

Meeting the World’s Evolving needs for a More Sustainable Future: How to Realise a Circular Approach to Drug-delivery-solutions

The world is looking for companies across all industries to take leadership positions that not only advance their traditional business metrics, but more importantly improve their impact on the environment and people’s lives around the world. When it comes to sustainability, there is not a single easy solution to solve all issues. Instead, taking a holistic view across various aspects of our business has led Aptar along the path to meeting its sustainability goals. Companies are increasingly adopting the principles of the circular economy where waste and pollution are eliminated or reduced as they are designed out of products throughout their lifecycle.

And it’s not just manufacturers who are supporting these potential solutions. Consumers are also demanding higher recyclability of products and are willing to pay more for them. In a recent Aptar Pharma survey conducted in 2022 with German, French and American participants, 77% of in total 840 respondents indicated that it was important or very important that the products they buy can be recycled. Further, 60% of respondents consider the recyclability of products when making purchasing decisions and 70% said they were willing to pay more for a product that they could recycle. Participants also voiced that they were willing to adapt their consumption habits to contribute to a reduced environmental impact, with six of ten respondents willing to use a refill/reload system to reduce environmental impact. These survey results confirm that consumer demand for increased sustainability, recycling and circular economy initiatives will be reflected in their buying decisions moving forward.

At Aptar, we’ve strategically assessed our businesses, which encompass pharmaceuticals, beauty, personal care, home care, food, and beverages, and have worked to embed sustainability throughout our business and within our product offerings. As the pharmaceutical industry is subject to very strict regulations, the introduction of such sustainability initiatives within our Pharma business must achieve not only the sustainability objectives but also maintain adherence to all regulatory, GMP (Good Manufacturing Practice) and quality requirements. We have categorised our sustainability programs into the three main action areas: Care, Collaboration and Circularity.

Care

As a company we show care to our employees, communities, and environment by continuously improving our impact and reducing our footprint. Our focus on care – for people and for our shared environment – as a key element of how we shape our future and achieve our objectives. Last year, Aptar named a Global Top 10 Female-Friendly Company by Forbes for its



progress on leading the way to support women inside and outside of their workforce. Notably, at Aptar in 2021, women accounted for 20 percent of leaders at the Vice President level and above. We have also grown our Employee Resource Groups (ERGs) to include the ALIGN Women’s Network, BOLD (Black/African American or African Descent) and ARC (LGBTQ+ community and their allies). We support these people focused initiatives, as Aptar firmly believes in the diversity and importance of every employee and the potential benefit they bring to Aptar, our customers and the world.

A second aspect of our care action area is reducing our footprint on the environment. We established a science-based target for the reduction of our Scope 1 and Scope 2 emissions by 28% by 2030 from a 2019 baseline. By the end of 2021, Aptar surpassed that goal by achieving 74% emissions reductions in 2021, well in advance of the original target date.

Aptar remained on track to achieve goals to source more renewable energy. In 2021, renewables accounted for 96% of electricity purchased, with the goal of 100% targeted by 2030. Also of note, 63% of Aptar’s facilities had achieved Landfill Free site certification at year-end of 2021 through our dedication to our internal waste reduction certification programs. We have additional sustainability targets related to both people and the planet and we remain committed to building a better future. (see table 1).

Our care action area demonstrates that through care for both people and the environment, Aptar can achieve broader objectives benefitting the company, customers and the planet.



Collaborate

We collaborate with customers, suppliers, industry coalitions and nonprofits to progress towards goals and better outcomes for people and the planet. These collaborations are important as they allow Aptar to gain and share knowledge and develop innovations that deliver economic, performance and environmental value.

Aptar's Sustainability Progress and Targets

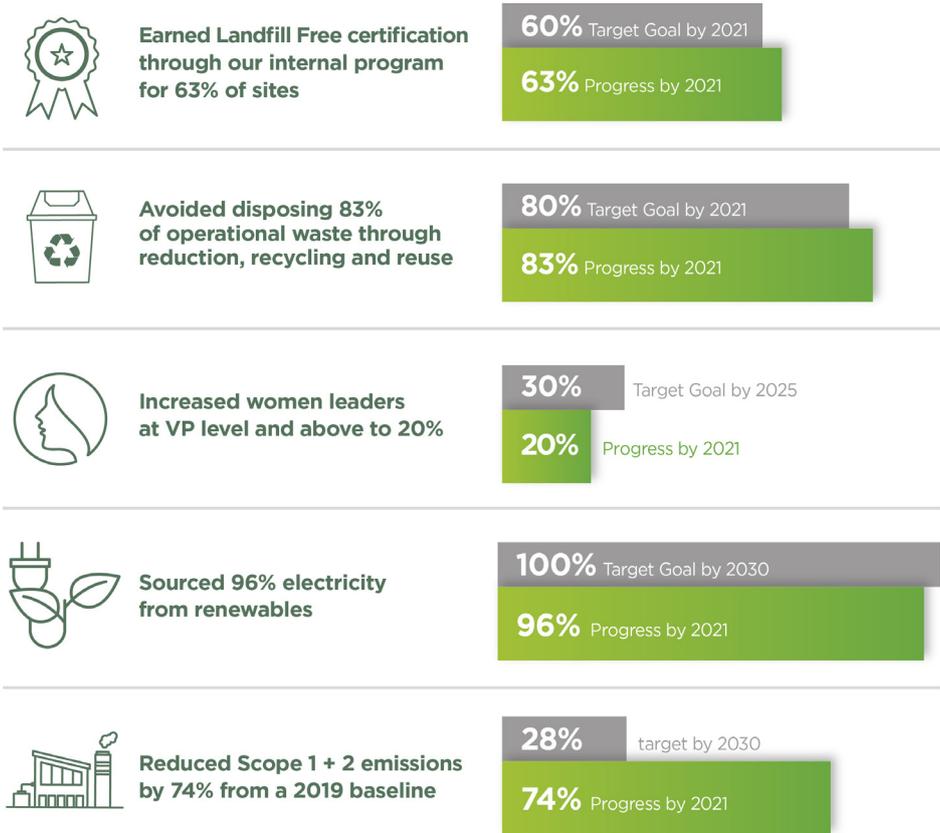


Table 1: Aptar defined corporate targets that aim at bringing forward our sustainability efforts. The group is on track and even surpassed some of the goals at year-end 2021.

Examples of Aptar's collaborations across segments and industries include:

- Partnering with PureCycle Technologies as its preferred technical partner to test and transform their Ultra-Pure Recycled plastic for food, beverage and cosmetics applications
- Active participation with the Ellen MacArthur Foundation (Cowe's, UK) as a signatory of the "New Plastics Economy Global Commitment", within a recyclability working group through the CE100 Network, and piloting their "Circulytics" circular economy assessment tool
- Expansion of domestic North American production of Activ-Film™ technology to ensure COVID-19 test kit integrity and accuracy through the support of a \$19 million U.S. Government contract
- Dedicated supplier engagement on sustainability objectives. By the end of 2021 Aptar had engaged approximately 40% of its supply base to manage their emission reduction efforts through a collaboration with EcoVadis

As system thinkers and change-makers, Aptar is committed to working alongside, and often leading, others by identifying solutions, processes and products that enable us all to move forward together.

Circularity

We are helping the industry advance system-scale changes that will benefit people today and generations to come by addressing climate change and waste crisis through Circularity.

The traditional take-make-dispose linear production cycle is rapidly being replaced with the concept of the circular economy or circularity. This circularity approach is based on developing designs and processes that emphasize resource reduction, extended use, reuse, recycling or composting of products or services and regenerate natural systems. These objectives must not compromise performance, safety or health requirements, which are especially important to Aptar Pharma's products as many save or improve human lives.

Aptar Eco-Design Tool Advances

Aptar partnered with an internationally respected consulting firm to develop an Eco-design tool that incorporates Lifecycle Assessment (LCA) functionalities that assess how products could impact the environment. The recently enhanced Eco-Design approach and LCA tools help our product design professionals better assess inputs and outputs and potential environmental impacts of the product system through the entire lifecycle of the product. Key performance indicators assessed by the tool is the CO₂ footprint, recyclability and circularity. The new tool is now applied to the development of every new Aptar Pharma product in order to enhance their circularity and reduce the CO₂ footprint of Aptar products globally.

Recyclable Metal Free Nasal Spray Pump Solution Using Eco-Design Tool

Aptar Pharma is in the advanced stages of developing a recyclable, metal free, nasal spray pump composed only of plastic components with no metal parts. This latest nasal spray pump was designed using our Eco-Design tool to maximise

recyclability from the earliest design stages. The full plastic nasal spray device will offer a very high degree of recyclability while delivering the superior level of reliability and precision expected of Aptar Pharma’s advanced nasal spray technologies including support for preservative free formulations. This metal free, nasal spray pump was primarily designed to provide a recyclable solution for nasal saline formulations and comparable nasal spray products (see table 2).

4Rs – Reduce, Reuse, Replace, Recycle

A concept that is critical to sustainability and engaging in the circular economy includes the four R’s. They are objectives to strategically Reduce, Reuse, Replace and Recycle at every opportunity throughout our business. Aptar Pharma has made great strides in many of these areas as part of our comprehensive sustainability objectives globally.

1. Reduce

As a drug delivery technology manufacturer, Aptar Pharma has been highly focused on ways to reduce the use of materials in device production and to minimise drug formulation waste. One effective way Aptar Pharma contributes to reduced material consumption is by designing drug delivery technologies that by function and inputs conserve materials when compared to other existing drug delivery technology options.

Aptar Pharma Ophthalmic Squeeze Dispenser (OSD) Compared to BFS Vials

Aptar’s unique multi-dose ophthalmic eye drop dispensing device has been designed for the ocular delivery of preservative-

free formulations. The design includes a purely mechanical tip-seal that eliminates the need for preservatives or additives such as silver ions to prevent contamination of the formulation. When compared to a traditional single-use blow-fill-seal (BFS) vials the OSD technology presents a more sustainable option for preservative-free eye drops. We recently performed an analysis that compares Aptar Pharma’s OSD against BFS vials for the same treatment course. For simplicity this comparison focuses only on the raw material extraction and production phase differences (see graphic 1).

With single-use BFS vials, residual medication must be discarded from opened vials after every use. With Aptar Pharma’s OSD, all of the medication can be used to the final drop. Based on a very conservative assumption a once daily treatment consists of 2 drops per eye with a 30–40 µl per drop, and 160 µl of product administered. These Blow-Fill-Seal (BFS) vials are filled with 300 µl of formulation in order to deliver the required dose, resulting in 140 µl of waste formulation. This discarded formulation represents approximately 46% of the total medication filled in each BFS vial.¹ A single OSD eye drop dispenser with a 10 ml fill can deliver approximately 60 days of this dosing regimen. It would require a pack of 60 BFS vials (18ml total formulation fill) to match the equivalent treatment duration of 60 days. The BFS single use vial treatment course would use nearly 10x the primary packaging material as compared to a single Aptar Pharma OSD² in order to deliver the 10ml of formulation to the patient/customer. With Aptar Pharma’s Ophthalmic Squeeze Dropper (OSD), one multidose device can deliver enough formulation for the entire

Aptar Pharma’s Sustainable Product Solutions

REDUCE	Ophthalmic Squeeze Dispenser (OSD)		<p><i>Sustainability advantages of multi-dose OSD over single-use BFS vials</i></p> <ul style="list-style-type: none"> Lower GWP due to <ul style="list-style-type: none"> • Reduced plastic packaging • Minimized formulation waste • Lower carbon emissions during transportation
	REPLACE	Pressurized Metered Dose Inhalers (pMDIs)	
RECYCLE	Proventu tube system		<ul style="list-style-type: none"> • Mono-material • Full recyclability • Medical grade polypropylene (PP) • Eliminates the need for a separate elastomer valve • Tethered cap
	Airless* Drug Delivery Systems		<ul style="list-style-type: none"> • Made of only polyolefins • Metal/Elastomer-free product pathway • High evacuation rate for efficient use and optimal recyclability • Excellent recyclability rating by cyclos-HTP certification • Feasible with renewable feedstock material (ISCC PLUS certification)
	Bag-on-Valve (BOV) continuous dispensing systems		<ul style="list-style-type: none"> • Compressed air/nitrogen propellant reduces greenhouse gas emissions • Recyclable aluminum • Removable actuators • Rated for good recyclability by cyclos-HTP certification
	In Development: Recyclable Nasal Spray Pump		<ul style="list-style-type: none"> • High degree of recyclability • Full plastic, metal-free • Preservative-free formulation support

Table 2: Aptar Pharma has a range of existing and optimised technology solutions that support a circular approach in drug delivery solutions. The most prominent examples for pharmaceutical products support the circular model through recyclability, material replacement or reduced resource strategies.

Comparing OSD with Blow-Fill-Seal (BFS)



Graphic 1: Aptar Pharma's multi-dose eye dropper for preservative-free formulations, OSD, has been compared to single-use BFS vials for primary packaging material use. Based on the standard OSD formulation volume of 10 ml, OSD offers an 83% reduction of primary packaging material as compared to BFS vials. OSD generates an 87% reduction in Global Warming Potential (GWP) based on the comparison with single-use BFS vials.

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) 1000 pieces stands for 1000 packaging units used for 10ml eye drops. For BFS that would be appr. 33,333 single use vials.

treatment with virtually no residual formulation to discard. Additional sustainability advantages for OSD over BFS vial eye drop delivery (based on materials 10 ml formulation volume requirement) includes:³

- Reduction of packaging materials reducing global warming potential (GWP) by 87%
- Use of 100,000 OSD devices instead of the equivalent 3.3 million single use BFS vials, saves 8,090 kg of CO₂ equivalents
- OSD generates lower carbon emissions during transportation than BFS. If you consider the volume and mass of both wasted formulation solution and bulky plastic waste differences, the OSD option would take considerably less space on a shipping pallet and consume less energy to transport, thereby markedly reducing the CO₂ footprint as it is transported to the consumer.
- 67% more medication per product unit provides up to 3x longer treatment duration
- Overall, Aptar Pharma's OSD greatly reduces plastic material use and minimises the waste formulation discarded as compared to single use BFS vial systems.

2. Reuse

Although reuse is an important part of the 4 R's it is more challenging than most to institute in the highly regulated pharmaceutical industry. The primary function of pharmaceutical drug delivery devices is to reliably deliver pure and efficacious drug product to the patient in a form that meets current regulatory and safety requirements. Reuse of such devices is difficult in the medical space as the units are typically self-contained and sealed against external contaminants. As a practical safety measure reuse of such devices is generally not

feasible and would clash with current regulatory requirements. Aptar Pharma continues to pursue the development of solutions enabling compliant reuse or refill drug delivery systems, made possible through innovative rethinking of our approach to such drug delivery systems. In fact, significant preliminary progress on reuse has been achieved with our Consumer Health Care lines, that can have a significant impact on the market overall. This is a complex challenge for the industry, but Aptar's efforts are positioning it to be a leader in the pursuit of solutions.

3. Replace

Aptar Pharma continues to seek ways to replace harmful or polluting technologies or materials with those having that have a less negative impact on the environment and support increased sustainability.

Sustainable Pressurised Metered Dose Inhalers (pMDIs)

With decarbonisation efforts in high gear in the respiratory or pulmonary drug delivery category, Aptar Pharma is fully engaged in helping our clients in the transition from the current widely used hydrofluoroalkane (HFA) propellants, such as HFA 227 and HFA 134a and other Hydrofluorocarbons (HFCs). They are now restricted as part of the Kigali Amendment (2016) to the Montreal Protocol, which seeks to phase down HFA/HFC use by 85% by 2047. Both patient safety and functional drug delivery aspects must be proven in studies before converting existing products to a new propellant. HFO1234ze and HFA 152a are two potential low global warming potential (GWP) propellants under assessment at Aptar Pharma. Ongoing studies are underway, involving multiple Aptar Teams, to ensure both mechanical and chemical compatibility between Aptar's metering valve technologies (and respective materials) and the propellants and respective formulations (including any necessary

excipients). HFA 152a has undergone exhaustive full inhalation propellant toxicology studies showing promising results and no adverse findings to date. The University of Manchester has also demonstrated that replacing HFA 134a with HFA 152a would reduce climate change and global warming impacts of inhalers in the UK by 90–92%.⁴

HFO1234ze has the potential to provide an even greater GWP reduction of 99% with more research and data being developed with customers and partners. However, less toxicology and safety data is available within the public domain to date, while additional toxicology data may be shared with interested clients under confidential disclosure. Aptar Pharma chose to work on replacement options seeking beneficial alternatives to current pMDI propellant gases. When customers eventually transition to these new alternative propellants, Aptar Pharma will be there to support them with data and services. Aptar Pharma supports customers with device selection, formulation development, analytical services and regulatory support. To help further de-risk and accelerate our clients' low GWP pMDI propellant replacement programs, Aptar Pharma also provides mixing and filling services at its Le Vaudreuil facility. The facility recently installed and validated an ATEX rated filling suite, where our technical experts work hand in hand with customers utilising pMDI propellants in our pilot plant, in order to efficiently develop and optimise device-ready formulations. Aptar Pharma also offers proprietary and novel Respitab™ technology that eliminates the need for the mixing process, saving cost and reducing risk. Our SmartTrack™ tool can be applied to make clinical endpoint studies redundant, saving time and money. Most critically, Aptar Pharma offers regulatory support including clinically relevant *in-vitro/in-silico* methods to eliminate the need for clinical endpoint studies. Aptar understands the complex requirements of converting to more environmentally friendly propellants and is fully equipped to support customers making these important advancements for a more sustainable future.

Chemical Phase-Out

Another example of replacement includes our Chemical Phase-Out Initiative. Aptar is committed to the Chemical Phase-Out of a number of potentially hazardous substances that

are commonly used in consumer packaging by 2025. This includes the elimination of these chemicals in the packaging production process or replacement with an alternative substance. We have used the chemical phase-out initiative as an opportunity to also improve the recyclability of our packaging and in anticipation of future regulations. We continuously monitor the regulatory environment and work towards alignment with our practices, particularly in the pharmaceutical sector where regulations are among the strictest.

Phasing chemicals out typically requires that each impacted packaging item must undergo extensive product-process performance and robustness testing to ensure both performance and safety.

4. Recycle

Recyclability is critical to our device designs as we move forward. One measure of our success is through the classifications we receive for our technologies from institutions such as the cyclos-HTP. cyclos-HTP is a reputable German organisation that assesses product packaging recyclability and responsibility for European countries and provides classifications for individual devices or packaging systems. Aptar Pharma is constantly looking for opportunities to improve the recyclability of their products through both design and innovation. This drive to improve Aptar's devices through innovative design for recyclability has led to favourable ratings from cyclos-HTP for a number of our systems. As a member organisation of RecyClass, an organisation dedicated to the enhancing the recyclability of plastics, we are continually evaluating our products and optimising them for higher levels of recyclability. These recyclability improvements include designing mono-material systems that enable simple and complete recycling of devices without compromising functionality or safety. We also shift 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 or material separation steps. Aptar 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.



Graphic 2: The mass balance approach allows for accountable use of renewable feedstock in production. ISCC Plus certification, as achieved for Aptar Pharma's Airless® production site in Villingen, Germany, makes it possible to specifically track and allocate renewable feedstock use to individual product batches.

Proventu – Mono-material Recyclability

The strategic development of mono-material systems is one way to increase a product's recyclability. Proventu is the company's first mono-material tube system designed to meet pharma product standards. Every part is composed entirely of medical grade polypropylene (PP). This eliminates the need for a separate elastomer valve that would reduce the recyclability. The tethered cap allows for one-handed closing and enables the entire device to be recycled with ease. Aptar Pharma strives to design and implement mono-material and highly recyclable systems as part of its recyclability programs.

Airless+ – High Recyclability Rated

Aptar Pharma's Airless+ range of highly recyclable products for dermal drug delivery benefitted from using our Eco-Design tools. Tighter regulations regarding patient protection outlined in US Pharmacopeia (USP) <661> for "Plastic packaging systems and their materials of construction" were addressed in the design stage by using medical-grade resins in the manufacture of the device. Airless+ dermal delivery systems deliver precise dosing and a high evacuation rate that results in leaving a minimal amount of residual semi-solid formulation in the device when fully utilised. With only moulded components and no metal parts, the systems in the majority of the applications can seamlessly go into existing recycling streams with no additional preparation. Airless+ systems meet cyclo-HTP's (Aachen, Germany) certification requirements and are rated "Class AAA" with an "excellent recyclability" rate (for raw, natural packaging without décor and label).

Bag-on-Valve (BOV) – Rated for Good Recyclability

Aptar Pharma's Bag-on-Valve (BOV) continuous dispensing systems incorporate the circular economy and patient care considerations in one device line. The BOV system completely separates the product from the propellant providing a clean and advanced nasal or dermal delivery system. The compressed air or nitrogen propellant reduces greenhouse gas emissions compared to other commonly used propellants. The BOV system may contain recyclable aluminium, have removable actuators and offer high-evacuation rates, all contributing to higher recyclability. Designed for recyclability, our BOV systems achieved the cyclo-HTP qualification for "good recyclability" (Class A) of the raw packaging assembly. This certification was specifically assigned for Aptar Pharma's BOV 30 ml, Pacifica Actuator (71% recyclable) and the BOV 400 ml, Nasal EP Actuator including cap and standard aluminium can. The Aptar Pharma BOV system provides industry leading nasal or dermal drug delivery with strong recyclability characteristics sign.

Supporting Mass Balance

Aptar Pharma's sustainability objectives have continued to gain traction across the company. Another initiative we have successfully implement is the use of plastic resins following the mass-balance approach. Mass-balance is a system that is designed to trace the flow of materials through the complex value chain. It essentially tracks and securely documents the amount and sustainability characteristics of circular and/or bio-based content. Plastic components using resins following the mass balance approach will allow for gradually increasing the share of bio-based or circular feedstocks used in your production process. Having this knowledge gives you control over your material composition and allows you to make claims, based on the verifiable records you maintain (see graphic 2).

At Aptar Pharma, our Villingen and Mezzovico sites have deployed mass-balance approaches and achieved the ISCC PLUS certification from the International Sustainability & Carbon Certification organisation. The ISCC is composed of over 200 international stakeholders and provides the leading sustainability certifications across a range of industries. As a result, we have been able to incorporate renewable feedstock into our production sites, with the program continuing to expand to other sites.

For example, our Airless+ systems are manufactured in a facility that earned both ISO 14001 and ISO 50001 certifications and is certified for renewable feedstock use. With International Sustainability Carbon Certification (ISCC) PLUS qualifications, the mass-balance approach offers accountable renewable material flow across the value chain.

A successful mass-balance implementation could also help to lower the CO₂ footprint of the product in a verifiable way. Aptar Pharma will continue to expand the application of the mass-balance approach across products and sites to help achieve its sustainability objectives and lower the CO₂ footprint of its drug delivery products.

Dedication to Sustainability

Aptar Pharma has demonstrated that a lot can be accomplished in a short period of time when it comes to sustainability and the circular economy. But we are not even close to being done. We have more long-term objectives for future phases of our sustainability plans centered around our main action areas of Care, Collaboration and Circularity. Aptar Pharma stays ahead of the curve, keeping its eye on rapidly changing demands of consumers, customers and regulators. Doing our part for sustainability, recyclability and participating in the circular economy, Aptar Pharma will continue towards the future we all strive for on a healthier planet.

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2. Calculation based on 10ml packed in 37.2g, hence 18ml packed in 66.6g (60 vials BFS) versus 10ml packed in 6.2g (one OSD)
3. 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.
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