represent a significant risk of disruption (Figure 6).

Established remanufacturing schemes in the medical sector have so far been largely limited to low-volume, high-value equipment, such as General Electric's medical imagers.[15] The labour-intensive processes required can be expensive, slow and non-scalable, which may not be a serious issue for small quantities of manually assembled multimillion-dollar imaging equipment, but is not viable for high-volume and relatively low-value products, such as disposable SUDs. For remanufacture to be considered a serious proposition in these areas, an approach more like design for manufacture and assembly (DFMA) is required.

Research into remanufacturing automation is being carried out by the University of Birmingham and Wuhan University, supported by Chinese national standards bodies in collaboration with BSI, and is reported on annually at the International Workshop on Autonomous Remanufacturing (IWAR). Drug delivery device remanufacture needs to operate at volume, speed, reliability and, crucially, low processing costs to pay for itself.

RECOVERY – THE ELEPHANT IN THE ROOM

A significant challenge for drug delivery device remanufacturing is how to achieve useful device recovery rates (how many you can get back) and recovered device yield rates (how many of those are of any use). Recovery of hospital-based devices, such as surgical equipment, has seen success due to its closed-loop nature, but devices released to the public outside of clinical environments are particularly problematic. Novo Nordisk has admitted problems to date[13] and, in September 2021, GSK reported that, after 10 years in operation, its pMDI recycling scheme only had a 0.4% recovery rate. The most sophisticated remanufacturing operations will fail if they have no used products to remanufacture, which has been an intractable issue for most organisations attempting this approach with medical devices.

Incentivising patients and users to return used devices is difficult. With low-residual-value devices, deposit return schemes (DRSs), where users are offered cash rewards for returning devices, need to offer a sufficient amount for users to bother. If this is more than the residual value of the device, the scheme will lose money – assuming the device is actually usable at all. If patients are asked for an additional deposit at the dispensing point that will be returned when a used device is returned, treatment is no longer free at the point of use, with all the political problems that implies. Insisting that patients return used

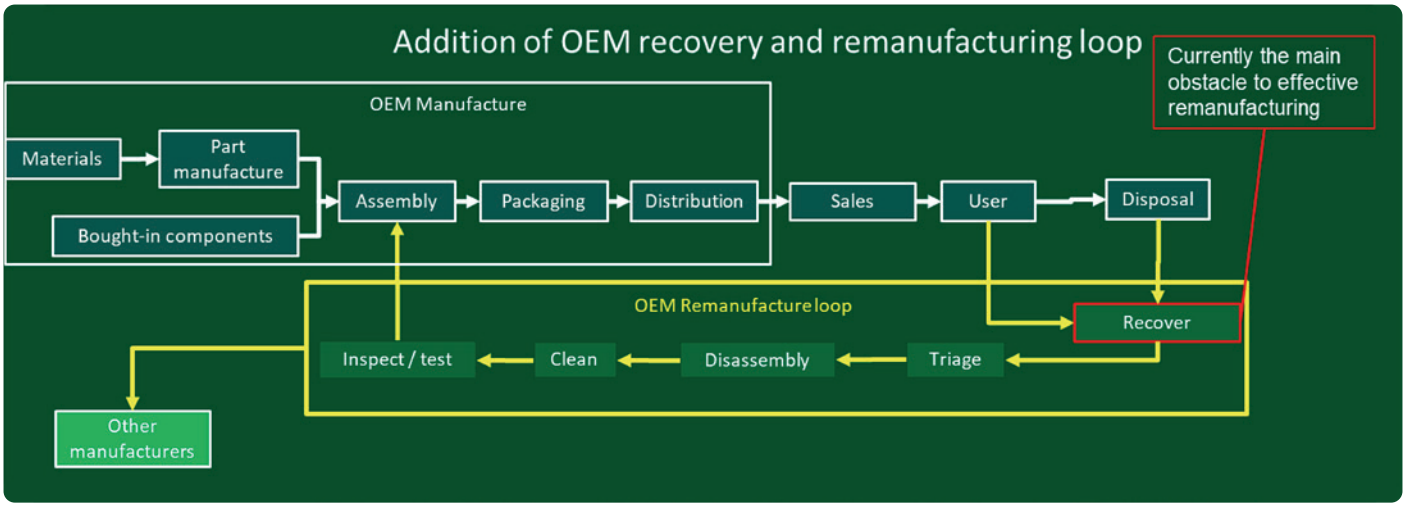

Figure 6: Diagram of a circular manufacturing model based on remanufacture by the OEM.

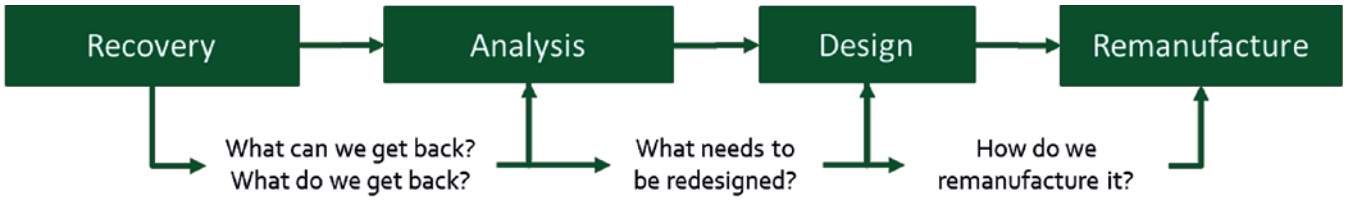

Figure 7: The route to establishing a remanufacture-based paradigm starts with recovery of existing devices for analysis to inform future designs.

devices in exchange for new ones raises the possibility of doctors refusing life-critical treatment to patients who lose or forget their old devices. The consequences of that are as obvious as they are unacceptable. True change requires a change in patient culture to drive an attitude that throwing your used device away is no longer acceptable. While history shows cultural change can be both difficult and slow, it could perhaps be achieved by helping patients understand the environmental and financial impacts of not complying with sustainable practices. This could be combined with schemes to make return as convenient as possible and by providing benefits to patients, such as helping to "de-clutter". Pilot schemes in the NHS to encourage the return of walking aids may offer some useful learning points.

Successful recovery schemes for high-volume, low-value products, such as plastic water bottles, coffee pods and aluminium drinks cans, have been developed in other industries, although their success rates are still in question. Approaches such as reverse vending machines,[16] DRSs and loyalty card points schemes are established in the food packaging industry. These have the potential to be adapted for use in medical devices, and new technologies, including unique low-cost part-marking solutions from Polytag, offer potential solutions for the tricky EU Medical Device Regulations (MDR) requirement to ensure the number of reuse cycles for each component are tracked and limited. Automated used-product picking systems can identify and pick devices from refuse streams in real time and can carry out superficial inspection and sorting activities. As with remanufacturing operations, used device recovery must be automated, scalable, reliable and cost effective.

IMPLEMENTING REMANUFACTURING

For organisations looking to implement a circular or spiral economy model, assuming that useful quantities of usable used devices can be recovered, the question remains – where to start? It is a complex and rapidly-evolving landscape. Successfully integrated product designs and manufacturing solutions have been established through the familiar DFMA approach, but now design for remanufacture must also be considered. Designers do not yet know what this process looks like, in no small part because it is still evolving. Designers also need to understand what the remanufacturing process needs from their designs, but this process does not yet exist. Ideally, designers need to understand what the different routes for each recovered component are likely to be so that they can optimise the design accordingly.

> "Successfully integrated product designs and manufacturing solutions have been established through the familiar DFMA approach, but now design for remanufacture must also be considered."

Experience from other industries has shown that 100% component reuse is unrealistic, so designers need to differentiate and plan to separate the remanufacturable "core" from components that can be discarded. This will require a change in requirements specifications and design verification testing procedures for multiple-lifetime parts, which will be different from the specifications for disposable items. Counterintuitively, the part count may need to go up to facilitate the separation of worn and contaminated features from reusable ones that were previously considered the same part.

The amount of plastic used in some parts may also need to increase to improve long-term robustness, and different materials may need to be considered. Increasing the amount of plastic, however, only becomes an issue when devices are discarded rather than reused, and a primary aim of remanufacturing is to reduce the number of discarded devices. Disassembly will also need to be considered, possibly using automation, but in such a way that patient safety is not compromised. Designs must also mitigate against the risk of users accidently taking devices apart.

So where do designers start? They start by looking at existing used devices. As stated earlier, without an effective device recovery scheme, the entire remanufacturing approach is pointless, so establishing an effective used device recovery scheme – at least as a pilot or feasibility study – must come first. This provides designers with evidence of real-life degradation in existing mechanisms that can be used as a basis for more robust remanufactured product designs. Recovered devices reveal how they have been used, abused, damaged, worn, contaminated and broken.

This, in turn, informs the design process as to which elements in the design need to be replaced and which need to be reinforced to provide reliable long-term use as part of the remanufactured core (Figure 7). This process can then inform the critical risk analysis required by the regulatory authorities, backed by physical evidence, and has the additional benefit of providing increased levels of post-market surveillance data, assuming this data makes its way back to the original equipment manufacturer (OEM). Indeed, this is something called for in recent changes to the EU MDR by the EU Medical and Healthcare Regulatory Authority.

Improvements in device reliability can reasonably be expected to result from these insights. If "smart" devices are recovered, there is the further possibility of adding self-diagnostic functionality whereby the device can directly communicate with the remanufacturing facility to tell remanufacturers what has happened to it, how much it has been used, if it has suffered

any serious abuse and therefore whether or not it is worth reprocessing.

Once all these factors have been assessed, the design can feed into strategies for:

- Reprocessing and remanufacturing, including what components need to be disassembled
- Disposal, remanufacture, repair and upgrades
- Decontamination and sterilisation processes
- Inspection and test requirements
- Considering variabilities
- Process automation.

The objective will be a design that is optimised for multiple usage cycles, with an evidence-based risk management strategy, and a manufacturing and remanufacturing solution able to deliver at maximum yield and minimum cost.

FUTURE DEVELOPMENTS

There is more detail to consider – including how to manage legacy components, design verification testing and accelerated life testing to cover extended product lifetimes – but there are also hidden benefits. Recovery of used smart devices can give access to device performance and anonymised patient usage data, improving their value as diagnostic tools and providing valuable clinical insights into patient population behaviour. Remanufacture of smart drug delivery devices can improve affordability without sacrificing profitability by amortising high manufacture and component costs over multiple usage cycles. Additionally, as stated earlier, incorporating a self-diagnostic capability in smart devices could improve yield and quality in remanufacture by enabling devices to communicate directly with automated remanufacturing facilities.

Longer term, redefining the relationship between manufacturer and patient to revolve around regular return, remanufacture and upgrade of familiar devices could improve patient confidence and establish a "lock-in", where patients are unlikely to switch to a different supplier. Some manufacturers may even consider transitioning to a "product-as-a-service" model, where ownership of the device remains with the manufacturer and the user pays for the use of the device as a service – suppliers maximise the value of their investment by keeping items in circulation while continuing to collect revenue for their use. Examples from other industries include the automotive sector, where 82% of new cars are leased in the UK using a similar business model.[17]

The refurbished medical equipment market was valued at US$9.82 billion (£8.86 billion) in 2019 and is expected to reach $23.91 billion by 2026 with a compound annual growth rate of 11.80% over the forecast period.[18] Sustainable manufacturing in the medical sector is a serious business – the medical device business should take it seriously.

ABOUT THE COMPANY

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

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ABOUT THE AUTHOR

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

SUSTAINABLE DESIGN FOR MEDICAL DEVICES

How do you meet environmental and sustainability objectives when designing medical devices? And what design considerations enable the technical cycles, known as the 4R loops of circular economy: reuse, repair, remanufacture and recycle? In this article, Stefano Vicenzetto, Systems Engineer at Flex, explores the Flex approach to design for environment for medical devices.

As companies comply with growing consumer and regulatory demands to meet sustainable targets, they are conscious that sustainability starts from the cradle. Design for environment (DfE), once considered a value add, is quickly becoming a necessity for medical product companies, and a top priority for designers.

> "Linear product lifecycles are giving way to circular models that are healthier for the environment."

Linear product lifecycles are giving way to circular models that are healthier for the environment. Sustainable new product design should require less raw material extraction, produce less waste and target the 4R loops: reuse, repair, remanufacture and recycle (Figure 1), all of which extend the lifespan of products, offering environmental and economic upsides.

DESIGN FOR ENVIRONMENT FRAMEWORK

For medical devices, Flex's approach is to consider DfE through three activities (Figure 2):

- Lifecycle assessment
- Eco-value analysis (on existing products)
- Environmental value engineering (on new products).

The Lifecycle Assessment

The first step is to evaluate the environmental impact of a product, based on the analysis of several parameters, including:

- CO_2 emissions
- Energy consumption
- Water consumption
- Recycling rate (percentage of material recycled)
- Recovery rate (percentage of material used to generate energy when the product reaches the end of life).

The assessment can be performed on medical devices already in-market to calculate a baseline of their environmental impact – or on new medical products under development to verify if the proposed design meets sustainability requirements (Table 1).

The Eco-Value Analysis

Existing medical devices, already in-market, can be analysed against the following criteria:

- Materials used
- Product durability
- Energy efficiency
- Ease of disassembly and reassembly
- Ease of maintenance and repair.

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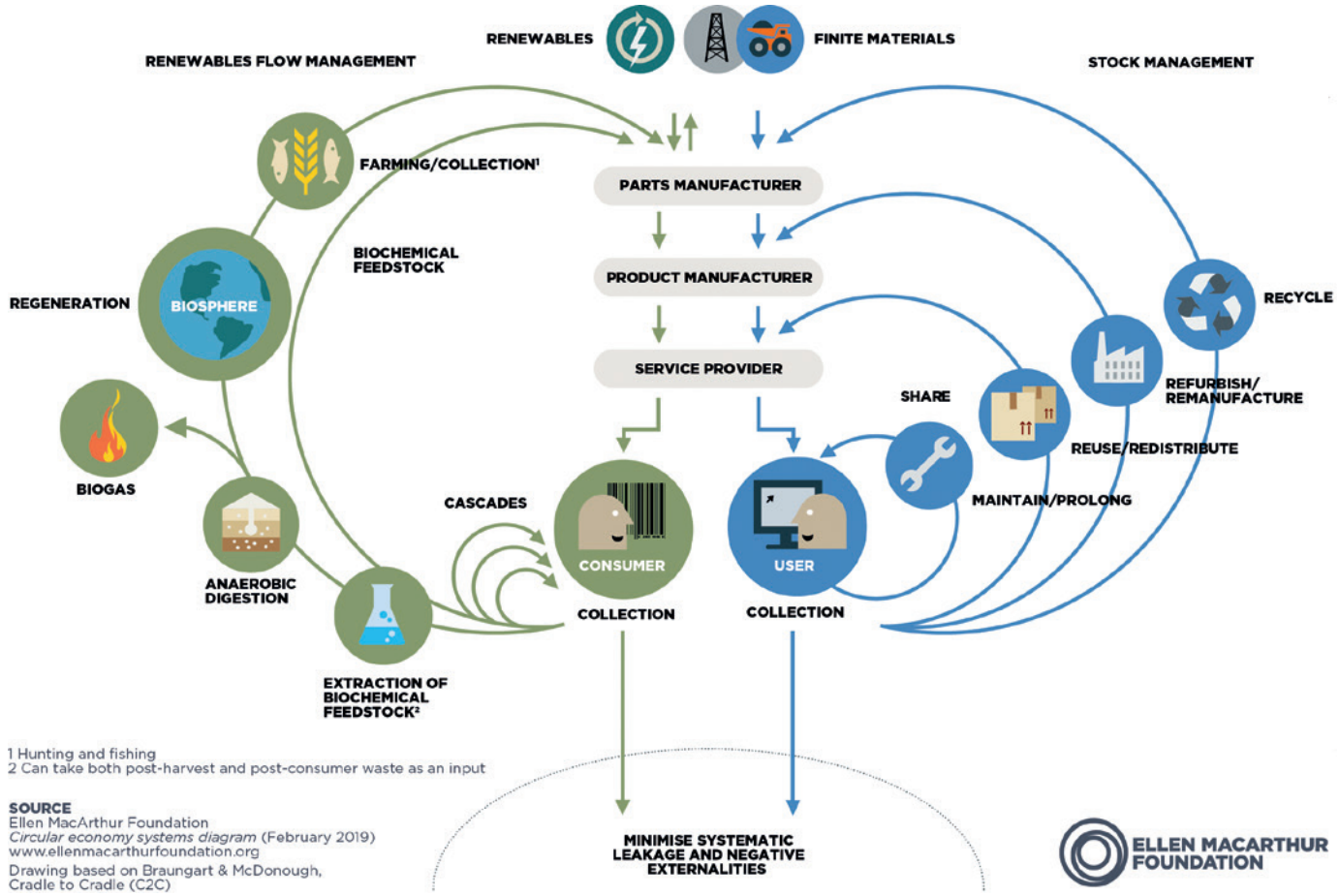

Figure 1: Technical cycles (4R loops on the right) of the circular economy.

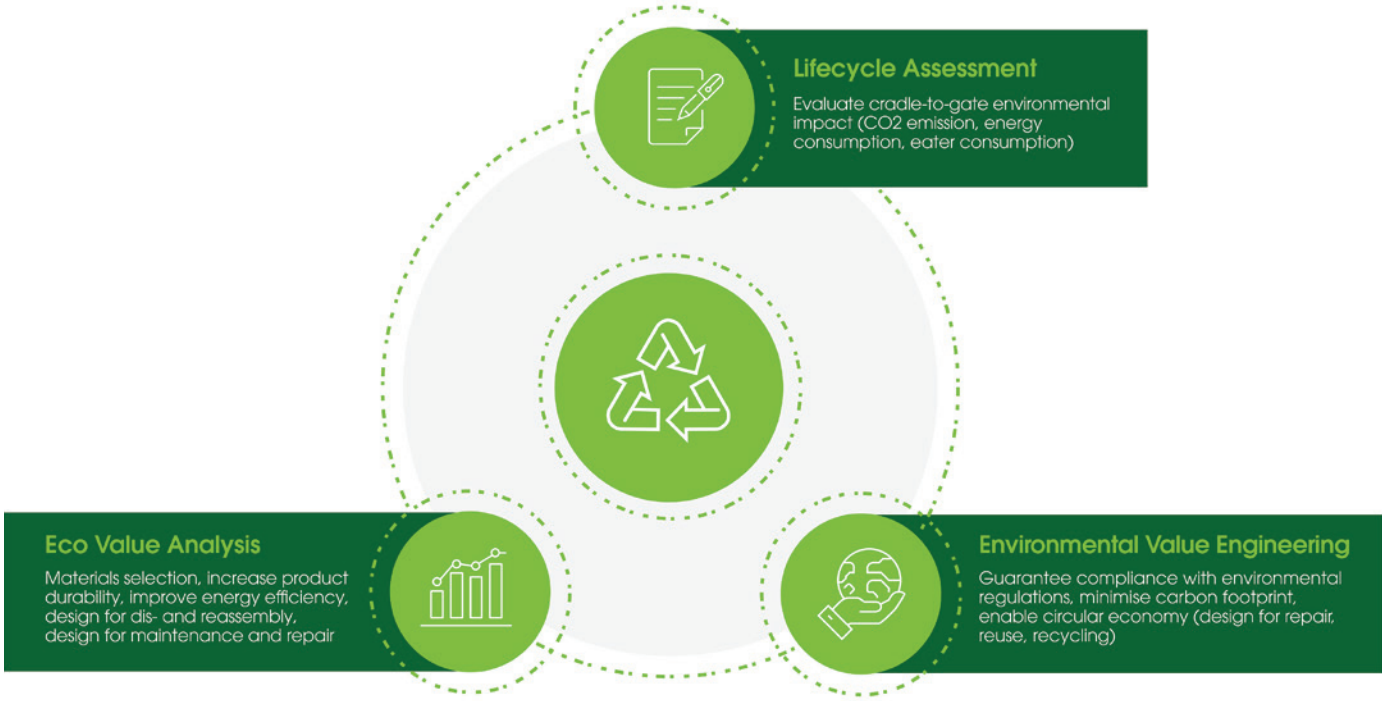

Figure 2: Flex's design for environment service portfolio.

"Each product is designed to be durable, minimising the need to repair or replace the device."

Waste type	Weight (g)	CO_2 Emissions (g)	Energy consumption (MJ)	Water consumption (m^3)
Battery	50.0	287.4	5.1	0.0034
LCD	4.3	911.1	14.4	0.0162
Metal (aluminium)	0.8	7.0	0.1	0.0001
Metal (brass)	8.0	36.1	0.6	0.0006
Metal (stainless steel)	21.7	93.4	1.6	0.0015
Metal-plastic (Motors)	25.0	203.0	2.9	0.0027
PCBA	25.0	5297.3	83.5	0.0940
Plastic (POM)	1.5	6.4	0.1	0.0000
Plastic (PC)	8.3	75.0	1.3	0.0002
Plastic (PC-ABS)	88.2	715.0	13.5	0.0020
Total	**232.8**	**7631.8**	**123.2**	**0.1207**

Table 1: Lifecycle assessment example for a medical device. (LCD = liquid crystal display; PCBA = printed circuit board assembly; POM = polyoxymethylene; PC = polycarbonate; and PC-ABS = polycarbonate/acrylonitrile butadiene styrene.)

Once an evaluation of these factors is complete, it is possible to envision where the medical product can be better designed to improve the environmental impact and the economic value of materials, parts and product recovered.

Environmental Value Engineering

For a new device, Flex integrates the product development process for a new medical design, subjecting it to the same analysis and design guidelines adopted in the eco-value analysis to meet the sustainability requirements of new products:

- Guarantee compliance with specific environmental regulations
- Minimise carbon footprint (i.e. carbon footprint lower than a predefined target)
- Enable circular economy (design for reuse, repair, recycling)
- Sustainable packaging, where possible.

Other considerations

DfE applied to medical devices must also consider specific challenges, such as biohazardous waste, which can limit the opportunity for product reuse, and biocompatibility requirements that may inhibit the use of recycled materials.

MEDICAL DESIGN GUIDELINES

Materials Selection

The medical design teams at Flex consider multiple aspects when selecting the right materials. Initially, they factor in and comply with regulations – such as the Restriction of Hazardous Substances and the Registration, Evaluation, Authorisation and Restriction of Chemicals – that restrict the presence of hazardous substances. Governments and standards bodies around the world are regularly updating regulations to increase the variety and volume of materials that can be used. Prudent product companies stay ahead of the regulations by expanding the list of restricted materials themselves.

The next step is to examine materials for their weight, durability, ease of recycling and ability to support effective 4R loops.

A material's carbon footprint is also considered. For example, climate-neutral polycarbonate can be used when designing innovative plastic solutions that are generated by virgin biomass (vegetation) and cooking oils. In some cases, these thermoplastic materials can reuse the tooling previously designed to host standard fossil resins and therefore avoid the need for additional investment.

Product Durability

Flex's design for reliability approach for medical devices means each product is designed to be durable, minimising the need to repair or replace the device. By increasing the reliability and modularity, some parts may be reused to support refurbishment or redeployment of those parts to other devices.

Reusable parts are typically components with a longer lifetime and lower failures in time. They are activated when required within the device and, like all the other subsystems, may include a self-test/diagnostic mechanism to flag up a fault in the device.

Energy Efficiency and Batteries

The energy efficiency of the medical device is equally important. In battery-powered devices, smaller and more efficient batteries will mean less-frequent charging cycles and, as batteries are hazardous waste, a lower impact on the environment when the batteries are replaced. For some devices, Flex uses disposable printed batteries, based on non-toxic materials like zinc. This allows the batteries to be disposed

> "The implementation of effective 4R loops requires products that can be efficiently and economically disassembled and reassembled."

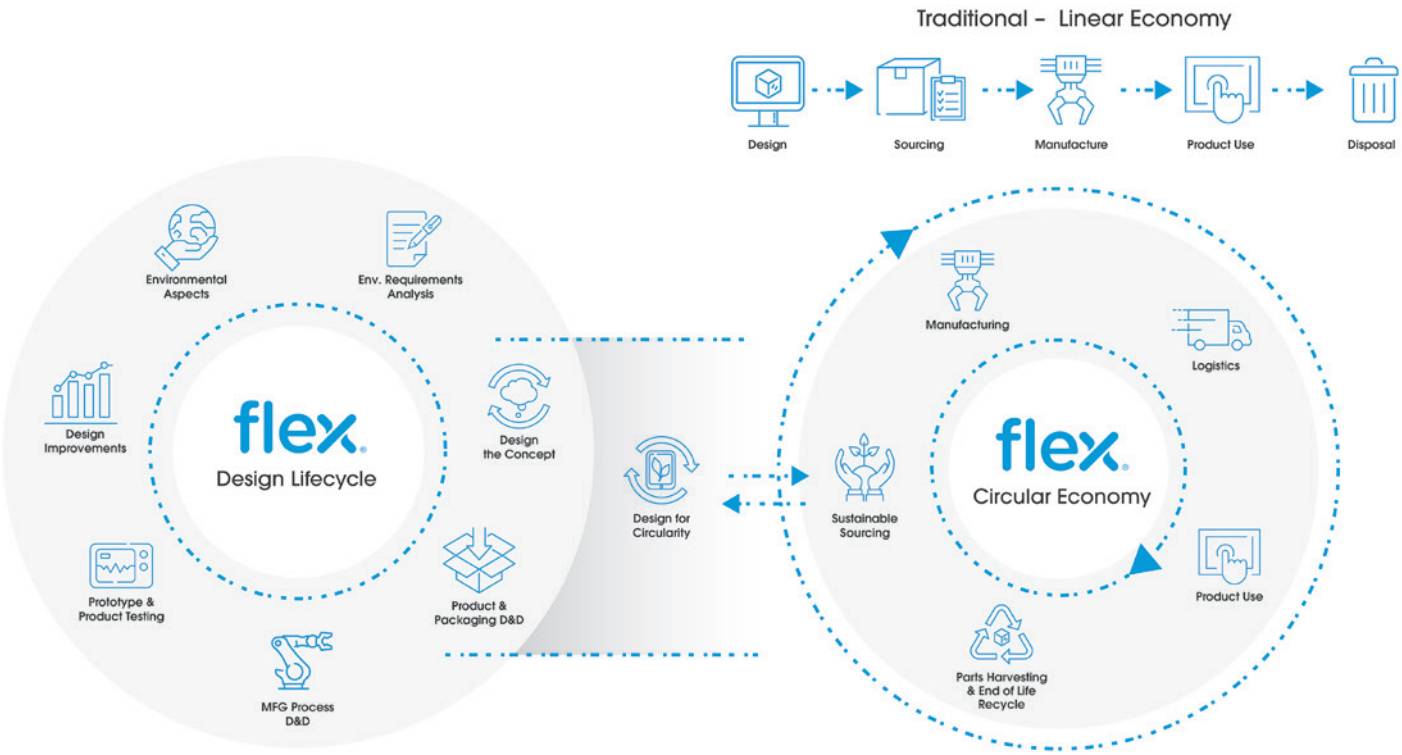

Figure 3: Linear versus circular economy.

> "The lifespan of the medical device can be further extended where a modular design has been used."

of in regular domestic waste bins, where local regulations allow. Any battery used should conform to safety standards such as the CE mark.

There are several power reduction elements that can be applied to medical devices, including adopting low-power technology, implementing low-power modes when not in use and separating the power supply for different parts of the product, depending on use.

Ease of Disassembly and Reassembly

The implementation of effective 4R loops requires products that can be efficiently and economically disassembled and reassembled. In this sense, it is important to minimise the use of glues and welds that can be difficult to remove without damaging parts of the product and that could contaminate other materials in the device. It is also important to ensure the design facilitates both automated assembly and manual disassembly.

Ease of Maintenance and Repair

While a firmware upgrade can increase device longevity and is a normal part of device maintenance, the lifespan of the medical device can be further extended where a modular design has been used. A modular design can allow easier access to each module, including the battery for testing, repair, replacement or upgrading, as necessary. It also ensures hazardous substances are isolated.

CONCLUSION

DfE services support medical device companies through cost-effective lifecycle assessment, environmental impact evaluation, material selection, durability testing, energy efficiency and ease of disassembly of the product and its parts (Figure 3).

The result is a medical device that is optimised for sustainability and uses low-power technologies, less hazardous substances and advanced non-toxic battery technology that allows for ecological disposal. Smart and sustainable design also allows for efficient assembly and disassembly to allow repair, refurbishment and reuse of parts, and easy upgrades to firmware and hardware. These elements combine to deliver a medical device with a minimised carbon footprint.

ABOUT THE COMPANY

Flex is the manufacturing partner of choice that helps a diverse customer base design and build products that improve the world. Through the collective strength of a global workforce across 30 countries and responsible, sustainable operations, Flex delivers technology innovation, and supply chain and manufacturing solutions, to diverse industries and markets.

ABOUT THE AUTHOR

Stefano Vicenzetto, Systems Engineer, has been working at the Flex Milan medical design centre for more than 12 years. He has broad experience of working with medical companies to identify needs and product requirements. Mr Vicenzetto leads product development for systems requirements throughout the whole development cycle, architecture design and risk control. Within Flex, he is also a lead on design for circularity.

CLIMATE CHANGE AND THE PHARMACEUTICAL INDUSTRY: TOO LITTLE, TOO LATE?

In this article, Catriona Eldridge, Materials Scientist, and Omar Shah, Materials Engineer, both of Springboard, discuss the findings of a recent investigative assessment into the environmental impact of healthcare products, and consider whether or not the pharmaceutical industry is doing enough to combat climate change.

Governments and companies across the world have made ambitious commitments to reduce their environmental impact. For example, at the COP26 climate change conference in November 2021, 55 countries committed to developing low-carbon healthcare systems and 20 committed to developing net zero healthcare systems, with deadlines ranging from 2030 to 2050.[1] What is the pharmaceutical industry doing to help meet these targets, and is it enough?

Governments are increasing the pressure on companies to improve their sustainability. For example, the EU Corporate Sustainability Reporting Directive will take effect from January 2023,[2] expanding both the number of companies required to report their emissions and the scope of that reporting. Mandated reporting will now include Scope 3 greenhouse gas emissions (Figure 1), as well as requiring reports to be assured by third parties, as well as to be computer readable. These laws will apply to large or listed companies within the EU, including non-EU companies with significant activity inside the bloc. Taken together, these new requirements will significantly alter the landscape of climate-related reporting. It will be significantly easier to investigate the environmental impact of a company and to hold them to account.

> "Despite having seemingly large environmental impacts, good early interventions, such as pMDIs, in fact avoid greater environmental damage by preventing more serious interventions later on."

Globally, the healthcare industry accounts for approximately 5% of emissions.[3] However, unlike other, less necessary, sources of emissions, such as air travel for leisure, it is not possible to reduce emissions from the healthcare industry by simply reducing the amount of activity. This article will discuss the findings of an investigative assessment of healthcare products' environmental impact. Especially in patient-led care, the investigation found

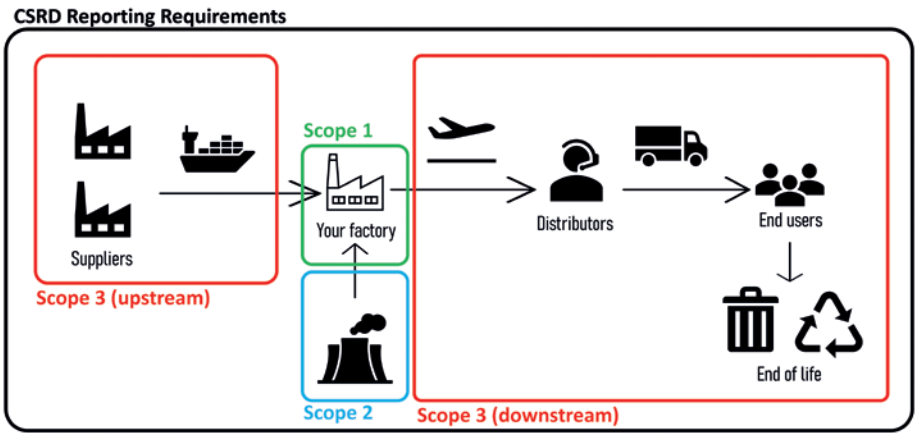

Figure 1: An illustration of Scope 1, 2 and 3 emissions in a value chain, with definitions of the different scopes.[3]

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that, despite having seemingly large environmental impacts, good early interventions, such as pressurised metered dose inhalers (pMDIs), in fact avoid greater environmental damage by preventing more serious interventions later on.[4] As such, a more nuanced solution is required to reduce emissions in the industry.

PUBLIC COMMITMENTS

Of the 10 largest pharmaceutical companies by sales, all have committed to reducing their environmental impact. Some began reducing emissions as early as 2000, but some have only begun making serious, quantified commitments since 2019. Predominantly, these commitments focus on CO_2 equivalent (CO_2e) emissions, plastic waste or water use within the operations of the company – that is, Scope 1 or 2 CO_2e emissions and plastic waste or water use within the direct control of the company.

Some of these targets are highly ambitious, such as Novartis' target to be carbon neutral across their entire value chain by 2030,[5] or AstraZeneca's "Ambition Zero Carbon" to be carbon negative across their entire value chain by 2030.[6] Some are less ambitious, with later deadlines and smaller reductions.

Only seven of these emissions-based commitments were accredited by the Science Based Targets initiative (SBTi).[7] The SBTi encourages companies to set science-based net-zero targets and assesses whether targets are in line with a 1.5°C future. Across the industry, the general trend is to make large commitments on the easy wins, focusing on a company's own operations, with more limited commitments in more difficult areas, such as Scope 3 emissions or water use.

Scope 3 emissions, however, made up approximately 80% of the reported emissions from these companies. Figure 2 illustrates some typical proportions of Scope 1, 2 and 3 emissions. Scope 3 emissions are still a consequence of a company's actions and, to a great extent, can be changed by decisions taken by that company. Given that Scope 3 emissions constitute the majority of the total emissions involved, meaningful targets must involve reductions in Scope 3. The largest quantified Scope 3 reduction target the assessment found was 50%, whereas a typical target was only 20%.

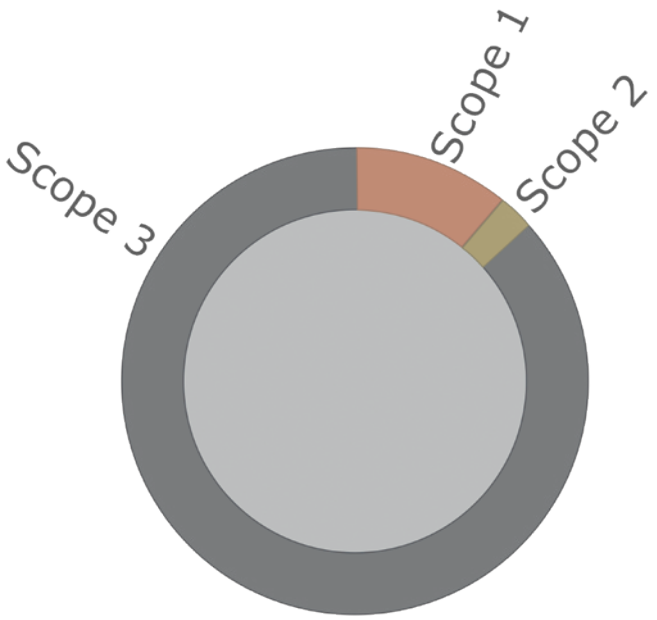

Figure 2: An illustrative graphic of the typical proportions of Scope 1, 2 and 3 emissions among the top 10 pharmaceutical companies.

> "Several methods are being used to try and reduce emissions – such as designing new products, improvements to the manufacturing process and the Energize initiative to enable suppliers to buy renewable energy collectively."

Changes are being considered or implemented from the level of individual devices and manufacturing sites, all the way up to business-wide strategies. Several methods are being used to try and reduce emissions – such as designing new products,[8] improvements to the manufacturing process[9] and the Energize initiative[10] to enable suppliers to buy renewable energy collectively. Some companies have also installed renewable energy generation directly on their own sites.

For example, GSK is altering some of its synthesis pathways to use enzymes, delivering massive efficiency savings. Johnson & Johnson has changed some of its packaging, using materials and methods that are novel to the pharmaceutical industry, meaning that the change required serious investigative work to meet regulations. Both of these measures are good examples of the scale of change required – on average, these 10 companies still need to reduce even their Scope 1 and 2 emissions by half. In a highly regulated industry such as pharmaceuticals and healthcare, these changes take time and must therefore be started now.

PROGRESS – TOO LITTLE, TOO LATE?

Are these efforts succeeding? Across other industries, the outlook is poor – large companies are failing to meet their emissions targets by as much as 60%, and a report from the NewClimate Institute found that none of the 25 large companies they investigated in 2021 were achieving a high standard of improvement.[11]

Among pharmaceutical companies specifically, progress so far has been mixed. A few companies set climate-related targets as early as 2010 or 2000. GSK, for example, set a target of reducing water use by 20% between 2010 and 2020, and reported a successful reduction of 30% in 2020.[12] Similarly, Merck aimed to reduce greenhouse gas emissions by 10% between 2010 and 2015, and managed a 13% reduction.[13]

However, other targets were not met – seven out of the 10 largest pharmaceutical companies either failed to meet, or failed to report, the outcome of at least one of their targets. Some only fell a little short; for example, a target to reduce waste to landfill by 100% only reduced waste by 85%. Others failed badly, such as one company that published a target to reduce water discharge by 4% over two years, but actually increased water discharge by 15%.

Several companies have openly stated that they will use carbon offsetting or compensation, despite the well-documented issues around these practices. Firstly, it is clear that there is already an urgent need to decarbonise global economies and further reduce the amount of carbon dioxide already in the atmosphere by capturing carbon.[14] The second issue is that carbon offsetting methods are widely unaccountable, with flaws including:

- A lack of additionality, where credits are issued for carbon offsetting that would have occurred anyway
- Carbon "leakage", where credits are issued for halting an activity that actually continues in a different location.[15]

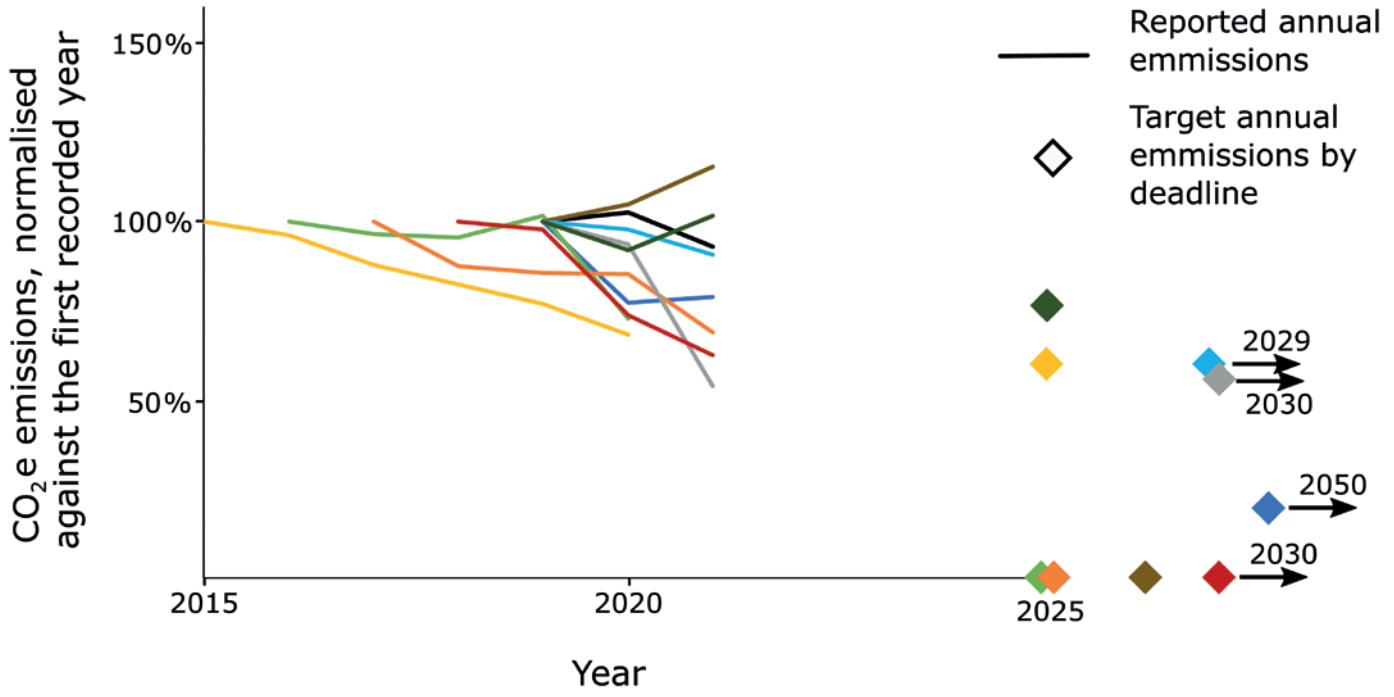

Figure 3: A graph showing the reported Scope 1 and 2 emissions from the top ten pharmaceutical companies, where available. The emissions are normalised against the first reported year's emissions. The diamonds indicate the target annual emissions these companies have committed to reaching.

"Some companies seem to be struggling with the sheer scale of this task; for some of the companies in the assessment, emissions increased from 2020 to 2021."

The work that remains is daunting, but necessary. The typical reduction over the last two reported years was 7% for Scope 1 and 2 emissions, and 6% for Scope 3 emissions. Five of the 10 largest pharmaceutical companies increased their emissions over the last two reported years. Figure 3 shows the reported Scope 1 and 2 emissions, where available, since 2015, normalised against the first reported year, as well as the targets that these companies are aiming for. Among the companies investigated in the assessment, the average reduction in Scope 1 and 2 emissions they needed to make annually to reach their target was 15%. Now, some must make reductions as large as 25%.

Some companies seem to be struggling with the sheer scale of this task; for some of the companies in the assessment, emissions increased from 2020 to 2021. One was able to report a 53% reduction in water usage at one manufacturing site, but this took over a decade. Another company was able to report a 3% reduction in energy consumption, but only because natural disasters had closed multiple production sites.[14] Many companies are still assessing the true size of their environmental footprint, carrying out internal investigations and beginning conversations with suppliers. This is only the first step in reducing emissions and, as self-imposed and external deadlines move ever closer, the time available to make these changes is slipping away.

Of all the pre-COP26 targets the assessment was able to find for the top 10 pharmaceutical companies, only half were achieved.

WHAT TO DO NEXT?

Some avenues companies could explore include lifecycle assessments of existing business strategies and devices; root cause analyses of inefficiencies, pinpointing the main problems with a device or logistical set up; moving on to concept generation and feasibility assessments (including sustainability) for the solution; and potentially, where the necessary changes are significant, re-evaluating the entire product development process, from blue sky concept generation to manufacture, verification and validation. Given that climate change has been on the agenda for over a decade now, most of the low-hanging fruit may already be gone.

In the authors' experience, it is critically important to have both breadth and depth of skills to tackle these problems. The authors have found that engineering and scientific expertise, alongside a strong understanding of the business objectives, regulatory requirements and, vitally, industry experience are all needed to assess such problems clearly and then to find workable solutions and implement them successfully.

Companies will need to develop industry-specific strategies around supplier selection and management, and to design products with the logistical and manufacturing implications in mind. Cold chain transportation, for example, is energy intensive, but could be minimised with thoughtful drug formulation and good

"Companies will need to develop industry-specific strategies around supplier selection and management, and to design products with the logistical and manufacturing implications in mind."

device design. Similar savings could be made in a variety of device types if world-class expertise and insight are applied to the project during the early design stages.

The targets set at and around COP26 were a good and necessary start. Moving further into the 2020s, however, it is clear that a serious effort from all parts of the pharmaceutical industry is required if these goals are going to be met and further climate harm minimised. Following the implementation of the EU Corporate Sustainability Reporting Directive, many companies will be forced to quantify and report their emissions to stakeholders, such as their shareholders, governments and, of course, themselves.

If you recognise any of these issues and would like to discuss how Springboard can assist your organisation, please get in touch with Catriona Eldridge at catriona.eldridge@springboard.pro

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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ABOUT THE AUTHORS

Catriona Eldridge is a Materials Scientist at Springboard with a range of experimental experience including mechanical testing and thermal analysis and a broad knowledge of engineering materials and manufacturing methods. She completed her MSc at the University of Cambridge (UK), with a focus on nanostructure materials. Ms Eldridge's work at Springboard involves both new product design and applying scientific analysis to issues in existing products in order to find solutions.

Omar Shah is a multi-skilled Engineer and Materials Scientist at Springboard, specialising in metallurgy and material processing. He has experience in corrosion, mechanical and microstructural testing, and mechanical engineering design. He completed his MSc at the University of Cambridge (UK), working with the Rolls Royce University Technology Centre developing novel titanium alloys. At Springboard, Mr Shah uses his broad knowledge base to identify and solve cross-disciplinary problems.

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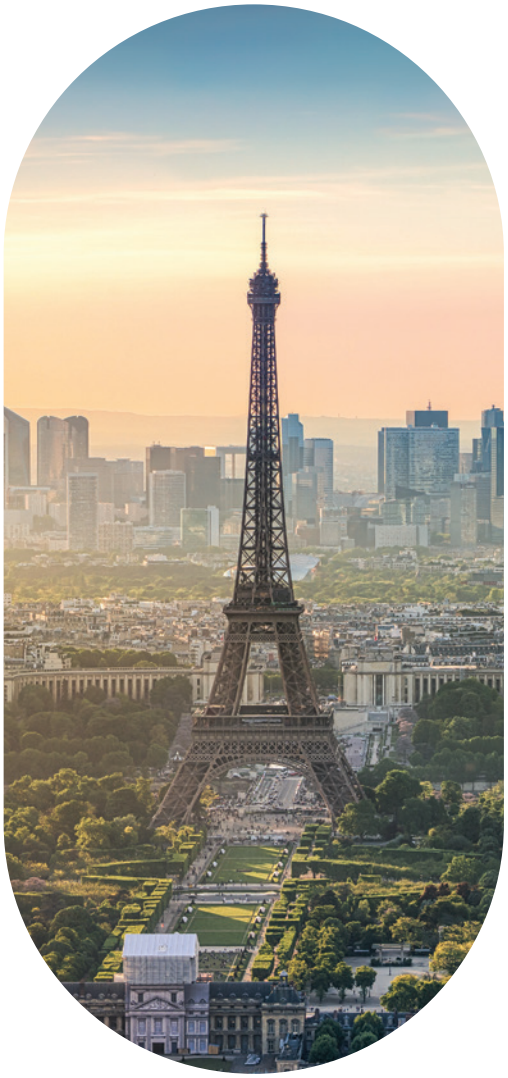

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Publication Month	Issue Topic	Materials Deadline
November 2022	Pulmonary & Nasal Drug Delivery	Deadline passed
December	Connecting Drug Delivery	Deadline passed
January 2023	Skin Drug Delivery: Dermal, Transdermal & Microneedles	Dec 8, 2022
February	Prefilled Syringes & Injection Devices	Jan 5, 2023
March	Ophthalmic Drug Delivery	Feb 2, 2023
April	Pulmonary & Nasal Drug Delivery	Mar 2, 2023
Apr/May	Drug Delivery & Environmental Sustainability	Mar 16, 2023
May	Delivering Injectables: Devices & Formulations	Apr 6, 2023
May/Jun	Novel Oral Delivery Systems	Apr 20, 2023
June	Connecting Drug Delivery	May 4, 2023
Jun/Jul	Industrialising Drug Delivery	May 18, 2023
September	Wearable Injectors	Aug 3, 2023
October	Prefilled Syringes & Injection Devices	Sept 7, 2023
Oct/Nov	Drug Delivery & Environmental Sustainability	Sept 21, 2023
November	Pulmonary & Nasal Drug Delivery	Oct 2, 2023
December	Connecting Drug Delivery	Nov 7, 2023

YPSOMED
SELFCARE SOLUTIONS

YPSOMED'S TWO-STEP APPROACH TO ACHIEVING NET ZERO

In this article, Sebastien Gerner, Corporate Sustainability Manager at Ypsomed, discusses the company's approach to achieving its net zero objectives, both looking back at Step One of Ypsomed's approach and outlining the upcoming Step Two.

INTRODUCTION

The climate crisis demands that all players in all industries do their part towards achieving net zero greenhouse gas (GHG) emissions. The pharmaceutical industry is no exception to this, and many companies have set themselves ambitious targets in their drive to net zero. However, reaching net zero as an industry requires collaboration across the supply chain, from materials producers to drug and device developers to logistics companies and healthcare providers. Some payers, such as the UK NHS, are using their influence to push this agenda by adopting purchasing policies that only permit working with suppliers that can demonstrate progress in reducing their carbon footprint.[1]

A major part of reaching net zero will be the transition to a circular economy (Figure 1). Historically, most industries have operated on a linear economic model, where raw materials are extracted from the environment, processed into a product, distributed to consumers and then disposed of. A circular economy closes this loop by looking at product end of life and, rather than simply disposing of a used product, reintroducing it to the start of the value chain – either as raw materials via recycling or as a new product via refurbishment.

Creating a circular economy presents a particular difficulty in the drug delivery industry, as any recycling programme has to contend with safety and regulatory concerns surrounding medical waste. However, this is far from an insoluble problem – some companies, such as Johnson & Johnson[3] and Novo Nordisk,[4] have launched take-back schemes to encourage recycling of their drug delivery products.

> "Ypsomed is committed to doing its part in the drug delivery industry's drive towards net zero and has made a commitment to reduce its carbon footprint and promote the circular economy."

Ypsomed is committed to doing its part in the drug delivery industry's drive towards net zero and has made a commitment to reduce its carbon footprint and promote the circular economy. The company's net zero goals are:

- Net zero operational (Scope 1 and 2) CO_2 emissions by 2030
- A selection of products with net zero emissions by 2030
- Net zero emissions across the company's entire value chain (Scope 1, 2 and 3) by 2040.

A significant step in achieving these goals has been the development of YpsoMate Zero – the world's first net zero autoinjector.[5] However, this is only one part of what Ypsomed has achieved with

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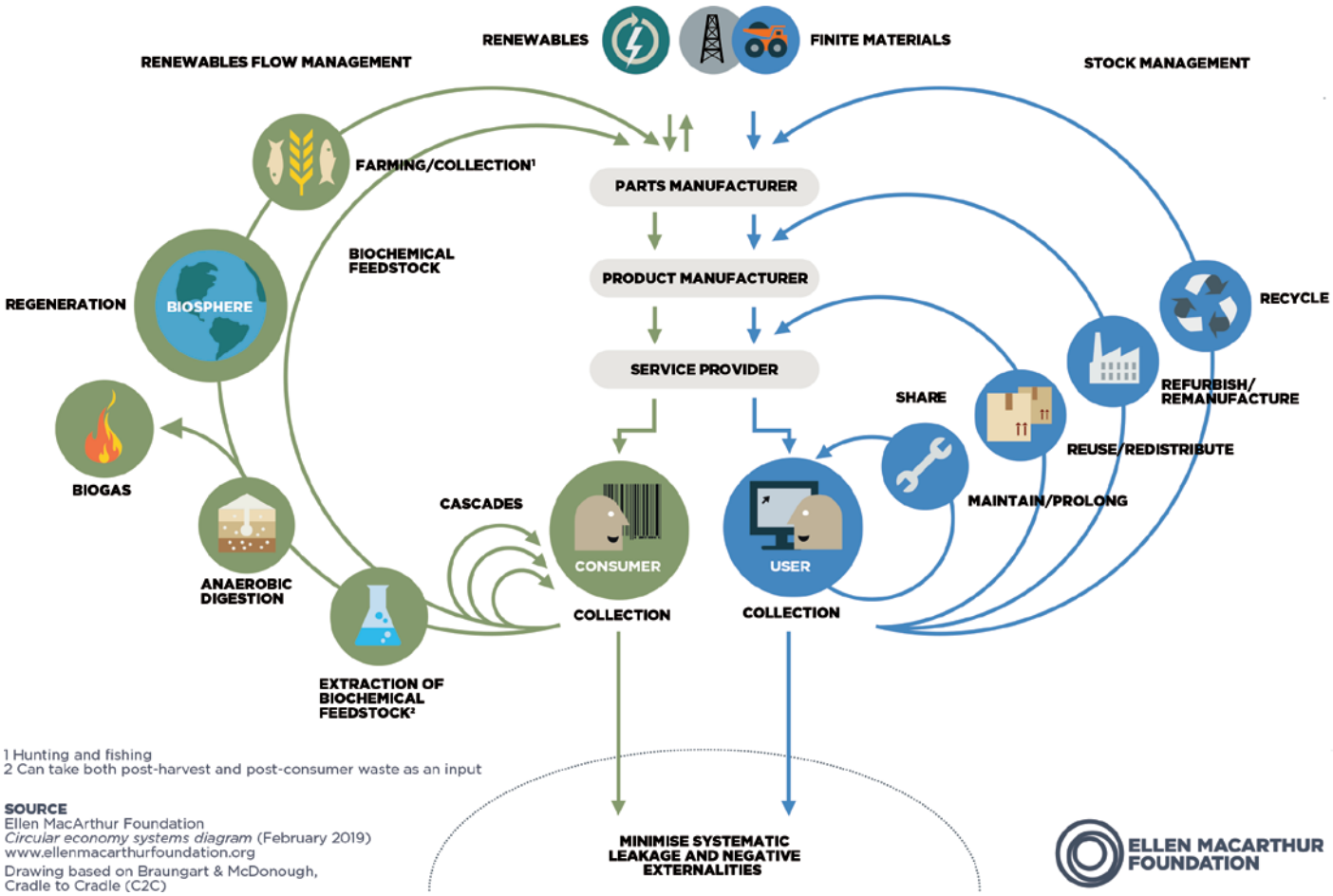

Figure 1: The circular economy closes the loop by recycling products at their end of life and reintroducing them as feedstock for the next generation of products.[2]

respect to its sustainable development goals in the past year.[6] Ypsomed also transitioned to sourcing 100% of its electricity from renewable sources and is an active founding member of the Alliance to Zero,[7] which encourages collaboration between various members of the pharmaceutical supply chain and marked its one-year anniversary at the PDA Parenteral Packaging Conference in Basel (Switzerland) this year.

YPSOMED'S ZERO PROGRAMME

To meet its sustainability targets, Ypsomed has adopted the Zero Programme – a systematic approach towards achieving drug delivery platforms that are produced with net zero emissions and is embedded in the company's overall corporate sustainability strategy. The Zero Programme takes an iterative approach to emission reduction, with each step building on the last. Step One targeted an overall reduction of 40% and Step Two is targeting up to 70%.

Looking Back at Step One

Ypsomed began Step One by conducting a cradle-to-gate lifecycle assessment (LCA) of YpsoMate (Figure 2). The LCA revealed that the vast bulk of GHG emissions came from those associated with the materials used in

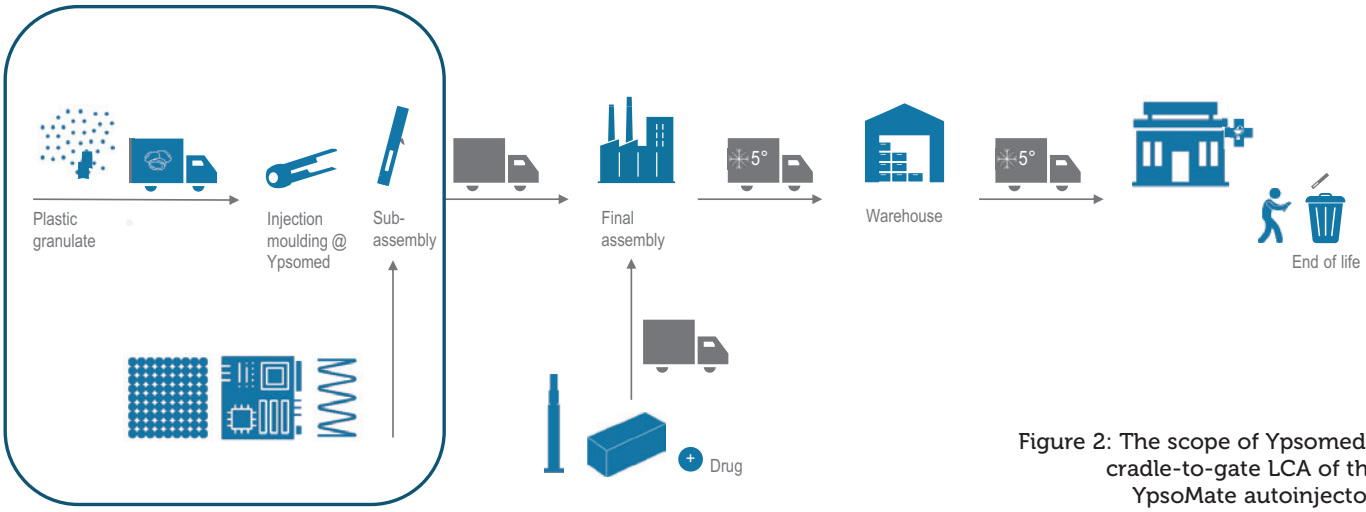

Figure 2: The scope of Ypsomed's cradle-to-gate LCA of the YpsoMate autoinjector.

"With the results of Step One of the Zero Programme now accounted for and available to customers, Ypsomed is now looking to go further in the drive towards net zero with iterative improvements in Step Two."

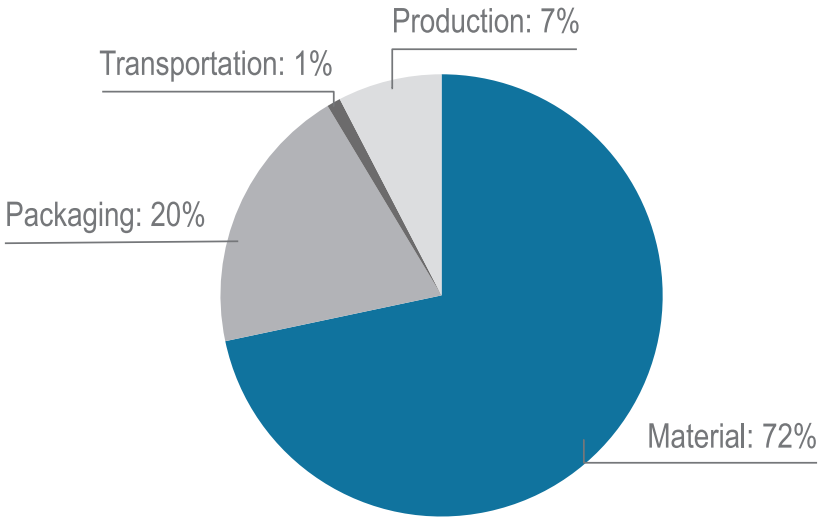

Figure 3: The LCA of YpsoMate conducted at the start of Step One of the Zero Programme revealed that over 90% of the carbon footprint comes from materials and packaging.

production (72%), with the second-highest contributor being those associated with packaging (20%), as shown in Figure 3. Both of these sources of GHG emissions are Scope 3 emissions, meaning that reducing them required working with suppliers across the supply chain to bring down YpsoMate's carbon footprint.

Step One has now been achieved with the successful development and uptake of YpsoMate Zero by customers. Step One reached its 40% reduction in carbon emissions (Figure 4) by investigating two key avenues – chemically identical bio-based plastics for parts manufacture and the use of recycled polyethylene terephthalate (rPET) as a packaging tray material.

Drug delivery devices are naturally held to a very high standard for quality, and their constituent materials are no exception. As such, when developing YpsoMate Zero it was imperative for Ypsomed to use an identical grade of plastic granulate to manufacture parts from, but from a sustainable source. The solution to this challenge is the mass-balance approach (Figure 5).

Following the mass-balance approach, bio-based feedstock, such as that derived from waste materials or biogas, is fed into the plastic production process along with conventional fossil-based feedstock. At this point, the two become indistinguishable and segregated bookkeeping is used to keep track of the proportion of the output plastic granulate that can be sold as bioplastic – the proportion of bio-based feedstock in is equal to the proportion of bioplastic out. In this way, plastic granulate producers can guarantee chemical equivalence between their conventional and bio-based products, while also clearly differentiating between them.[8]

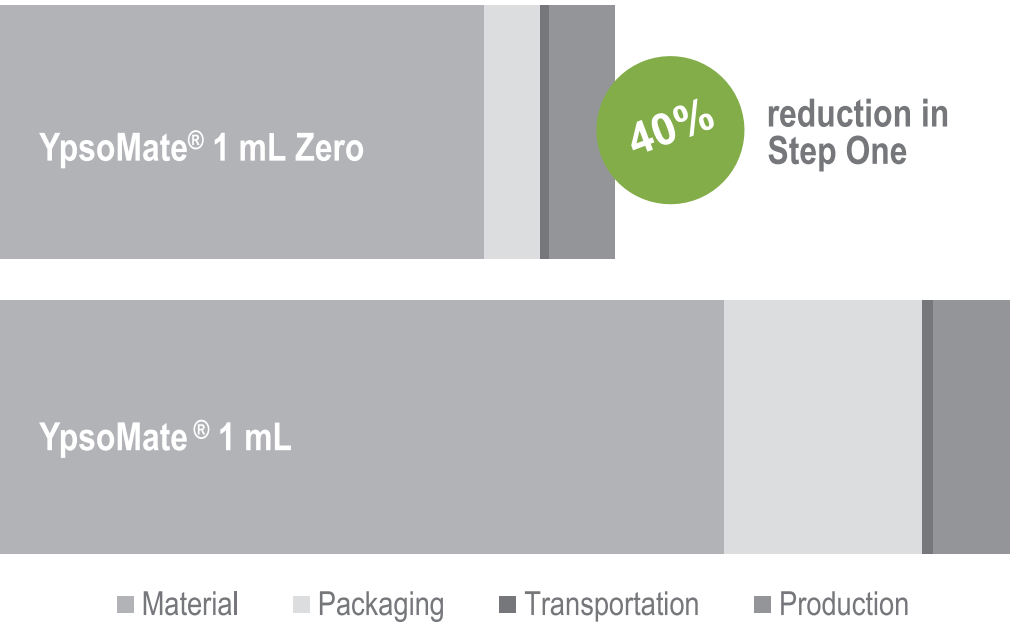

Figure 4: Step One of Ypsomed's Zero Programme has already achieved a 40% reduction in GHG emissions.

Looking Ahead to Step Two

With the results of Step One of the Zero Programme now accounted for and available to customers, Ypsomed is now looking to go further in the drive towards net zero with iterative improvements in Step Two. The aim for Step Two is to reach a carbon footprint reduction of up to 70% from the current YpsoMate platform. The first step in achieving this aim is again to consider where the GHG emissions associated with YpsoMate come from.

Being the largest contributing factor, materials are going to continue to be a key focus going forwards. Bio-based polymers from sustainable sources, produced using the mass-balance approach, will play a major role in further reducing the GHG emissions associated with the plastic granulate used to make the component parts of YpsoMate. However, to realise the goals of Stage Two, Ypsomed is going further, evaluating wherever possible the use of alternative materials.

The other primary area for improvement is packaging. In Step One, Ypsomed achieved a reduction in carbon footprint by switching from PET to rPET as a packaging material. In Step Two, Ypsomed is investigating the possibility of achieving further reductions by looking at alternative materials, such as pulp- or fibre-based packaging. These materials are

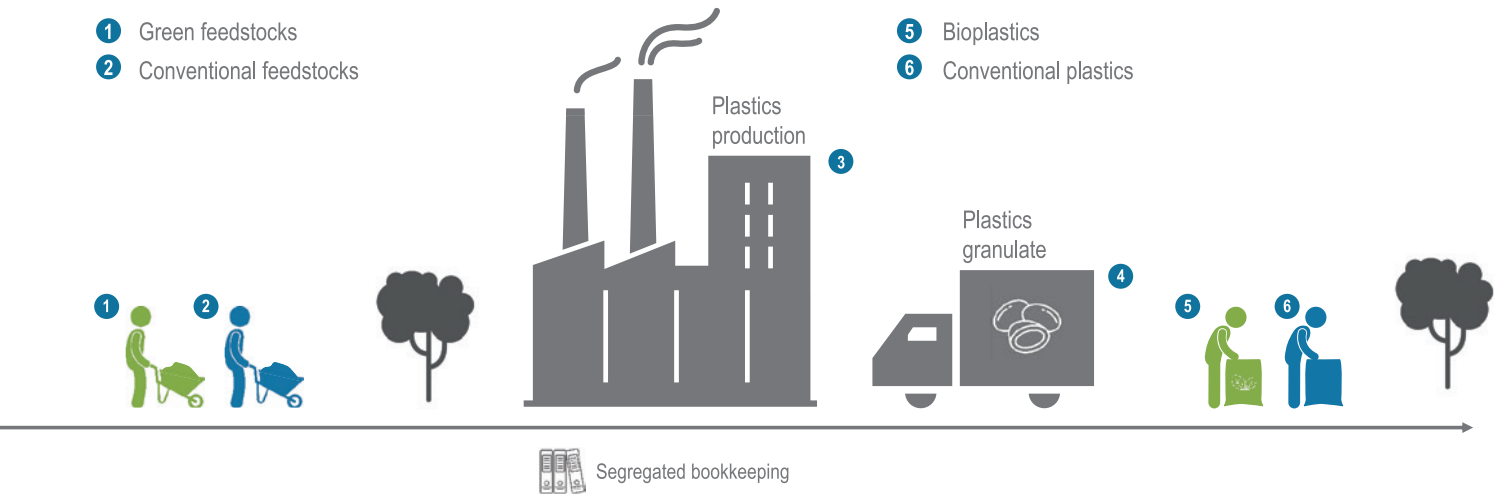

Figure 5: The mass-balance approach to plastic granulate production.

entirely derived from plant matter and are significantly more sustainable than conventional fossil-based plastics.

ISCC+ Certification

A fundamental part of Ypsomed's approach is ISCC+ certification. The International Sustainability & Carbon Certification (ISCC) is an organisation that provides a globally recognised certification system dedicated to supporting companies in the production of their products in an environmentally, socially and economically sustainable manner. The ISCC is a major proponent of the circular economy, material traceability and the mass-balance approach, among other such sustainable practices. The ISCC+ certification covers not only an individual product, but its entire supply chain, accounting for Scope 1–3 emissions.

Ypsomed has achieved ISCC+ certification and sees applying its principles to all the company's products as critical to achieving its net zero objectives. Ypsomed encourages all its customers to also apply for the ISCC+ certification; the benefits for pharmaceutical companies that apply the certification to their products include the added value of the certification and carbon credit accounting.

ENVISIONING A POTENTIAL STEP THREE

The Zero Programme's process of improving sustainability won't stop once Step Two's aims have been achieved. The programme is designed as a systematic, iterative approach that can achieve real, step-by-step targets on the road to net zero emissions. Once Step Two has been successful in creating a significant reduction in YpsoMate's carbon footprint, further LCAs will reveal the key target areas for improvement. Realising the aims of Step Three will likely involve further investigations into ways to reduce Scope 3 emissions and may involve new ways of tackling emissions generated by production, transport and logistics, should the proportion of emissions associated with those areas increase relative to materials and packaging.

One possible objective on the horizon is deeper consideration of YpsoMate's end of life. As mentioned earlier in this article, recycling is a uniquely difficult prospect for drug delivery devices, considering the special care required for the disposal of medical waste – especially with products that include needles. Because of this, Ypsomed is already developing towards circular device partnership for its disposable autoinjectors, including partners from the industry. It is expected that governments and regulators will encourage the development of such schemes, along with the infrastructure and social habits required to get the most out of them. Devices designed using a platform approach, such as YpsoMate, will be best placed to adapt to this new model, being best suited for part recycling and part reuse, where possible.

SUMMARY

With the successful development of YpsoMate Zero, Ypsomed is leading the way in the drug delivery industry's drive to net zero. However, this achievement is only Step One of YpsoMate Zero; Step Two aims to build on the 40% reduction in emissions achieved by Step One and go further – pushing beyond a total 70% reduction.

With the vast majority of the company's emissions now being Scope 3, Ypsomed is working extensively with partners in the drug delivery and pharmaceutical industries to bring down GHG emissions across the whole supply chain as part of the Alliance to Zero, a global, non-profit membership association for pharma and biotech companies that facilitates working towards common sustainability goals by connecting suppliers, pharma companies and service providers. The Alliance to Zero works to reduce waste and emissions, encourage collaboration, facilitate traceability and establish industry-wide key performance indicators for sustainability – goals Ypsomed is proud to be a part of.

Ypsomed is ISCC+ certified, demonstrating its commitment to achieving sustainability across its supply chain. As part of this commitment, the company is continuing to work with suppliers to reduce the carbon footprint of the materials and packaging used in its products, which currently account for over 90% of its total GHG emissions. This includes transitioning to chemically identical bio-based materials manufactured under the mass-balance approach, as well as investigating alternative and recycled materials wherever possible, such as rPET and pulp-based packaging.

With the climate crisis upon us, collaboration across the supply chain will be critical for the pharma and drug delivery industries to reach net zero, and Ypsomed is ready to do its part.

ABOUT THE COMPANY

Ypsomed's comprehensive drug delivery device platforms consist of autoinjectors for prefilled syringes in 1 mL and 2.25 mL formats, disposable pens for 3 mL and 1.5 mL cartridges, reusable pen injectors, ready-to-use prefilled wearable patch injectors and injection devices for drugs in dual-chamber

cartridges. Unique click-on needles and infusion sets complement the broad self-injection systems product portfolio.

With over 35 years of experience in the development and manufacture of innovative injection systems, Ypsomed is well equipped to tackle digital healthcare challenges and has strategically invested in the development of connected solutions and therapy-agnostic digital device management services. Anticipating the future needs of patients, pharmaceutical customers, payers and healthcare professionals, Ypsomed moves beyond manufacturing connected sensors. Ypsomed's smart device solutions strive to transform patients' lives by capturing therapy-relevant parameters, processing them to facilitate self-management of chronic diseases and integrating these insights with digital therapy management ecosystems.

The company leverages its in-house capabilities in electronics, software and connectivity for the development of new devices and digital product systems. Ypsomed is ISO 13485 certified and all its processes comply with design control and cGMP guidelines with operational QA/QC experts on-site at each location. Ypsomed's FDA-registered manufacturing facilities are regularly inspected by pharma customers and regulatory agencies to supply devices for global markets, including the US, Europe, Japan, China and India

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ASSESSING THE ENVIRONMENTAL IMPACT OF GLOBAL SUPPLY CHAIN LOGISTICS AND SUPPLIER SELECTION

In this article, Alastair Willoughby, Head of Mechanical Engineering at Team Consulting, looks at the factors affecting sustainability when considering global supply chain logistics and supplier selection.

Increasingly, medical device developers are considering ways to build sustainability into their device designs, from low-impact polymers to reducing device complexity. While this has an important role to play in reducing overall emissions, in reality, the design of the device often makes up only a small part of its overall environmental impact. Transportation, especially carbon-costly methods such as air freight, often contributes a much larger carbon output than the device manufacture itself. If companies are serious about meeting their carbon targets, it is essential to consider factors such as global supply chain logistics and supplier selection throughout the device development.

Building an evidence-based understanding of the environmental impacts of different supplier choices, transportation routes and design decisions is no easy task. There are many factors and complexities to take into account, from manufacturing methods to energy sources to power them. Luckily, tools such as lifecycle analysis (LCA) can help decision makers to navigate these complexities, enabling insight-driven decisions to be made throughout a development.

WHAT IS LCA?

LCA is a methodology for assessing the environmental impact of a product or process over its lifetime. It can be used to assess the carbon footprint of multiple aspects of a development, from individual parts to transport options and manufacturing processes. The stages and approaches of an LCA are set out in ISO:14040, covering four main stages (Figure 1):

1. Goal and scope definition
2. Inventory analysis
3. Impact assessment
4. Interpretation.

LCAs are used across multiple industries, meaning there is often public data available for certain processes that can be fed in. In the medical industry, however, there is typically less data available for medical-specific processes, such as how much energy is required to run a clean room for use during an assembly process. Research, coupled with a strong understanding of these industry-specific processes, is often needed to build a more complete representation of the data needed for a medical device LCA. It is also important to note here that, while an analytical tool, there will always be some scope for interpretation in the results. However, it is still a valuable tool for helping to shape our thoughts and decisions.

LCA SCOPE DEFINITION

The scope of an LCA can vary, depending on your goals and the data available. As illustrated in Figure 2, a cradle-to-gate LCA considers the process from raw material extraction to the point the product is ready for transport distribution, i.e. the factory "gate". A cradle-to-grave LCA considers a much wider scope, including the transportation, distribution and use of the product, as well as disposal and waste. A cradle-to-cradle LCA can also be conducted, which considers reuse and recycling as well.

The scope you choose for your development will often depend on what you are trying to achieve. You may be trying to simply benchmark your device, for example, or perhaps you are interested only in what you have direct control over in the development process. How much data is available, as well as its reliability, can also impact the scope of your LCA.

Within your scope definition, what you choose to include and not include can make a lot of difference to the overall picture your LCA provides. For example,

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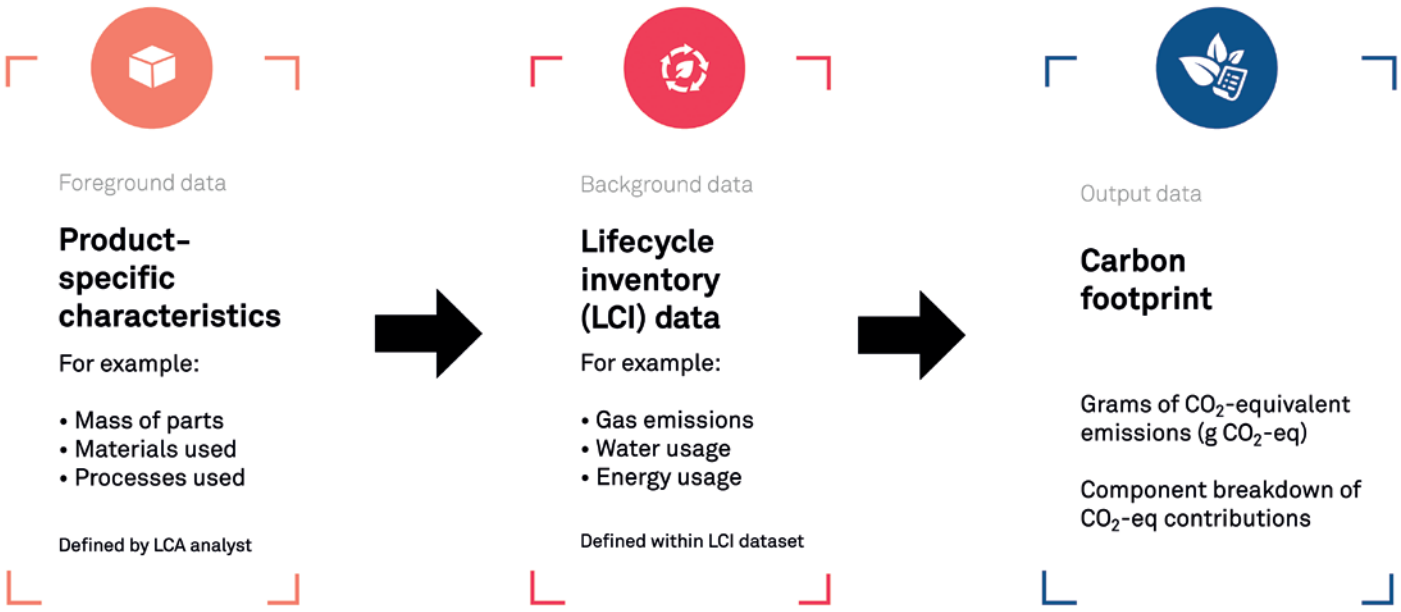

Figure 1: LCA process for medical device development.

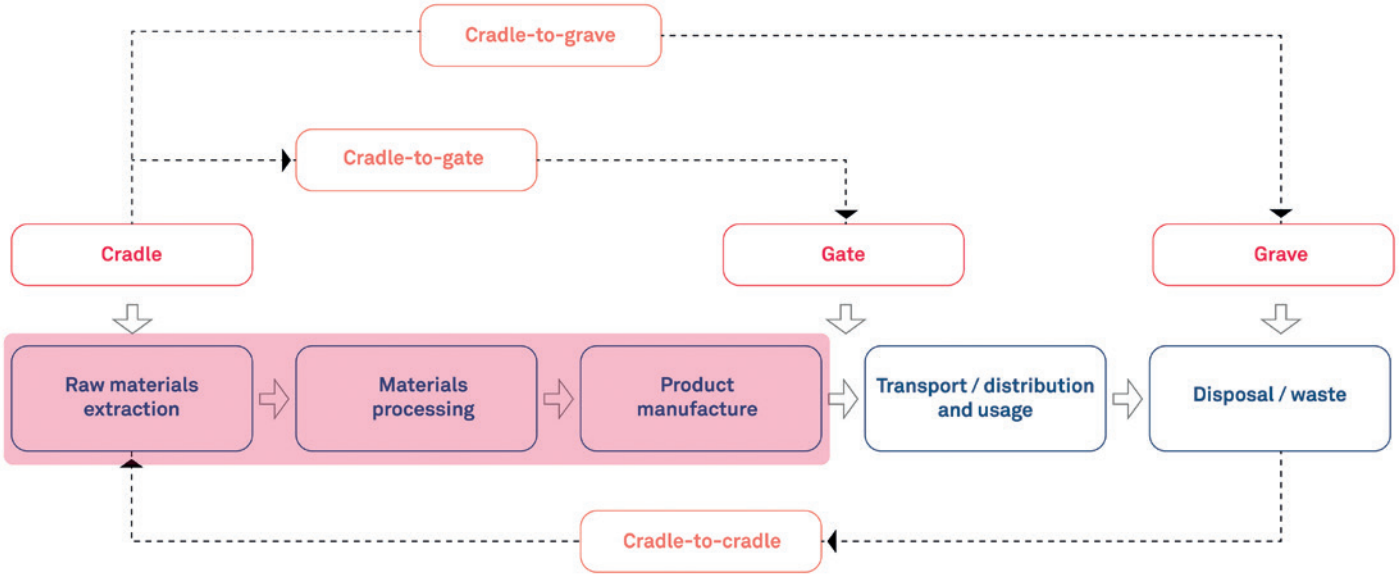

Figure 2: Example of LCA scopes.

a simplified cradle-to-gate LCA assumes that transport only takes place after the manufacturing process. A more comprehensive representation of this process would also take into account the transport of materials and components within the manufacturing stages too, for example.

WHAT SHOULD AN LCA COVER?

As mentioned, an LCA can have a broad or relatively narrow scope. The following aspects are some of the most important to consider when determining the environmental impact of a device.

Device Components

A basic LCA for a medical device might only cover the components of a device and the carbon footprint they create.

> "Selecting a manufacturing plant in a country heavily reliant on coal-fuelled power will create more carbon output than one in a country using more wind and solar energy."

This can be useful for understanding the impact of different parts and features of the device, such as connected add-ons. It can also help to understand the impact of different manufacturers and suppliers. For example, selecting a manufacturing plant in a country heavily reliant on coal-fuelled power will create more carbon output than one in a country using more wind and solar energy.

While these insights can be used to inform design decisions, the device components are only part of the wider picture. To fully understand the environmental impact of your development, you also need to consider transport and packaging.

Transport

The location of the organisations involved, materials that need to be shipped between organisations, and the route and method of transport all play a significant role in a product's overall carbon footprint. For example, a sub-assembly in the Far East could be sea or air freighted into Europe where it is then assembled into the device.

This additional travel can lead to a major increase in carbon footprint, especially when using carbon-costly methods, such as air freight. Factors such as temperature control during shipping and the volume and duration of the material also need to be considered.

Transit Packaging

When shipping devices or components over any distance, transit packaging will be required. For example, syringes will typically be placed in single-use trays and tubs, which will then be placed into bags, boxes and pallets. Sub-assemblies for autoinjectors often need to be transported before being put together into the final device, each of which require packaging. Once completed, the device will then also be placed into its final consumer-facing packaging. Often, transit packaging is not reused, meaning the manufacturing carbon costs of this packaging, alongside the weight it adds to shipping and subsequent carbon footprint, also need to be considered as part of the total impact.

A COMPARISON OF DIFFERENT LCA SCOPES

To illustrate the difference between different LCA scopes, three LCAs were conducted based on the same fully functional autoinjector with needle safety system. The device is made up of 12 components.

Simple LCA

The graph in Figure 3 shows the results of a simple LCA, which focuses on the manufacture of the device components and primary pack. The resulting carbon output is 141 g CO_2 equivalent (eq). An assessment of this level might be suitable if you are a device developer and primarily interested in the sustainability factors you have most control over – such as the impact of adding or removing features or components or making changes to the material used. However, as noted before, this makes up only part of the wider picture.

Complex LCA

In Figure 4, we can see a more complex LCA that goes a step further to not only consider the device components but also the energy associated with assembling the device, syringe filling and final packaging. In this assessment, the assembly and product packaging increase the carbon output by around 86%, from 141 to 263 g CO_2 eq.

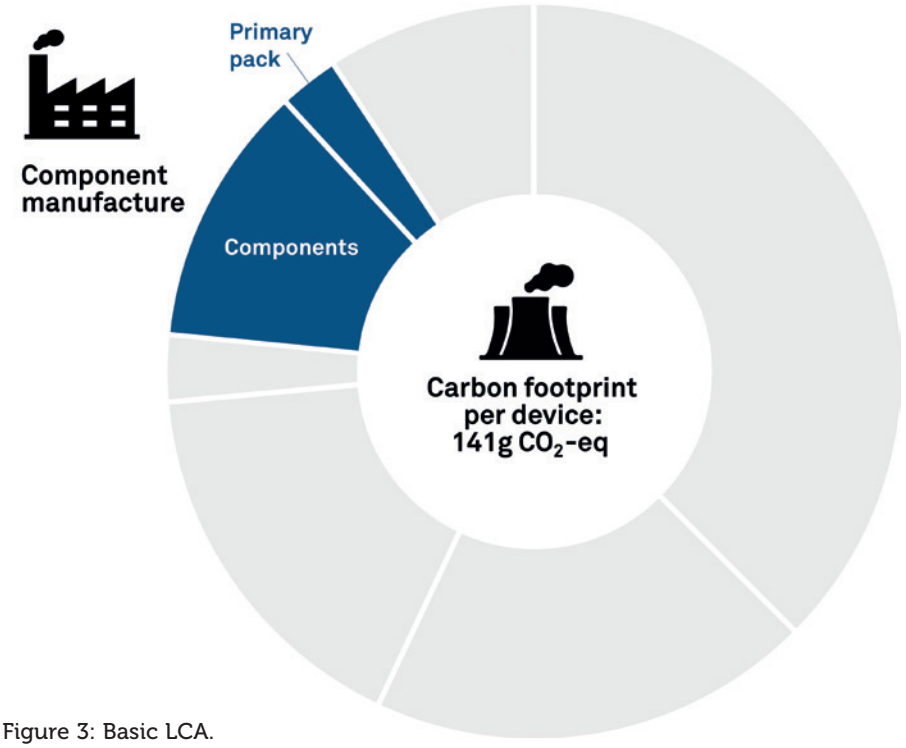

Figure 3: Basic LCA.

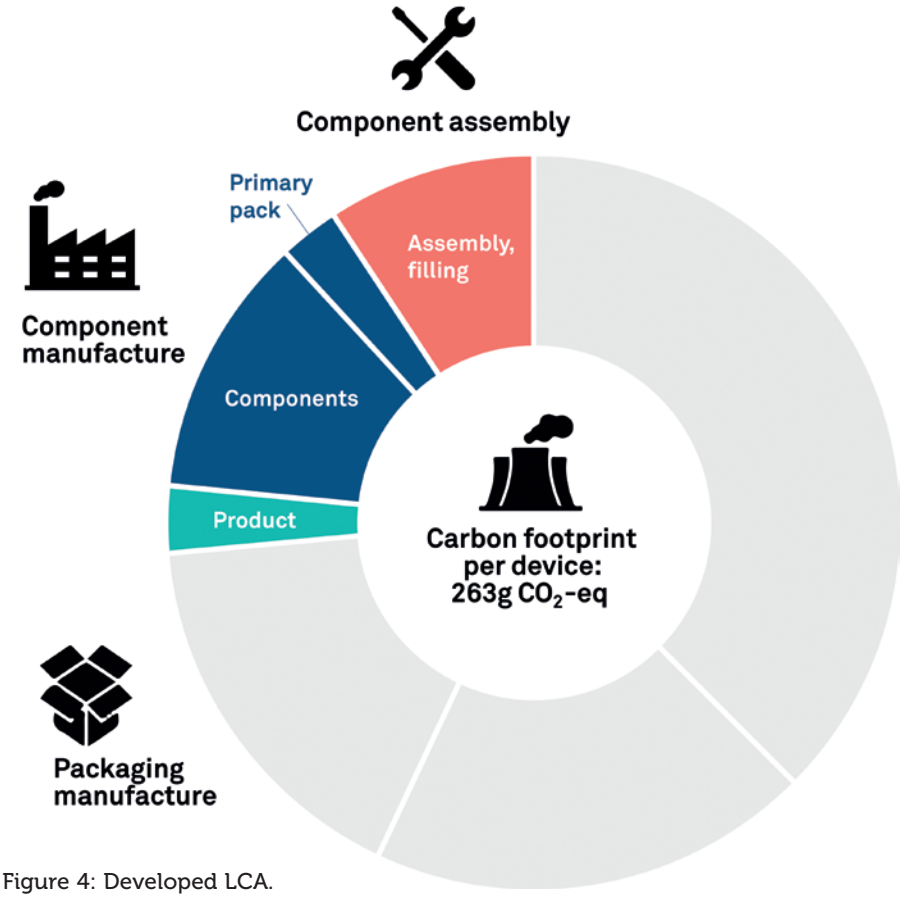

Figure 4: Developed LCA.

"Device developers should also consider decisions that could help improve other carbon-costly factors, such as transit packaging."

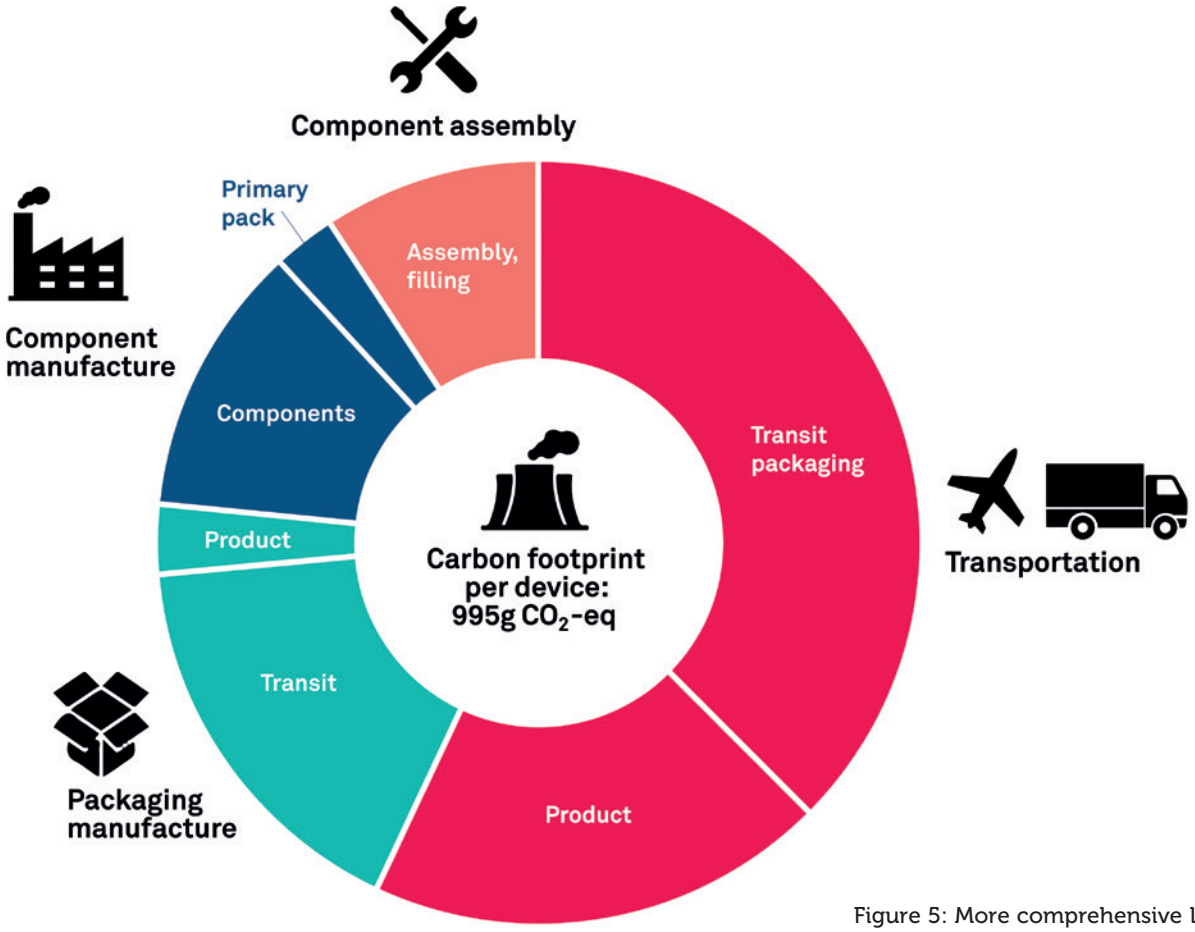

Figure 5: More comprehensive LCA.

A More Comprehensive LCA

Figure 5 shows the results of an LCA that includes shipping and transport during the various stages of device development. While shipping routes and methods vary with each device, it has been assumed that some components and assemblies are made in the Far East and then air freighted to Europe. Other components have been analysed as being made in Europe and transported on the ground via lorries. The carbon footprint of manufacturing the drug has not been included in this assessment. However, the mass of the drug has been factored in as it is transported for assembly. The assessment also does not include shipment to a distribution centre or to consumers, covering transport only to the point it is manufactured and ready to distribute – the final gate. In this example, if the product was assembled in Europe but needed to be distributed in the US, this could add a significant carbon footprint to the overall results.

Within the scope of this LCA, transport makes up almost two-thirds of the product's overall carbon footprint, increasing the total to 995 g CO_2 eq. While air freight makes up a disproportionately large part of this, it is notable that around two-thirds of the transport carbon footprint was produced from transit packaging alone. Clearly, factors such as these should be a priority for device manufacturers to consider.

HOW CAN WE INFLUENCE OUR CARBON FOOTPRINT?

Design Decisions

Some of the common approaches currently being considered around sustainable medical device development focus on the device itself, aiming to minimise or improve the sustainability of the materials used, simplify the device where possible and design for end of life. While these are important steps, device developers should also consider decisions that could help improve other carbon-costly factors, such as transit packaging. For example, if two sub-assemblies are required, they might be nested together to reduce the volume of packaging.

Packaging

In addition to minimising packaging through design choices, more sustainable packaging choices can also be implemented. We are already seeing improvements made in this space, such as reducing the material thickness in thermoformed trays. At scale, this could greatly reduce the manufacturing requirements, material mass and carbon impact of transit packaging.

There is also the potential to reuse packaging. While there are, of course, challenges around this, such as quality management and maintaining cleanliness, integrity and traceability, packaging is still one of the easiest elements within the product lifecycle to reuse without significant energy input.

> "Device developers should be actively questioning suppliers about their sustainable practices and credentials, as well as their plans and targets for the future."

Procurement Decisions

Another factor that can influence environmental impact, particularly for pharmaceutical companies, is who you are

buying from and how you are moving products. Where your supplier is based and how they plan to transport products to your distribution or assembly sites should be an important question when making your procurement decisions. Of course, you may be limited in supplier choice for certain technologies but, where there is a choice, factors such as location, energy efficiency and eco credentials should be considered. Device developers should be actively questioning suppliers about their sustainable practices and credentials, as well as their plans and targets for the future. Procurement groups should also consider the impact of different shipping routes as part of contract negotiations and shipping plans.

SUMMARY

Identifying the carbon footprint of your device development is a complex task. However, it is an important one if we are to truly make changes that will reduce our environmental impact. How you define the scope of your LCA plays a major role in identifying where changes could really add value. As device developers, it is important to consider not just the environmental impacts of manufacturing a device itself but also wider impact factors, such as transit packaging and transport, which often contribute the most carbon footprint. By considering the supply chain from the start of the development and procurement process, as well as making more sustainable design choices, we can begin to enact real positive change.

ABOUT THE COMPANY

Team Consulting is a leading product development consultancy focusing on the pharmaceutical and healthcare industries. The company is an acknowledged expert in drug delivery technology and device development, working with large pharmacos to innovative start-ups across Europe, the US and beyond. Combining expertise and experience in industrial design, engineering and human factors, Team helps its clients to develop medical devices from early concept through to commercial launch. The company is accredited to ISO13485:2016.

ABOUT THE AUTHOR

Alastair Willoughby is Head of Team Consulting's mechanical engineering group as well as lead for its cross-functional sustainability offering, where he works with his team to create robust device designs and conduct sustainability analysis. He is an experienced engineer in the parenteral device space with over 15 years' experience in technical consultancy, having previously worked for Bespak (Cambridge, UK), where he played a significant role in the development of a novel autoinjector technology, taking it from concept through to scale-up. Mr Willoughby has an MEng in Engineering from Cambridge University (UK).

SUSTAINABILITY MEASURES ARE THE KEY TO MEETING ESG COMMITMENTS

In this article, Matthias Birkhoff, Vice-President Business Development, Aptar Pharma, and Christophe Marie, Global Product Sustainability Director, AptarGroup, discuss the advances Aptar Pharma has made in delivering on its sustainability objectives.

Climate change is a challenge that impacts us all. Around 70% of the world economy is now covered by net zero targets,[1] with most companies having some form of climate strategy or commitment in place. However, without a clear focus and meaningful measurement standards, there is a risk that such plans will result only in empty promises and greenwashing. In fact, the NewClimate Institute reviewed the environmental strategies of 25 global companies and found that their climate pledges were often ambiguous and actual emission reduction commitments were limited.[2] Therefore, the question must be how to reach those goals and fulfil what has been agreed.

Overall, one clear and overarching target has been set – 1.5°C. That's the global climate change goal world leaders have agreed to strive for. By limiting the planet's warming to 1.5°C, or 2.7°F, by 2100, the hope is to stave off severe climate disruptions.

It is not just politicians that are driving change; environmental stability is becoming an increasingly high priority for consumers as well. In fact, over the past five years, there has been a 71% rise in online searches for sustainable goods globally, according to the Economist Intelligence Unit.[3] In addition to climate change, consumers have placed more emphasis on how products can be made more sustainable by design and through recycling.

In a 2022 Aptar Pharma survey, conducted with German, French and American participants, 77% of 840 respondents indicated that it was "Important" or "Very Important" that the products they buy can be recycled (Figure 1). In addition, six of 10 respondents noted that they consider the recyclability of products when making purchase decisions. A total of 70% of respondents also said that they were willing to pay more for a product that they could recycle. In summary, these responses clearly demonstrate that public opinion has started to shift towards demanding more sustainability initiatives that protect the environment.

Pharmaceutical drug delivery solution manufacturers, such as Aptar Pharma, must address the calls to address climate change and incorporate other sustainable benefits into their products, all while maintaining patient safety and compliance within a strict

"Pharmaceutical drug delivery solution manufacturers, such as Aptar Pharma, must address the calls to address climate change and incorporate other sustainable benefits into their products, all while maintaining patient safety and compliance within a strict regulatory environment."

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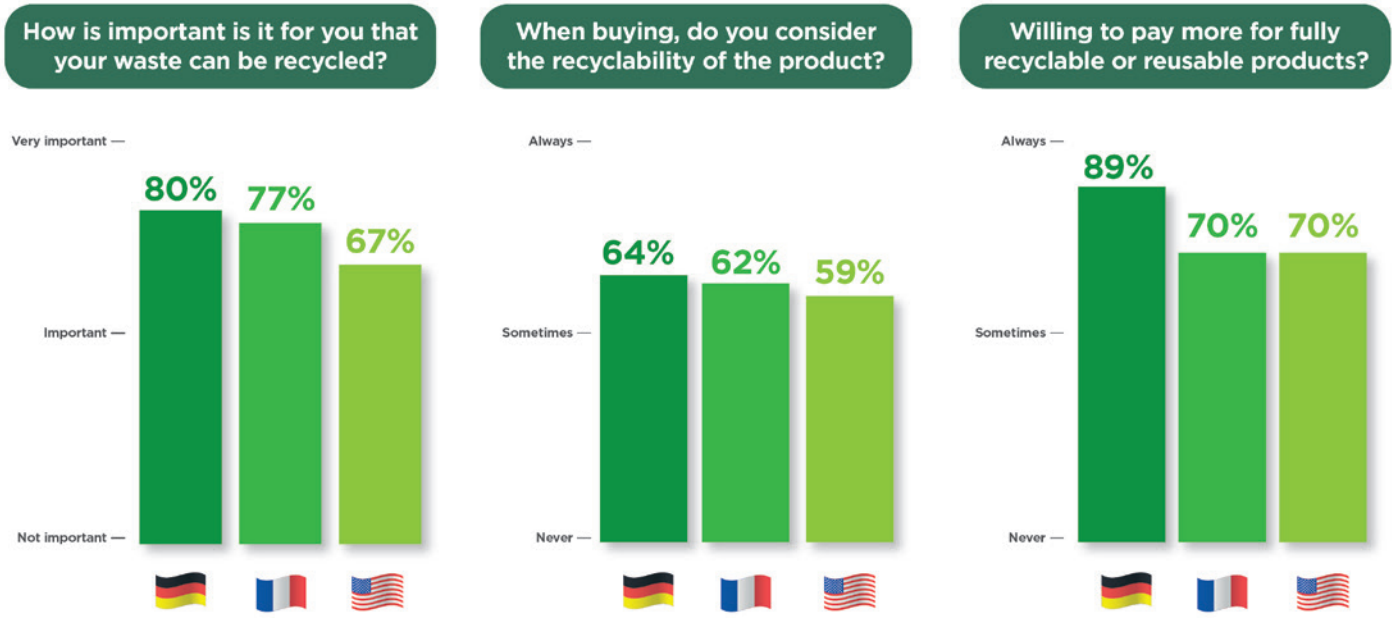


Figure 1: International research on consumer sentiments on recyclability and reusability.

regulatory environment. Interestingly, the pharmaceutical industry appears to be taking on more ambitious objectives than most, committing to a reduction in emissions of 45.8% in 12 years compared with an average target of 44.6% across other industries in the same timeframe.[4]

By all means, the industry has good reasons to be ambitious. In 2018, researchers at McMaster University (Hamilton, Canada) conducted a study of CO_2 emission levels generated by the automotive industry compared with the pharmaceutical industry. The study considered the direct emissions generated by operations and indirect emissions created by the energy purchased by the industry. The researchers found that the pharmaceutical industry generated 52 megatons of CO_2 emissions in one year, compared with 46.5 megatons generated by the automotive industry over the same period.[5] Achieving the goals that the pharmaceutical industry has committed to will require a concerted effort across the entire value chain, as challenges in this highly regulated industry remain increasingly complex. All this requires close study of the current products and an understanding of their environmental impacts, which then allows companies to strategically optimise existing products or design even better new ones.

An immediate action taken by Aptar Pharma to address some of these complex issues has been to change the way it designs its products. As of 2022, Aptar Pharma has committed to design sustainability and circularity into new product development programmes. This could help position the company ahead of today's tightening regulations and contribute to a more sustainable future.

To make new device design more effective, Aptar Pharma has co-developed an eco-design tool with Sphera (Fishburn, UK) that incorporates lifecycle assessment (LCA) perspectives to help design new products that minimise their impact on the environment. Sphera is a leading provider of environmental, social and governance (ESG) performance and risk management software, data and consulting services with operations around the world. The eco-design tool incorporates the assessment of inputs, outputs and the evaluation of a product's environmental impact throughout its entire lifecycle. Calculating the CO_2 footprint, recyclability and circularity are key measures that will help guide Aptar Pharma to design every new or improved drug delivery system to enhance its sustainability performance. The first step towards making progress on product development is often studying existing products more closely.

OPHTHALMIC SQUEEZE DISPENSER COMPARISON

One analysis-worthy example is Aptar Pharma's ophthalmic squeeze dispenser (OSD), a preservative-free multidose eyedropper system. Such eyedropper systems offer a convenient alternative to the single-use vials that are widely used for ophthalmic treatments. By closely studying the OSD's use, properties and how it impacts the environment, it is possible to support better product selection choices between drug delivery options.

Aptar Pharma recently conducted a study that compared its OSD for preservative-free formulations, with single-use blow-fill-seal (BFS) eye drops on a number of sustainability measures. The study compared only the OSD and BFS formats of a specific commercially available eye-care product, allowing for a direct comparison. Due to the complexity of the entire product lifecycle, Aptar Pharma focused on three measures for the same dosing regimen: plastic waste, CO_2 impact and formulation waste volumes. This study did not assess additional factors, such as energy consumption in manufacturing, resin transportation and other factors in its calculations, on the assumption that these other aspects would be largely net comparable on a global warming potential (GWP) basis and for simplicity of comparison.

Plastic Material Reduction With Aptar Pharma's OSD

A single multidose OSD unit typically contains 10 mL of formulation liquid. A typical selling unit for single-use BFS vials would include 20 ampoules of 0.3 mL fill volume each (for a total formulation volume of 6 mL). To perform a meaningful analysis of equivalent plastic material use, the impact of formulation waste and CO_2 on the data must first be normalised.

A single OSD unit containing 10 mL of formulation weighs 6.2 g. The same 10 mL of formulation packaged into single-use BFS plastic vials requires just over 33 vials, which would weigh 37.2 g. The majority of this weight is attributable to the plastic vial materials.

"At this scale and by this measure, 100,000 OSDs would save more than 8,000 kg of CO_2 over the BFS format, which is the equivalent amount of CO_2 generated by more than five round-trip flights between Paris, France, and Beijing, China."

Therefore, 10 mL of an eye-care medication packed in BFS vials uses five times more primary packaging material than the same formulation volume packaged in an OSD multidose eyedropper. Because of this sizeable weight difference and based on Aptar Pharma's LCA calculations (made with Aptar Pharma's eco-design LCA tool, no third-party review was conducted and secondary packaging/cartonnage were not considered), this translates into a CO_2 impact for the OSD that is six times lower than that of the BFS equivalents.

By extension, at a commercial scale, based on comparable 10 mL fill volumes, 100,000 of Aptar Pharma's OSD devices are equivalent to 3.3 million BFS single-use vials (1 OSD: 33 BFS). At this scale and by this measure, 100,000 OSDs would save more than 8,000 kg of CO_2 over the BFS format (Figure 2), which is the equivalent amount of CO_2 generated by more than five round-trip flights between Paris, France, and Beijing, China (82,000+ km total distance).[6] This demonstrated reduction in primary packaging materials using the OSD option also translates into reduced pack sizes, which reduces the number of pallets and shipping volume needed to ship the product, which will also result in reduced carbon emissions generated through the transportation process.

Minimising Formulation Waste With Aptar Pharma's OSD

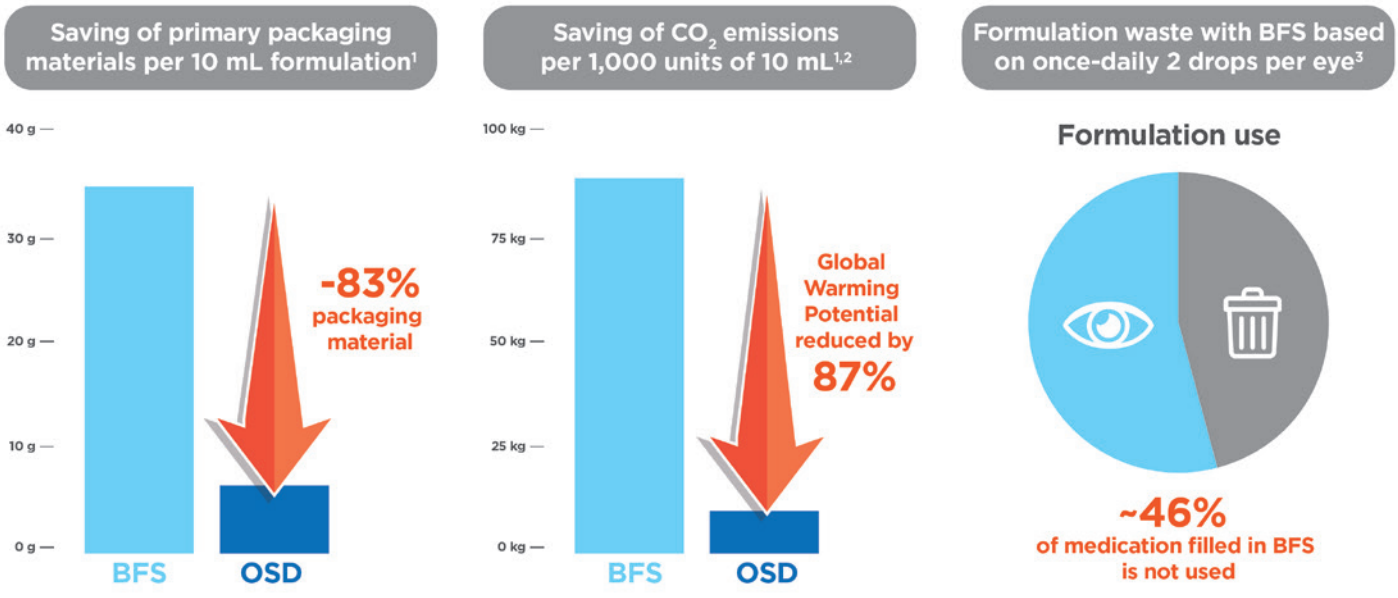
Aptar Pharma also assessed the difference in the amount of formulation solution wasted with both packaging options. It found that OSD devices provide environmental advantages over BFS with respect to minimising formulation waste. A typical dosing regimen for an eye condition could be two drops per eye per day, for as long as 60 days, which was the model for this comparison. A typical drop size volume for either eye-drop dispenser type would be approximately 40 µL per drop. Therefore, patients would use 160 µL of formulation delivered as drops per day, for a total of 9.6 mL used over the course of the entire 60-day treatment.

One major difference between OSD and BFS vials is that each BFS vial must be discarded immediately after opening and administration because the BFS vial cannot maintain formulation sterility or protect against contamination. Each BFS vial is filled to 300 µL, with 140 µL of formulation discarded as waste from each vial (Figure 2). Aptar Pharma's OSD device deploys a mechanical tip seal to protect the contents of the multi-use unit from external contamination and can safely administer 250 doses from a single unit with a single 10 mL fill.

As BFS vials are sold in selling units of 20 vials, the patient would need to purchase three selling units, or 60 vials, to complete a 60-day treatment course, whereas with the OSD, only one dropper bottle would be required to complete the entire treatment. Additionally, the OSD has a high-evacuation rate, delivering virtually all its 10 mL fill volume without waste.

Therefore, over the course of the 60-day treatment regimen, the BFS vials would result in 140 µL per vial, a total of 8.4 mL, of formulation solution being discarded as waste, whereas virtually none (1–5 µL) of the formulation would be wasted from the single OSD device. When scaled to 100,000 OSD units (which is equivalent to 3.3 million BFS vials), the total additional formulation waste volume produced by BFS vials is more than 460 L of formulation solution.

A single OSD device with 10 mL fill provides access to 67% more formulation and three times the treatment duration per selling unit compared with BFS vials (20 vials per package). In terms of the primary packaging materials, the treatment course requires 60 BFS vials versus a single OSD device, and almost 10 times more packaging material is consumed through the BFS packaging option. In summary,



1) All calculations have been made with Aptar's EcoDesign LCA tool. No third party review was conducted. Secondary packaging/cartonage has not been considered in this approach.
2) 1,000 units of 10 mL stands for 1,000 packaging units used for 10 mL eye drops, i.e. 1,000 OSDs compare to appr. 33,333 BFS single-use vials.
3) Daily dosing scheme: 2 drops per eye at a drop size of 30–40 µL. BFS vials are filled with 300 µL formulation each, as a consequence at least 140 µL per vial are not used.

Figure 2: Comparison of packaging material waste, CO_2 emissions and formulation waste between Aptar Pharma OSD and BFS single-use vials.

Aptar Pharma's multidose OSD eye-drop device provides substantial savings in plastic and formulation waste, as well as a reduced CO_2 footprint, based on Aptar Pharma's comparative analysis.

This OSD comparison serves as a strong example of how much can be done to reduce environmental damage through the data-driven selection of a device option that meets the same drug delivery requirements but reduces waste and increases efficiency. Imagine how much more can be done now that Aptar Pharma has dedicated itself to optimising existing devices and designing all new devices with sustainability and circularity objectives as primary drivers. The company has successfully implemented these types of initiatives with a range of different product lines towards meeting Aptar Pharma's broader long-term environmental objectives. The following are some examples of how Aptar Pharma has been successful in optimising its existing products or services, and how it has started to design circularity and sustainability into the new devices it makes.

pMDIs AND SUSTAINABLE PROPELLANTS

Propellants used in medical devices have come under new and tighter regulations designed to reduce their environmental and GWP impact. Aptar Pharma recognised some time ago that propellants presented a problem that needed to be addressed. As a result, it engaged in supporting its clients who were researching new propellant options that are suitable for Aptar Pharma's pressurised metered dose inhaler (pMDI) devices and would reduce the overall GWP. Companies are targeting the reduction of commonly used propellants, such as hydrofluoroalkanes (HFAs) and hydrofluorocarbons (HFCs), by 85% by 2047, as they have been designated as restricted materials in the Kigali Amendment (2016) to the Montreal Protocol. The challenge with introducing new propellants is that both patient safety and functional drug delivery aspects must be proven in studies before existing products can be converted to using a new propellant.

HFA-152a and HFO-1234ze have been identified as two potential propellants with a considerably lower GWP and are therefore currently under assessment at Aptar Pharma. HFA-152a has undergone extensive study, including full inhalation toxicology studies, and has shown strong results with no adverse findings to date. By replacing the current propellant, HFA-134a, with HFA-152a, there is the potential to reduce climate change and global warming impacts of inhalers in the UK by 90%–92%, according to a study by the University of Manchester (UK). HFO-1234ze has the potential to deliver an even greater GWP reduction of 99%, but safety and toxicology data available in the public domain are currently limited. Aptar Pharma remains committed to supporting its customers with a range of services to help de-risk and accelerate their low GWP pMDI programmes, including the optimisation of a new metering valve technology platform that demonstrates improved chemical and functional compatibility with both HFA-152a and HFO-1234ze propellants.

RECYCLABLE SYSTEMS BY DESIGN

Historically, recyclability was not a primary consideration in the development of drug delivery devices. The primary focus was always to create devices that reliably and safely delivered the required drug dosages to the patient with convenience. Today, those functional parameters are still just as important but now improving the recyclability of the devices during the design stage has taken on significantly more importance.

> "This drive to improve Aptar Pharma's devices through innovative design for recyclability has led to favourable ratings from cyclos-HTP for a number of its systems."

This drive to improve Aptar Pharma's devices through innovative design for recyclability has led to favourable ratings from cyclos-HTP (Aachen, Germany) for a number of its systems. These recyclability improvements include designing mono-material systems that enable simple and complete recycling of devices without compromising functionality or safety. Aptar Pharma has also shifted to using medical-grade source materials for pharmaceutical applications that support recycling capabilities. Higher levels of recyclability can also be achieved by eliminating harder-to-recycle device component materials, such as metals, so that the entire device can be recycled without significant intervention. Aptar Pharma has looked at a variety of ways to enhance the recyclability of its products and invested in making these opportunities a reality across a number of its product lines.

The Recyclable Nasal Spray Pump

Aptar Pharma is currently developing a new recyclable nasal spray pump that incorporates a mechanical tip seal feature for preservative-free multidose formulations. Any metal components of the spray mechanism have been removed, and the innovative technical design is based on plastic components only. The full plastic spray pump thereby achieves very high recyclability ratings and is specifically designed for use with nasal saline or comparable formulations.

Proventu Mono-Material Tube Systems

Aptar Pharma has developed its first mono-material tube system, called Proventu, which was designed to meet pharma product standards using an eco-design approach. All device components are made entirely of medical-grade polypropylene, enhancing the recyclability of the system to full recyclability. The mono-material device can be placed directly into existing recycling streams when emptied after use. This is just one example of Aptar Pharma's drive to implement mono-material system designs to enhance the recyclability of its products and have a positive impact on the environment.

Rated for Recyclability

Aptar Pharma's Airless+ dermal drug delivery systems use the company's eco-design tools to meet the tightened US Pharmacopeia <661> regulations, excluding metal parts and using medical-grade resins. The Airless+ system efficiently dispenses its dermal formulation leaving only minimal volumes when fully used, making the device easy to recycle directly in existing recycling streams without further preparation. It achieved a "Class AAA" with an "excellent recyclability" rate of 96%–98% as rated by cyclos-HTP.

Aptar Pharma's bag-on-valve (BOV) continuous dispensing systems are another example of designing recyclability into the device. The BOV system can include recyclable aluminium, removable actuators and offers high product evacuation rates making them easily recyclable. Designed to use compressed air/nitrogen propellant systems, they reduce greenhouse gas emissions compared with other

Figure 3: Overview of Aptar Pharma's product solutions, supporting sustainability targets in drug delivery.

common propellants found in similar applications. The BOV systems achieved a "good recyclability" rating (Class A) of the raw packaging assembly from cyclos-HTP.

Both these examples demonstrate the importance of designing recyclability into devices from the start. This enables the device to be easily recycled and reduces the environmental impact of the product across its entire lifecycle.

THE IMPORTANCE OF MASS BALANCE

Aptar Pharma has also taken more holistic approaches to reduce its carbon footprint in a sustainable and responsible way. Aptar Pharma has successfully begun to implement a mass-balance accounting system to increase the use of more sustainable inputs, such as bio- or circular feedstocks, that could reduce its CO_2

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Matthias Birkhoff is Vice-President Business Development at Aptar Pharma. In this role, he is responsible for Aptar Pharma's Eye Care programme and co-ordinates research and development activities, microbiological assessment and commercial strategies. Before joining Aptar Pharma in 1998, Mr Birkhoff began his career in pharmaceutical sales at a major multinational pharma company. Prior to his roles in business development and marketing at Aptar Pharma, he was responsible for sales in the Asia-Pacific region. He studied medicine at the University of Dusseldorf (Germany) and holds a nursing degree.

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

footprint. Aptar Pharma has already implemented mass-balance systems at some of its sites.

Mass balance is a system designed to document and track the flow of materials through the value chain, including the amount and sustainability characteristics of circular and/or bio-based content in products. This approach gives Aptar Pharma control over material composition and supports claims about device material composition through the associated documentation and records. Several Aptar Pharma production sites have implemented a mass-balance system and achieved ISCC certification,[7] allowing them to incorporate renewable feedstocks into production. A mass-balance system allows a company to maintain better data regarding material flows and allows for more flexibility around controlling feedstock profiles, producing more sustainable products. Aptar Pharma is expanding the mass-balance approach and ISCC certification to additional sites across its network to achieve even greater sustainability improvements.

> "Aptar Pharma has successfully begun to implement a mass-balance accounting system to increase the use of more sustainable inputs, such as bio- or circular feedstocks, that could reduce its CO_2 footprint."

CONCLUSION

Aptar Pharma has successfully developed drug delivery systems that reduce raw material and plastic waste, offer enhanced recyclability, reduced or replaced inputs and minimised formulation waste. It has also successfully instituted new systems and philosophies, such as mass balance and the circular economy across its business that will enable the company to measure and improve on the successful achievements of its environmental objectives to date (Figure 3). As a market leader in pharmaceutical drug delivery systems, Aptar Pharma has demonstrated that a company-wide strategic effort can quickly produce positive results for the environment. Its commitment to the environment is long term and there is still much more to do. Aptar Pharma will continue advancing its sustainability objectives while maintaining the highest standards of quality and functionality for its products and services, ultimately enabling patients around the world to achieve better and healthier lives.

Aptar Pharma strives to maintain industry leadership in pharmaceutical drug delivery technologies while also taking an emerging leadership position in the industry for its environmental and sustainability efforts. What could be more important than improving people's health and the planet we all share together?

ABOUT THE COMPANY

For pharma customers worldwide, Aptar Pharma is the go-to drug delivery expert, from formulation to patient, providing innovative drug delivery systems, components and active material solutions across the widest range of delivery routes, including nasal, pulmonary, ophthalmic, dermal and injectables. Aptar Pharma Services provides early-stage to commercialisation support to accelerate and de-risk the development journey. With a strong focus on innovation, Aptar Digital Health is leading the way in developing digital health solutions to help improve the patient treatment experience. With a global manufacturing footprint of 14 manufacturing sites, Aptar Pharma provides security of supply and local support to customers. Aptar Pharma is part of AptarGroup, Inc.

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

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

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

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

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

A journey of a thousand miles begins with a single step. To find out how Aptar can help you on your sustainability journey, to learn more about our initiatives and to read our 2021 Corporate Sustainability Report, visit **www.aptar.com/esg/reporting-center/sustainability-reports**

Delivering solutions, shaping the future.

Aptar pharma

CONSIDERING THE SUSTAINABILITY IMPACT OF CONNECTED INHALERS IN THE TREATMENT OF ASTHMA

Here, Iain Simpson, PhD, Director, Front-End Innovation, Phillips-Medisize, and Vinith Bhandari, Graduate student from the University of Cambridge, consider the sustainability impact of device connectivity specific to asthma inhalers through the reduction of greenhouse gas emissions.

In recent years, there has been increasing interest in the use of electronic drug delivery devices, based on the belief that these devices can offer patients the benefits of personalisation and ease of use. Furthermore, the use of electronics enables drug delivery devices to connect to smart devices and the internet, allowing data to be shared with other stakeholders in the healthcare ecosystem. This can enable remote monitoring, especially around measuring and improving medication adherence, as well as supporting better and more integrated disease management.[1]

> "The shift from single-use disposable devices to electronic, reusable devices can have a positive impact for both sustainability and the patient experience."

However, at the same time, global concerns around sustainability have impacted nearly every industry, and healthcare is no exception. At first, the addition of electronics might appear counterintuitive to sustainability objectives. However, the shift from single-use disposable devices to electronic, reusable devices can have a positive impact for both sustainability and the patient experience.[2]

This article explores whether device connectivity specific to inhalers used to treat asthma can positively impact overall sustainability by reducing greenhouse gas (GHG) emissions, on the basis it might reduce consumption in other parts of the healthcare system.[3] The work presented in this article is the result of a research project conducted by Vinith Bhandari, as part of an MPhil in Therapeutic Sciences at the University of Cambridge and supported by Phillips-Medisize, a Molex company.[4]

Initial research established that, while relatively limited research has been published on reducing the environmental impact of chronic disease treatments, significant work has been done on asthma, especially by the UK NHS. The data are available to understand in detail how different aspects of the treatment pathway impact the associated GHG emissions. With the introduction of smart connected inhalers, such as Digihaler® by Teva (Tel Aviv, Israel), and connected add-on sensors, such as those provided by Propeller Health (WI, US), there is an opportunity to consider how technology can support more sustainable healthcare pathways for the disease. As a result, research has focused on asthma and connected inhalers. This article also considers how the approach might be applied to other disease areas.

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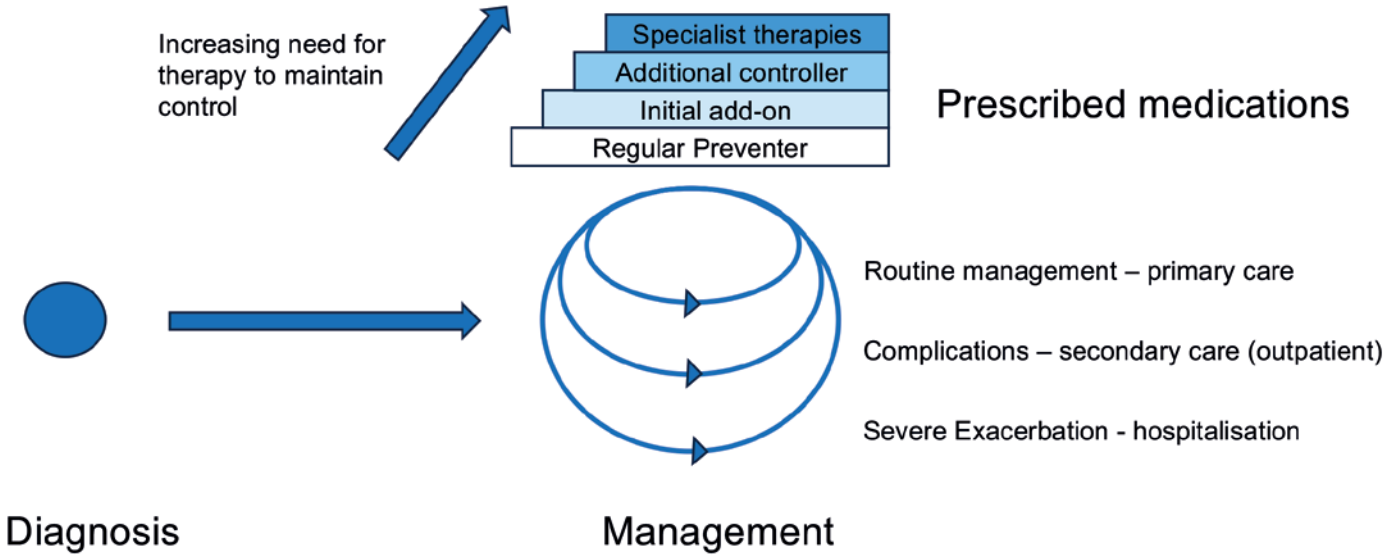

Figure 1: Simplified pathway for the diagnosis and management of asthma.

"A key objective in asthma management is to minimise the amount of medication required to achieve adequate asthma control."

ASSESSING IMPACT OF CONNECTED INHALERS ON THE TREATMENT OF ASTHMA

Nearly 8 million people in the UK have been diagnosed with asthma (around 12% of the total population), with about 5.4 million receiving asthma treatment, according to the British Lung Foundation, as of 2018. Annually, about 160,000 people are diagnosed with the disorder in the UK, accounting for about 2%–3% of all primary care consultations.[5] Most cases of asthma (~85%) in the UK are managed in the primary care system, but complications can result in increased medication use and the need for hospital treatment, often in the form of emergency admissions. Asthma is one of the most significant drivers for the NHS in terms of cost and demand on resources. It is estimated that 46% of asthma deaths could be avoided with better routine care.[6] In fact, the total number of deaths in England and Wales from asthma in 2017 was reported to be 1,320.[7]

Figure 1 shows a simplified pathway for the diagnosis and management of asthma. Asthma in the UK is principally managed in primary care, involving general practitioner (GP) visits and prescriptions. Patients who have difficulty in managing their disease in this way may be referred to secondary care for consultations and training. Failure to manage the disease may result in more severe exacerbations that can result in emergency and inpatient hospital care. In terms of medication, inhaled therapy is the standard treatment option for patients with asthma and chronic obstructive pulmonary disease (COPD). Pressurised metered inhalers (pMDIs) are the most commonly used inhaler type, although dry powder and soft mist devices are also in use.

A key objective in asthma management is to minimise the amount of medication required to achieve adequate asthma control. There are two main types of inhaled medicines; preventers, which are regularly taken prophylactically to control asthma, reducing the risk of an acute attack; and relievers, which are used when a patient is experiencing asthma symptoms. A key issue in asthma disease management is that patients tend to be non-adherent to preventer use, leading to an overdependence on reliever treatments.[8] As discussed later in this article, this has an adverse impact on associated GHG emissions as well as on effective disease management.

The compressed propellants, usually hydrofluorocarbons (HFCs), that are used to expel the drug from pMDIs are considered to be GHGs and account for approximately 3% of the NHS carbon footprint (and 13% within primary care).[9] Chlorofluorocarbons (CFCs) have already been replaced by HFCs, but HFCs are also expected to be phased out eventually. Recent National Institute for Health and Care Excellence's guidance recognises that sustainability should be considered when selecting which type of inhaler to use and further understands that greater use of other inhaler types could reduce emissions.[10] However, there are trade-offs around cost and availability of the formulations in alternative formats that must be considered.

Another impact on associated GHG emissions is the number of hospitalisations associated with asthma. Between 2008 and 2012, there were around 60,000 admissions and a total of 200,000 bed days of care related to asthma annually, of which around 70% were considered avoidable.[11] This additional care adds significantly to costs and GHG emissions and is considered an undesirable healthcare outcome.

THE ROLE OF CONNECTED HEALTH IN ASTHMA MANAGEMENT

Digital services using connected smart inhaler devices have the potential to improve the management of asthma. Results from pilot studies have shown positive outcomes. For example:

- Propeller Health reported an 18.5% reduction in the use of reliever therapy for an intervention group using its connected device technology compared with a control group.[12]
- In an electronic adherence monitoring study in children with asthma, a sustained improvement in adherence rates (70% compared with 49% in the control group) was seen, leading to a decrease in hospitalisations.[13]

- Other studies have also shown that high adherence can cause a significant reduction in hospitalisations – up to 39.5%.[14,15]
- Research using machine learning has shown that it is possible to predict exacerbations based on data recorded in a daily patient asthma diary.[16]
- Increased use of reliever therapy (something that could be monitored using smart devices) has also been associated with increased exacerbation risk.[17]

However, larger systematic reviews have shown less promising results, according to an analysis of several studies on adherence interventions, including patient education, reminders, simplified dosing and counselling.[18,19] These reviews found that, although some interventions had a positive effect on adherence and outcomes, no single strategy demonstrated improvement in all settings. More work is certainly required to fulfil the potential of connected health in asthma treatment, but it seems likely that the introduction of optimised digital solutions can positively impact outcomes with a reduction in reliever therapies and hospitalisations.

RESEARCH METHODOLOGY

Two main steps were used in this study to consider how connected health might reduce the GHG emissions associated with asthma disease management. First, the GHG emissions associated with traditional asthma treatment in the UK were estimated. Then it was considered how a connected health intervention might influence the care pathway, which could reduce GHG emissions. To estimate the sustainability

	Unit of measurement	GHG emissions (kg CO_2e)	Fresh water use – direct (m^3)	Fresh water use – indirect (m^3)	Waste generated (kg)
GP consultation	Per consultation	1.10	0.01	2.27	0.19
Patient travel					
Self – to GP	Per single trip	0.56	0.00	0.10	0.00
Self – to elective care	Per single trip	2.90	0.00	0.53	0.00
Provided – non-emergency	Per single trip	7.90	0.01	25.80	0.13
Provided – emergency	Per single trip	36.00	0.03	91.20	0.53
Emergency department	Per day	14.00	0.11	20.80	0.29
Inpatient admission					
Low intensity	Per day	37.90	0.24	0.56	3.30
High intensity	Per day	89.50	0.96	2.90	13.00
Self-management					
Patient education session	Per session	1.60	–	–	–
Pharmaceuticals					
pMDIs	Per inhaler	24.0			
New inhalers	Per inhaler	10.0			

Table 1: The impact of parts of the care pathway and types of medication on GHG emissions.[21]

	Number of events/uses in UK (1,000s)	GHG emissions (tonne Co_2e)	Fresh water use – direct (m^3)	Fresh water use – indirect (m^3)	Waste generated (tonne)
GP consultation	75,000	8,250.0	42,000	17,025,000	1,425
Patient travel					
Self – to GP	75,000	42,00.0	0	750,000	0
Self – to elective care	160	464.0	0	84,800	0
Provided non-emergency	60	474.0	432	1,548,000	7.8
Provided emergency	31.2	1,123.2	936	2,845,440	16.5
Emergency department	31.2	436.8	3,432	648,960	9.0
Inpatient admission					
Low intensity	93	3,524.7	22,320	5,635,800	306.9
High intensity	1.8	161.1	1,728	245,880	23.4
Self-management					
Patient education session	500	800.0	–	–	10
TOTAL CARE PATHWAY		**19,433.8**	**70,848.0**	**28,783,880.0**	**1,798,684.0**
Pharmaceuticals					
MDIs	3,600	86,400.0			
New inhalers	1,800	1,800.0			
TOTAL PHARMACEUTICALS		**88,200.0**			
TOTAL		**107,633.8**	**70,848**	**28,783,880**	**1,798,684**

Table 2: NHS and other published data used to estimate the impact of the care pathways and medication use for the UK population.[21]

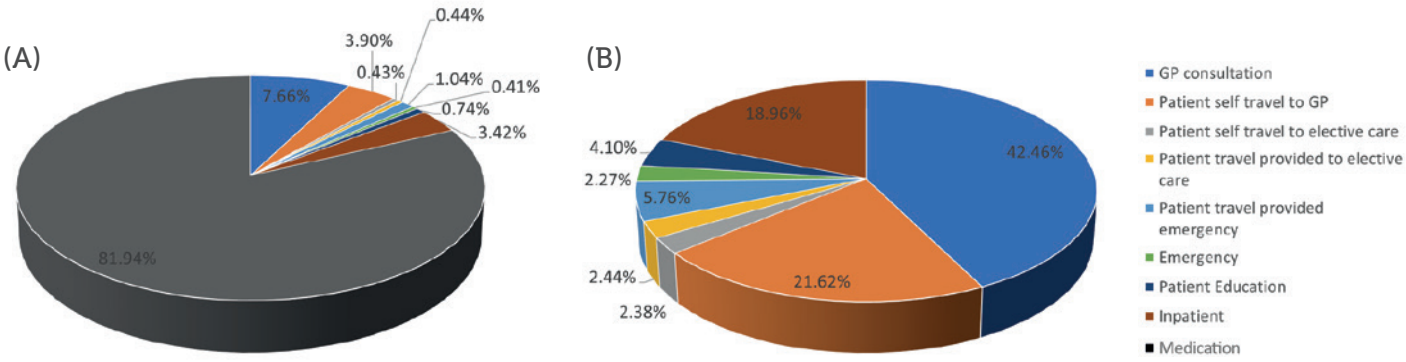

Figure 2: GHG emissions associated with the treatment asthma.

impact of asthma treatment, a model was built based on associated guidance provided by the Sustainable Healthcare Coalition (SHC).[20] The model estimates the environmental impact of a care pathway in terms of GHG emissions, freshwater use (direct and indirect) and waste generation. The following care pathway modules are considered: GP visits, emergency department visits, self-management, travel by patient, and inpatient admission and bed days of care.

Using data from the SHC model, Table 1 shows the impact of parts of the care pathway and the medication GHG emissions, water usage and waste production. NHS and other published data were then used to estimate the impact of the care pathways and medication use for the UK population. These data are presented in Table 2. It was then considered how a digital intervention using a smart connected inhaler device might reduce this impact by considering two scenarios: the reduction in the use of reliever medication through digitally mediated support and the reduction in the number of hospitalisations due to better patient support and the prediction of exacerbations using digital technologies.

RESULTS

Figure 2 shows the GHG emissions associated with the treatment of asthma in the UK. Figure 2a includes the contribution from the medication whereas Figure 2b focuses on the non-drug aspects of asthma care. As the data show, the overall impact on sustainability is dominated by the medication, which is to be expected given the high levels of pMDIs use in the UK. Pernigotti *et al* (2021) analysed the carbon footprint of inhalers in five different European countries, including the UK, and estimated that, by switching to switching to pMDIs using propellants with lower global warming potential or DPIs, and also considering device recycling, reductions in GHG emissions of up to 90% could be achieved.[21] Much of this sustainability gain would be achieved through use of these inhalers and is more about inhaler design and supply rather than an opportunity for a connected health intervention. However, they also considered improvements in clinical practice that could reduce the usage of reliever inhalers by switching to other inhaler types and estimated that these could reduce carbon dioxide equivalent (CO_2e) emissions by around 48%. In this case, a digital service that monitors inhaler usage and provides feedback and support could help this change in practice and claim some of this saving in emissions.

Focusing on Figure 2b and the care pathway without considering drug use, the potential to reduce hospitalisations through better disease and medication management was considered. This could be potentially mediated by a digital service that provides training support and early warning of exacerbations that might lead to hospitalisation by, for example, monitoring for increased reliever use. If it is assumed that a supporting digital service can help eliminate 60% of the potentially preventable hospitalisations, then the data in Table 3 show that around 12% of the total GHG emissions

	Current Practice		Future Practice (with connected health intervention)	
	Number of events/ uses in UK (1,000s)	GHG emissions (tonne Co_2e)	Number of events/ uses in UK (1,000s)	New GHG emissions (tonne Co_2e)
GP consultation	75,000	8,250.0	75,000	8,250.0
Patient travel				
Self – to GP	75,000	4,200.0	7,500.0	4,200.0
Self – to elective care	160	464.0	160.0	464.0
Provided – non-emergency	60	474.0	600.0	474.0
Provided – emergency	31.2	1,123.2	17.2	617.8
Emergency department	31.2	436.8	17.2	240.2
Inpatient admission				
Low intensity	93	3,524.7	51.2	1,938.6
High intensity	1.8	161.1	1.0	88.6
Self-management				
Patient education session	500	800.0	500.0	800.0
TOTAL CARE PATHWAY		**19,433.8**		**17,073.2**

Table 3: Total GHG emissions associated with the care pathways for current practice and proposed future practice.[21]

associated with the care pathway could be eliminated. Looking at other contributions, GP consultations (including associated patient travel) account for around two-thirds of the impact on the care pathway (excluding medicines). A digital service that allows remote monitoring and support could potentially reduce the carbon emissions from GP visits (both from the patient travel and possibly some of the consultation).

Van der Kamp *et al* (2020) have argued that experience of asthma management during the covid-19 pandemic can support the development of multi-modal eHealth platform technologies with the possibility that it could be adapted to the needs of specific healthcare systems, providing more personalised healthcare.[22] However, there have also been concerns that a lack of face-to-face contact with healthcare professionals could increase complications and a feeling of isolation, so such systems should not preclude face-to-face contact where it is preferred.

CONCLUSIONS

This study has demonstrated the opportunity for connected inhalers to have a positive impact on reducing GHG emissions in the treatment of asthma. It has also shown how they can potentially support a transition towards more sustainable medications.

There are limitations to the work: a full lifecycle analysis to consider the increased impact of a smart inhaler due to on-board electronics and off-device systems required to provide a connected health service was not conducted. However, previous work on the sustainability of smart autoinjectors suggests that these impacts can be reduced by a move from disposable to reusable devices.[1] Although inhalers tend to be multi-use, fully disposable devices, the industry is now seeing alternatives, such as the Boehringer Respimat® soft mist inhaler, offering versions that are refillable, along with devices such as Turbuhaler®, marketed by AstraZeneca, that allow the connectivity module to be transferred between disposable devices. Although further research would need to be conducted to fully demonstrate this hypothesis, the impact of the device contribution can be minimised compared with the potential benefits that it can offer.

No consideration was given to the ability of a companion connected health service to bring about the behaviour changes required to avoid excessive use of reliever medicine or to take action before a loss of treatment control leads to hospitalisation. But progress in these areas is being made and, eventually, the promising results from small studies will be scaled to larger real world populations.

In terms of the sustainability of drug-based interventions, asthma may be an outlier due to the GHG emissions associated with the pMDIs that are commonly used to treat the condition, resulting in a drug delivery system contribution that accounts for more than 80% of the total emissions associated with its treatment. Other than some telemedicine publications, little published data was found around the use of connected health to improve the sustainability of other disease treatment practices. Although GHG emissions associated with other medications are expected to be much lower, cardiovascular and psychiatric diseases, such as schizophrenia, are good examples where poor medication adherence can result in lengthy hospitalisations. As such, it is expected that the use of connected health can be extended to address both sustainability and healthcare outcomes. Fortunately, in many situations, better sustainability will be correlated with better healthcare outcomes so that their value to society is aligned and additive. It is also worth considering that digital therapeutics can avoid the use of chemicals to make prescription drugs, so this factor might also have a positive impact on sustainability.

It is hoped that this research will motivate others to explore in more detail how connected health can contribute to lower GHG emissions, as well as improving healthcare efficiency, patient experience and clinical outcomes.

ABOUT THE COMPANY

Phillips-Medisize, a Molex company, helps clients get from concept to care quickly while reducing the inherent risks of any new product journey. The company acts as a singular resource for its clients, offering robust end-to-end capabilities, including drug delivery device platforms. For over 60 years, pharma, diagnostic and medtech companies have trusted Phillips-Medisize to deliver quality products that help people live healthier lives.

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MAKING SUSTAINABILITY BY DESIGN
THE LINTEL OF SUSTAINABLE INHALER DEVELOPMENT

Here, Phil Seeney, Drug Delivery Specialist, Philip Winkworth, PhD, Technology Strategy Expert, and Craig Nelson, Consumer Products Specialist, all at PA Consulting, provide an insight into sustainability developments in the pharmaceutical industry.

Climate change and sustainability have become important drivers for much of what we do in our daily lives and in selecting the products we, as consumers, use. Government policy, international legislation and company strategies all attempt to address the sustainability challenge. Products such as medical devices, including inhalers, are no exception, with recent regulatory and advisory guidelines driving change, including:

- Targets/policies emerging in healthcare systems, such as UK NHS England targets[1] encouraging a switch to more environmentally friendly alternatives
- Earlier, similar guidance from NICE,[2] the MHRA consultation on new future device regulation looking at sustainability[3], and the emergence of the Sustainable Medicines Partnership[4] also encourage change

While currently there is no definitive "environmental" legislation that covers inhalers and other medical devices, we can anticipate it will not be long before legislation drives change or economics force change via national and supranational bodies, whose policies will impact the costs of material supply and demand (thereby cost). We have seen moves like these before, with the Montreal Protocol[5] limiting the use of chlorofluorocarbons (CFCs), which led to significantly increased costs for CFCs and, ultimately, a forced move by pharma to hydrofluoroalkanes (HFAs) across the industry.[6] With new legislation to protect the environment appearing inevitable, the impact can be limited by considering the apocryphal Benjamin Franklin saying, "By failing to prepare you are preparing to fail." Acting early will become paramount to achieve a commercial and sustainable advantage or, indeed, to survive.

> "The pharmaceutical industry is currently addressing the sustainability issue with a range of initiatives ahead of actual legislation being in place."

The pharmaceutical industry is currently addressing the sustainability issue with a range of initiatives ahead of actual legislation being in place, and this can be demonstrated by companies such as Chiesi, GSK, AstraZeneca, Takeda, Novo Nordisk and Merck & Co investigating and analysing their

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sustainability profiles and environmental impact at a company, supplier and product level.[7] This article mainly considers devices and their manufacture. However, it is increasingly seen that pharma companies are taking an even wider holistic approach to include the sustainability aspect of the manufacture and supply of the drug product (which, although not addressed here, follows similar principles of assessment).

Inhalers and inhaled products are nominally very small contributors to the overall climate budget (0.05% of all greenhouse gas emissions)[8] but significant in the specific sustainability picture for suppliers (e.g. GSK – 32% of its carbon footprint)[8] and healthcare providers like the NHS (4% of the entire NHS carbon footprint).[6,9]

Current inhalers present a number of issues from an environmental perspective, including the propellants used in pressurised metered dose inhalers (pMDIs) and the polymers used in dry powder inhaler (DPI) products, both of which are disposed of after a month of use. Inhalers, with their long-established design and delivery of essential therapeutics, represent a challenge for achieving sustainability targets. With the pressures from national policy, internally and from the wider public, a pre-emptive and rapid move towards more sustainable devices would seem prudent before legislation potentially enforces it on the wider landscape and potentially unprepared suppliers. However, there is not a universal inhaler that suits every patient and not all drugs are available in every type of inhaler in use. Inhalers do, therefore, present a distinct challenge here, given their current varied design(s) and the options available to prescribers.

> "Companies will be challenged to deliver not only better healthcare to patients but also healthier solutions for the planet."

A number of recycling schemes and initiatives have been piloted in the past with little benefit and the NHS has no plans for a national recycling scheme.[10] However, to encourage the move to a more sustainable future, there is clearly a need (and therefore an opportunity) to make a more fundamental change – a core change in culture – by designing new devices to better enable recycling and address the needs of patients and the planet. Companies will be challenged to deliver not only better healthcare to patients but also healthier solutions for the planet. Patients are, after all, consumers and, as such, receive constant stimulation to purchase and use more sustainable products.

Consumer products are going through a sustainability revolution and many companies are building brand loyalty and growing market share based on their "sustainability credentials" and awareness of how their activities are impacting the planet. Eventually, patients will expect and even demand environmentally sustainable medicines and will expect to be given a choice. Of course, as industry and healthcare professionals, we have a duty of care to ensure that patients are not pressured to change medication on environmental grounds alone; if there is a risk the alternative product puts the patient at increased health risk (either through its different drug or via a different delivery mechanism the patient cannot handle), then a change cannot be justified. Thus, the opportunity of starting from a blank sheet of paper and building in sustainability by design to create a new breed of inhalers increasingly seems the only viable option to achieve long-term sustainability and patient-care goals. Such an approach will enable companies to keep ahead of future legislation and provide potential competitive advantage, but in a way that does not compromise product performance or put the patient at increased risk. Quality by design (QbD) is already part of the culture for many drug delivery companies, but building in sustainability requirements (sustainability by design (SbD)) as a critical element of the quality management system (QMS) will mean that emerging designs will provide quality, maintain performance for patients, achieve sustainability goals and be better for the planet.

There are several ways to achieve such a redesign. Such an approach will demand that we explore these emerging critical elements in addition to the delivery performance and human factors that currently drive device design. PA's approach is to consider the technological, design and (importantly) the planetary health

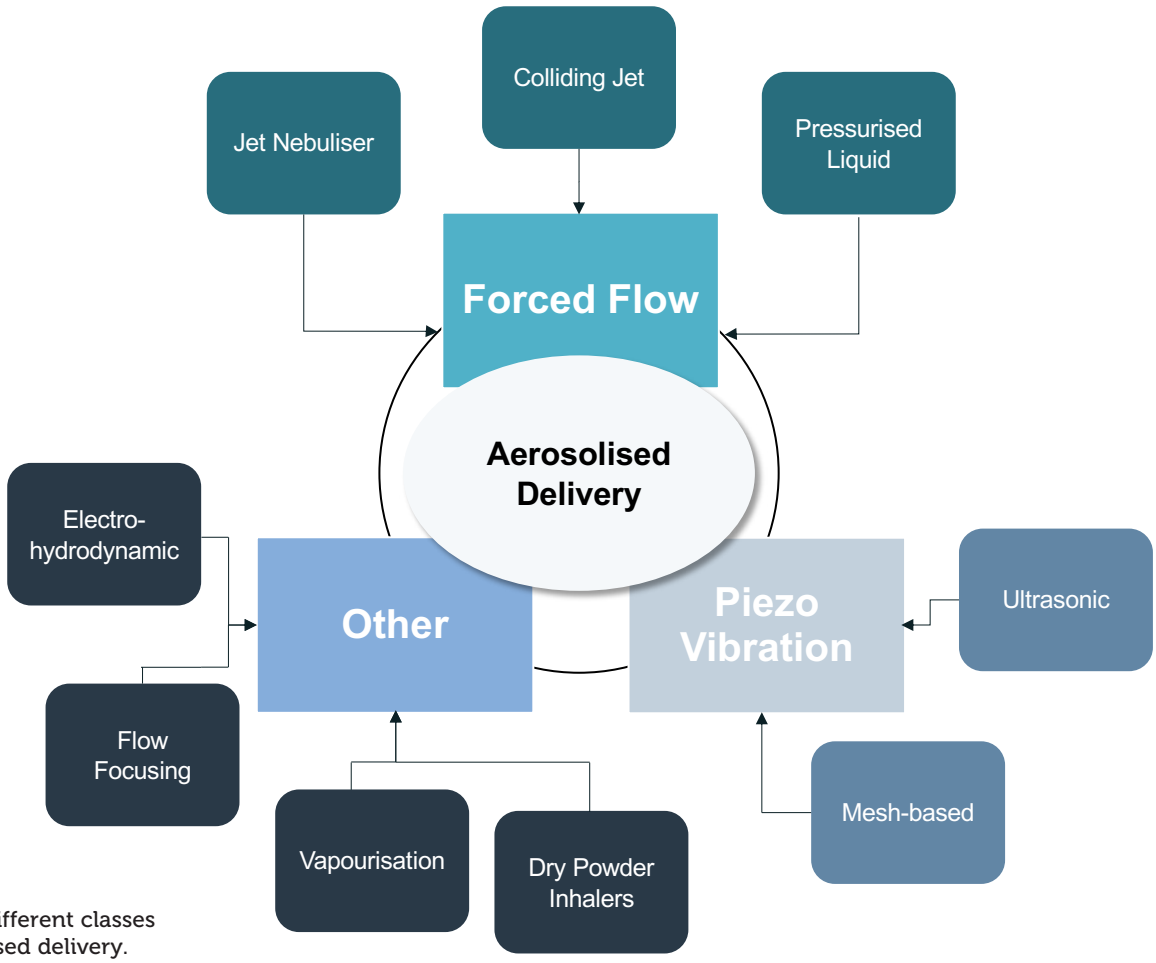

Figure 1: Different classes of aerosolised delivery.

aspects of future platforms and products. By focusing on these three pillars and incorporating learnings from the consumer and manufacturing sectors, we can design a new generation of inhalers fit for purpose, fit for the planet and fit for more demanding patients.

> "The long-term solution is to design the next universal platform for liquid inhaled drugs that can be adopted by the majority of pharmaceutical companies."

TECHNOLOGY

When considering technology, if we start from first principles, understanding how a formulation can be aerosolised may offer a route to a more sustainable product. Can we pick a more sustainable technology or method of delivery? Can we use alternative aerosolisation technologies that can deliver longer inhaler use and more doses over the life of the device, reducing the cost per dose – both financially and environmentally? Can we avoid the use of environmentally unfriendly propellants completely for liquid formulations? Of course, the answer to the latter question is "yes, potentially", since solutions already exist – but we can do more and, ultimately, create products that can be as cost effective as pMDIs without using environmentally damaging propellants. Given there is a wide range of alternative methods to aerosolise liquid formulations (Figure 1), there are potential alternatives to using propellants.

The technology decision is not as easy as assuming DPIs will remain more environmentally sustainable than pMDIs – they may have the high ground currently, but newer propellants promise to level the score once HFA152a and/or HFO 1234ze(E) are fully developed and launched – but they are not without issues.[6] Furthermore, DPIs tend to use a number of high-value engineering polymers in their make-up and may not be as sustainable as some believe. A further complication (or opportunity?) comes from the increased use of soft mist inhalers (SMIs) (e.g. Boehringer Ingelheim (Ingelheim, Germany), Merxin (Norfolk, UK), Pharmaero (Hovedstaden, Denmark) and Well-Bridge (Suzhou, China)) which, while possible alternatives to pMDIs, are currently too expensive to compete on a cost basis, but that could change with the development of simpler atomisation mechanisms and increased reuse with simple refill cartridges.

A propellant-free delivery approach may well lead to a lower overall global warming potential (GWP), but this is just one element of the overall design challenge. Creating a reusable device and reducing the environmental impact per dose is likely to deliver sustainability benefits but care must be taken to ensure that patient usability is not compromised. Furthermore, a key consideration will be the necessity of the chosen technology to deliver different, multiple drugs/combination therapies as well as different classes of drug.As inhalation continues to

show potential as a delivery mode of choice for biologics, a device that has the potential to deliver both small molecules and biologics will be more attractive from a commercial and sustainability standpoint. Enabling device circularity (the principle that at the ultimate "end of life", once the product can no longer be reused, it goes back into the supply chain, not landfill) **together with** creating a reusable platform suitable for delivering a wide range of therapies, maximises the useful life of the device and platform. Such an approach can improve the sustainability profile, compared with a single use, disposable design that is often limited to a smaller range of drugs (e.g. many monthly use DPIs).

To a large extent, the issues with most common current devices are hard-wired based on the technology choices made when they were developed, in some cases, decades ago. For example, pMDIs must use a liquid propellent which increases their GWP. Alternative propellants have the potential to improve the situation, but not remove the issue completely, due to propellants being fundamental to the design principle.

DESIGN

Historically, we saw the move from traditional CFC-based propellants to HFAs driven by environmental pricing pressures, but now even these second-generation propellants are falling out of favour as they are also greenhouse gases.[11] It is time to take the initiative and, while the suggestion to move away from pMDIs to DPIs may appear to make sense in the short term for some organisations (due to the impact of current propellants used), some patients cannot use DPIs and, furthermore, some medications do not exist in DPIs.[6] Therefore, a move to DPIs cannot be the only short-term solution and is certainly not a long-term solution. Surely the long-term solution is to design the next universal platform for liquid inhaled drugs that can be adopted by the majority of pharmaceutical companies (just as the pMDI was for many years) – this is a challenge we are now equipped to meet.

For polymer-based consumer products, we are all aware of the drive to move away from single-use products and the need to change the "everything is disposable" mentality of modern consumerism. Is now the time to transition this ethos into drug delivery products; is it feasible?

> "Packaging is also a key part of the environmental footprint."

PA believes it is. Completely redesigning the inhaler provides the opportunity to create a paradigm shift in selecting inhaler component and packaging materials and manufacturing methods, which enables us to reduce the overall carbon footprint and target extending the product life (to reduce the carbon footprint/GWP per dose). For device components, moving to a more sustainable source of currently used plastics is a conservative step.

Alternatively, a bolder move is to consider changing to some of the "greener" forms of polymer, where alternative, lower-carbon feedstocks – such as 100% bio feedstocks – are used. Furthermore, by enabling patients to reuse the devices for longer periods and by ensuring circularity of use – by creating systems for the easy return of used devices for material recovery/recycling – more sustainable inhalers will emerge.

Often, the packaging side of sustainability in medical products is ignored; it has rarely been more than a basic necessity. However, many patients are now stimulated by initiatives in consumer packaging and will demand more from their medical products brands. In a holistic approach to sustainability, packaging is also a key element of the environmental footprint and must be considered in the sustainable redesign process. Learning from the consumer and consumer healthcare industries, and considering materials such as cellulose fibre-based polymers, which can be more sustainable than their petroleum-based cousins, may help further improve the sustainability profile.

All good product designs should consider the design of the supply and distribution chains. However, to develop more sustainable products, the circular elements of the supply chain should be considered and thus, how best to supply, reuse and recover materials in a truly circular way. Returning recovered materials to the original supply chain may make it possible to improve a product's ultimate GWP. Unfortunately, this is not a given with drug delivery products due to the complex nature of the drug/device combination and the difficulties associated with separation and recovery of materials that could have drug still present. Thus, if we are ever to take on and address this problem, now is an ideal opportunity to consider the manufacture and recovery of materials in any new inhaler concept platforms – to build in QbD and SbD – considering the full environmental lifecycle and circularity. Frequently, manufacturing in wider product platforms has tended to favour specific geographies that provide the lowest cost offering for manufacture.

The supply chain, with more products containing thousands of parts, is complex and can involve increased environmental impact, increased GWP and increased carbon footprints for logistics/transport/supply chains. Furthermore, in many countries where the cost of production is low, the planetary cost of using carbon-intensive energy supplies, such as coal-fired power stations, is high and adds to the environmental cost of production. Thus, it is important that decisions based on sustainability and the environmental cost of production are considered, not just the financial manufacturing cost – the planetary cost of products has to be determined based on factual evidence and not unsupported dogma. An ill-considered approach can lead to low sustainability credentials due to large Scope 3 emissions,* leading to carbon-intensive product production.

As we progress through the next decade or so and consider alternative inhaler concepts, we may be able to consider a drive to be more local in the supply of raw material (where possible from circular recovery of used products and minimal virgin material). Inhalers are (after all) relatively simple, with typically less than 50 components compared with, for example, the thousands of components in a new car, and thus, the sustainability elements of inhaler and drug product manufacture may ultimately be driven by international and local legislation promoting or mandating local supply.[12] Therefore, conceiving and building a device that enables at least partially decentralised supply chains where, as far as possible, products are manufactured and assembled locally/nearer to where they are used by patients, could lead to more sustainable inhalers. Of course, there are risks associated with technology transfer and particularly method transfer in drug manufacturing and supply, but do we really have to manufacture in only one

or two locations and ship products all over the world? Furthermore, with the ongoing dynamic nature of the geopolitical landscape (e.g. current conflicts in Eastern Europe, price inflation for goods produced in China,[13] etc.), a federalised model that does not rely on specific countries or sites for non-specialised manufacturing and assembly will lead to more secure supply and a potential for sustainable competitive advantage.

PLANETARY HEALTH

Planetary health requires the consideration of a number of elements to achieve the desired outcomes for the planet, in addition to those for the patient. Four of the key elements are circularity, impact, wider infrastructure and equity of access:

- **By circularity**, we mean consideration and understanding of the recyclability and reusability of the inhaler and the materials used in its manufacture, together with the aim of returning recovered material to the original supply chain.
- **By impact**, we consider other sources or entities that increase carbon footprint or global warming potential within the inhaler circular life, as a whole.
- **By wider infrastructure**, we consider the supply, utilisation and logistics involved in the delivery, recovery and ultimate disposal of the inhaler.
- **By equity of access**, we consider how easy it is for all patients to access and use any new solutions proposed; are there any limitations to who can use it, are materials globally available so it can be produced anywhere across the globe, will patients of all socio-economic backgrounds be able to obtain it and use it?

For example, in the bigger picture, there are downstream environmental impacts associated with poor adherence and avoidable hospital admissions. By creating better designs, improving usability, adherence and product access, there will be a sustainability benefit as well as a major patient benefit. Assessment of each of these elements in a more holistic manner is important in demonstrating the true sustainable nature of any new inhaler concepts. Only by following a more holistic approach will we ensure that future inhalers meet (and exceed) future environmental legislation.

"The growing environmental, societal and policy pressures to be more sustainable will become an inevitable hurdle for the inhaled drug delivery industry if we do not take the opportunity to transition and change now."

This holistic assessment must be transparent and consider the complete end-to-end process (E2E), from supply through distribution and recovery of the device and, in a similar way, the manufacture, supply and filling of the drug product. By more deeply understanding and assessing the overall lifecycle process in terms of circularity, cost and carbon, planned changes or new concepts for a product can be quantified in terms of increasingly demanding sustainability requirements and a sustainable business case can be delivered. Such an approach that looks at E2E processes is likely to show that, from a sustainability perspective, current DPIs and SMIs may be better than current pMDIs; but they are not (in their present form) a sustainability silver bullet when considering the whole lifecycle of the inhaler.[14]

Furthermore, by considering and quantifying the wider benefits to patients and healthcare providers of a new design (whether that be increased access, improved adherence, etc.), we can demonstrate the broader healthcare system-wide impacts and value. Overall, this final assessment step in creating a new generation of inhaler will be a crucial step for the future. As regulators, specifiers and users begin to differentiate between devices using their overall carbon footprint and sustainability credentials, new technology and new designs will achieve little if the sustainability credentials cannot be demonstrated.

In summary, the growing environmental, societal and policy pressures to be more sustainable will become an inevitable hurdle for the inhaled drug delivery industry if we do not take the opportunity to transition and change now. While the figures for the global environmental impact of inhalers may be low, for individual companies and healthcare providers, they can be significant, and it is suggested that we both need and can deliver new inhaler concepts to make them better for patients, the planet and sustainable by design.

By focusing on the technology used, performance required, the design of materials, the inhaler and its supply chain, and by close consideration of the user and planetary needs – demonstrating sustainable credentials – we have the opportunity to deliver a paradigm shift. If we take these factors into account and see them as an opportunity to release ingenuity and help patients become more engaged with their devices, we can ensure inhalers have a long, sustainable future ahead.

PA believes that, as pharma companies transition from drug suppliers to partners caring for patients, there will be parallels to trends in consumer markets, increasing the importance of sustainability in brand reputation and patient retention. Convincing key pharma decision makers and global healthcare providers that customer choice is increasing is a challenge, but the shift is happening.

**(Emissions that are the result of activities from assets not owned or controlled by the reporting organisation, but that the organisation indirectly impacts in its value chain.)*

ABOUT THE COMPANY

PA Consulting is a global innovation and transformation consultancy with more than 4,000 specialists – strategists, innovators, designers, consultants, digital experts, scientists, engineers and technologists. PA has over 45 years' experience in the design, development, characterisation and evaluation of drug delivery devices. PA has dedicated inhaled and parenteral drug delivery teams, covering both conventional and smart connected devices using low-cost printed electronics and electronic-free acoustic connectivity. Services include complete device development, device identification, selection and customisation, device strategy, product characterisation, development of custom test equipment, human factors studies, design verification programmes and transfer to manufacturing. PA supports many organisations as they face the urgent need to address climate change and sustainability where consumers now expect organisations to keep people safe from the unintended consequences of technological progress.

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Philip Winkworth, PhD, is an R&D and Digital Strategy Expert and a member of the applied sciences team at PA Consulting, based in London. He holds a PhD in Process Organic Chemistry and has spent the past eight years working in life sciences consulting. He currently focuses on ensuring that company strategies take a wider, holistic view of the ecosystem that they operate in. This approach ensures that from conception through to launch, strategies will maximise the positive outcomes for both the company, the end user and the wider ecosystem. He is a firm believer that ingenuity will power a more sustainable future.

Craig Nelson is an experienced applied scientist within PA's Global Innovation and Technology Centre. He is a physical chemist by training, having carried out academic research in non-linear laser spectroscopy for analytical applications. Prior to joining PA, he worked for a UK defence contractor for 3.5 years developing laser and optical systems. He has been with PA for over 31 years and has carried out a wide range of product and process development programmes in both medical devices and consumer products. He has also conducted a large number of technology-based due diligence projects.

Recipharm

WHY PARTNERSHIPS ARE KEY TO A MORE SUSTAINABLE PHARMA INDUSTRY

In this article, Peter Hirst, PhD, Head of Commercial for Recipharm's Advanced Delivery Systems Business Unit, argues that careful selection of partners and better collaboration throughout the supply chain are key to optimising the sustainability of the pharmaceutical industry. He explores the challenges facing the creation of sustainable drug delivery devices and discusses the measures that suppliers to the industry are taking to support customers in achieving their sustainability goals.

Given the consequences of failing to act on climate change, governments worldwide are collaborating to enact legislation designed to reduce emissions of carbon dioxide and other industrial pollutants with a high global warming potential (GWP). For example, the Paris Agreement on climate change, adopted by 196 countries at COP 21 on December 12, 2015, commits signatories to take steps to limit global warming to below 1.5°C.

The pharmaceutical industry has an important part to play in achieving this goal. Increasingly, companies in the sector are looking to optimise sustainability, not simply to ensure compliance with government environmental legislation, but to play their own role in tackling global warming. However, the most fundamental action must come from all stakeholders in the pharmaceutical supply chain acting together to achieve a common goal.

> "Implementing sustainability measures directly contributes to ensuring that future generations can expect to live a long and healthy life."

LONG-TERM THINKING

Ultimately, the role of the pharmaceutical industry is to drive medical progress through novel research, and to develop and bring to market new medicines that improve the health and quality of life of patients. As such, the goal of minimising the sector's impact on the environment is a logical one – an improved environment has significant benefits for people's health and wellbeing. Implementing sustainability measures directly contributes to ensuring that future generations can expect to live a long and healthy life.

It is no surprise that the environmental impact of products and services now far higher up the list of priorities for pharmaceutical companies when engaging with suppliers. It is, in many cases, non-negotiable that each company has an effective plan to reduce carbon output and a sustainability strategy. A GlobalData poll conducted in January 2021 found that 43% of pharmaceutical company respondents considered environmental issues a priority for the industry. Within this, 52% noted that the most pressing issue was climate change.[1]

The responsibility to act rests with every stakeholder in the supply chain – from the manufacturers of the drugs themselves to the contract development and manufacturing organisations (CDMOs) that aid in bringing

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the drugs to market, along with every other step in between. When selecting a CDMO, pharmaceutical companies are increasingly using sustainability measures as critical selection parameters. Typically, these are based on the capability of the supplier to deliver solutions that will reduce the overall carbon footprint of their products.

LEARNING FROM THE PAST

History holds many lessons for pharmaceutical companies when taking action to reduce their environmental footprint. One such lesson is the transition away from the use of chlorofluorocarbons (CFCs) as propellants in inhalation drug delivery devices towards the use of hydrofluoroalkanes (HFAs) following the signing of the UN Montreal Protocol in 1987. CFCs were found to be highly damaging to the ozone layer, contributing to its depletion, so steps were taken to phase out their use, not just within the pharmaceutical industry, but across all economic sectors.

Now, the industry faces another shift as, subsequently, HFAs have been found to be a major contributor to global warming. Research by the University of Cambridge (UK) found that pressurised dose inhalers (pMDIs) using HFAs could contribute to an estimated 3.9% of the carbon footprint of the National Health Service in the UK.[2] GSK has calculated that 28% of its entire carbon footprint derives from patient use of its inhalers.[3] As a result, the industry is looking for alternatives to HFAs, which means engaging in discussions with vendors regarding alternative, greener forms of propellant.

An alternative avenue could be to switch patients to dry powder inhalers (DPIs) or reusable soft mist inhalers that do not use propellants (Figure 1). However, traditional DPIs use substantial amounts of plastic as part of their design, compared with pMDIs. Steps can be taken to redesign these devices to reduce the amount of material required, or to change to more sustainable bioplastics. The development of bioplastics has become a burgeoning industry with a strong market need, especially in the healthcare industry. As such, sourcing sufficient quantities of suitable medical-grade bioplastics may also present a challenge that will need to be overcome to ensure successful commercialisation

Figure 1: Soft mist inhaler.

Figure 2: pMDI valves and actuators.

IMPROVING EFFICIENCY

One of the most impactful ways in which pharma companies can build a more sustainable future for the industry is to improve efficiency through every stage of the drug development and manufacturing process. Alongside this, a greater emphasis on the recyclability of devices delivered to the end user is also crucial. This is especially the case for pMDIs, which often end up in landfill, leading to pollution from both plastic waste and their propellants being released into the atmosphere (Figure 2).[4]

For drug device design, a trend that will have a significant impact on the viability of sustainability efforts is the movement towards connected devices.[5] The existing problems the industry faces when drug delivery devices are thrown away are only magnified when the added components of connectivity technology are factored in, such as the inclusion of precious metals. Connected devices can play an invaluable role in disease management, ensuring patient adherence to their medication, but they need to be developed alongside a partner that is aware of the associated sustainability challenges to minimise their environmental impact.

CDMOs have a significant role to play in reducing the carbon footprint of a product. They must support pharmaceutical companies during the development and manufacturing process to ensure that production processes are as energy efficient as possible and that waste reduction is considered a priority. The good news on this front is that the rise of digital technologies is providing greater means of ensuring efficiency, such as the rise in the use of digital twin technology. Such technology is able to identify process improvements, with Accenture (Dublin, Ireland) recently reporting that it is possible to reduce process time, reduce cost of goods and lower greenhouse gas emissions significantly when employing digital twins.[6]

REGULATORY BACKING

To facilitate the work taking place to improve sustainability, the backing of regulators will be necessary, and those working in the industry must be ready to engage proactively in relevant discussions. For its part, the industry has already come together to create the Biopharma Investor ESG Communications Guidance 2.0,[7] which was developed to generate dialogue between companies and investors to communicate best practice on climate change and environmental issues, as well as other social and governance issues. Other projects have been initiated, such as the Science Based Targets initiative, which Recipharm is part of, where companies commit to taking the necessary steps to reduce their carbon footprint.

However, when drug device developers address questions over sustainability in design, action can be limited by the need to submit the new design to regulators. As each change to a medical device design needs to be assessed by the regulator, this means innovation in more sustainable design can take years. One move that could encourage faster adoption of sustainable design would be for an accelerated approval process for changes to components that are designed to reduce the carbon footprint. Overall, the regulators can play an important role in dictating the direction of travel on the issue by taking action to facilitate and encourage sustainability improvements across the industry.

WORKING TOGETHER

There is a shift across the pharmaceutical industry, and discussions about sustainability are taking place at the highest levels. A growing number of pharmaceutical companies are prioritising it when discussing projects with their CDMO partners. In the coming years, it will be essential for drug developers and their CDMO partners to work together on questions of sustainability, and to be ready with a sustainability agenda prior to beginning work developing a new product and delivery device. Discussions do not end at the primary source of a product's carbon footprint. As we begin to find solutions in this area, such as with alternative propellants or forms of delivery, work needs to be carried out simultaneously to understand the next largest contributor and potential remedies. The process of improving the sustainability of drug delivery products, and across the industry more broadly, is an ongoing one that will take time and persistence.

> "The process of improving the sustainability of drug delivery products, and across the industry more broadly, is an ongoing one that will take time and persistence."

At each stage of the drug development process there are steps that need to be taken, which is why open communication between pharmaceutical stakeholders about sustainability is so crucial. This extends to working alongside competitors, which is necessary because of the scale of the problem that climate change poses to everyone. Even healthcare providers have a responsibility to communicate with drug developers to give feedback on how the device is used and disposed of to better understand its environmental impact in the real world. Designing a drug delivery device that marks an improvement on what came before takes time and adds cost, which ultimately means that payers will have to consider paying more for a greener product.

There are good reasons to believe that such discussions between all stakeholders can be productive because everyone is on the same page. The overall aim of the pharmaceutical industry is to achieve the international community's target of net zero by 2050, and there are several companies working within the industry that have set themselves far more ambitious targets than this. With everyone understanding the importance of the challenge facing the world, the issues outlined in designing sustainable products can be overcome, but it will take a united effort across the pharmaceutical supply chain.

ABOUT THE COMPANY

Recipharm is a leading CDMO in the pharmaceutical industry, employing almost 9,000 people. Recipharm offers manufacturing services for pharmaceuticals in various dosage forms, production of clinical trial material and APIs, pharmaceutical product development and development and manufacturing of medical devices. Recipharm manufactures several hundred different products for customers ranging from big pharma to smaller research and development companies. The company operates development and manufacturing facilities in France, Germany, India, Israel, Italy, Portugal, Spain, Sweden, the UK and the US, and is headquartered in Stockholm, Sweden.

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Peter Hirst, PhD, Head of Commercial, Advanced Delivery Systems at Recipharm, has over 25 years of experience in the pharmaceutical industry with a wealth of knowledge and experience in drug delivery. Having completed his PhD in cystic fibrosis lung infections, Dr Hirst worked in a number of organisations supporting the development of pharmaceutical products that use drug delivery technologies. Dr Hirst has experience working with a wide range of organisations from small biotech start-ups through to large pharmaceutical companies.

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