Bio-based Plastics:
A Bridge to Sustainable Devices

There is one material used with ubiquity across the pharmaceutical industry. In one way or another, it enables nearly every drug treatment given today. It has become so fundamental to medicine, that it is treated in a vast number of cases as part of the medicine itself. It is used because of a well-understood and repeated safety record, and because it enables high-volume, reliable, and repeatable manufacture, and is made from a commonly extracted raw material.

It is, of course, the range of synthetic materials called plastics. Yet despite being easy to work with, and to make safe for medical use, it is difficult to manage at the end of its life, doubly so for drug-contaminated medical devices typically made from the higher-performing end of the plastic spectrum.

At end of life, plastic medical waste is either sent to landfill or incinerated. It is vanishingly rare for recycling to be considered.

Combination products, capitalised in the case of the FDA term 'Combination Product', consist of a device element and a drug element, which combine to provide the necessary efficacy – the drug formulation is designed to work with the device, and vice versa. Intrinsically, they are proven and regulated in combination.

Ideally, the often-plastic device element would be designed based on circular design principles, to eliminate waste and pollution, circulate products and materials (at their highest value), and regenerate nature, as defined by the Ellen MacArthur Foundation. Circular design in practice is typically achieved by design for device reuse or full recyclability. However, this switch does not come without possible impacts on usability, and therefore efficacy, and is currently not compatible at scale with the end-of-life disposal that is required today.

The environmental impact of plastic is also an important consideration for devices which are on sale today, or are soon to become marketed products, where expensive and time-consuming development work is already complete. Circular design should be pursued, but it cannot deliver an instant impact.

What we are left to work with then, is the plastic materials themselves. Even better if we can remove the dependence on the extraction of oil and gas for their production.

Vectura's Open Inhale Close (OIC) device is a good working example of the device element of a combination product. It has been developed with ease-of-use (to help patient compliance), and therefore medical efficacy in the hands of patients, at the core of its design philosophy. The OIC, therefore, makes great use of a small number of robust injection-moulded plastic components, and with conventional end-of-life considerations. The OIC Device has a significantly lower component count than other blister-based open-inhale-close DPI devices, including devices for which it was designed to be a substitutable generic device.

As a simple-to-assemble and lightweight dry powder inhaler, the OIC's environmental impact is driven predominantly by the volume and processing of the plastics used in its construction.

In using the OIC as a case study, plastic options are presented, explored, and, crucially, implemented into the OIC device with input from stakeholders across Vectura.

More Sustainable Plastics

There are options available when it comes to the origin and processing of the plastics. These are potential options for use in devices:

- **Conventionally recycled plastics –** products that contain post-industrial or post-consumer waste. These are not suitable for medical applications. Proving the safety of these plastics is close to impossible and the variability in product-quality challenging.

- **Closed-loop recycling –** returning moulded scrap to be resupplied. This is not suitable for medical applications. Regrind, where scrap moulded material is ground down and remoulded at the moulding site, is often forbidden, and this is a less-controlled version of regrind.

- **Chemical recycling –** products which are of virgin quality but produced with feedstocks derived from chemical recycling. This has the potential to meet the needs of medical device applications, however, it is not industrialised.

- **Bio-based plastics –** products made or derived from naturally occurring materials as a replacement for fossil feedstocks. This is suitable for medical applications and solutions are commercially available.

Bio-based Plastics for Medical Devices

In their manner of production, bio-based plastics for medical applications differ to what might conventionally be referred to as bio-plastics.

By mixing equivalent feedstocks to fossil-based materials with those derived from bio-based sources during polymer manufacture, and accounting for this in the output, identical bio-based and fossil-based resins can be produced at the same time. Figure 1 provides an overview of the production process for medical device plastics.

1. Green feedstock derives from bio-circular sources, for example, methane from anaerobic digester using only waste products
2. Mass-balanced approach means fossil and green feedstocks are mixed during production but accounted for separately
3. Segregated bookkeeping approach is certified by ISCC+
4. Bio-based resins are identical to conventional resins

This process means that for any given material, there can be a fossil-based version and a bio-based version that are inter-changeable with one another, at least from a technical perspective, with the regulatory impacts in need of consideration. As such, bio-based resins are available for many commonly used plastics in medical devices.

For Vectura's portfolio of devices, most of the plastic materials selected have bio-based versions commercially available.

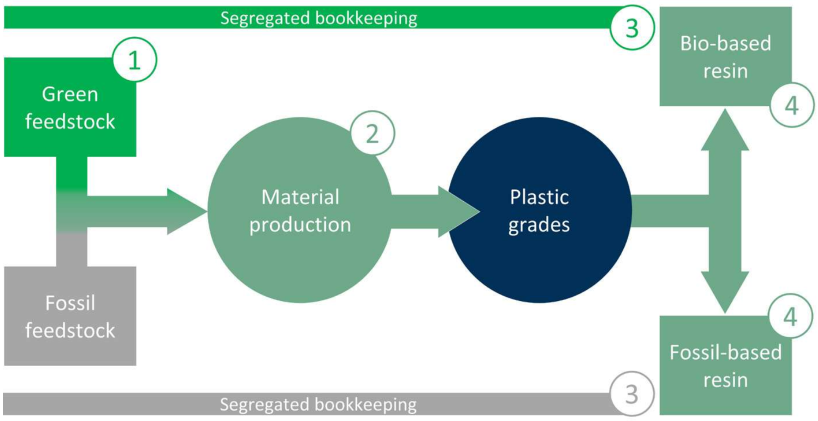


Figure 1: Medical device plastics production incorporating bio-based feedstocks

In the case of Vectura's OIC device, all injection-moulded plastics have a bio-based equivalent that can be used as a drop-in, provided the risk of the change can be adequately resolved, where that risk is primarily regulatory in nature, but may extend to supply chain risks.

Environmental Impact

The benefits of bio-based plastics on sustainability and the environment derive from reducing the need to extract and refine virgin raw materials. Typically, these are fossil in origin, but may extend to other mined substances. The effect is doubled given the bio-based feedstock source is waste, therefore endowing circular design properties into the material.

Using bio-circular (waste) sources reduces the negative externalities associated with other plant-based plastics (bioplastics), where the feedstock is usually a crop. This can compete with food-crop production and creates biodiversity loss as an opportunity cost from land use.

The lifecycle for carbon dioxide emissions from bio-based plastics are substantially reduced when compared with fossil-based equivalents. Figure 2 compares the emissions from device-plastics supply for three of Vectura's key drug delivery devices, all dry powder inhalers, using data from material suppliers. By considering the carbon footprint of the raw plastic material elements only, the actual carbon emission reduction can be easily derived for a typical annual production of three million devices, though this does not consider the full lifecycle of the device.

Further benefits include the localisation of feedstock production. Typical waste sources, invariably food waste, are universal, meaning the feedstock supply chain does not need to rely on geopolitics and the associated supply tensions placed by the global distribution of natural resources, as is the case with oil and gas.

Impact to the Medical Device

Of course, this seemingly straightforward switch has to consider the impact on safety and efficacy of the final drug product.

Documentation that defines material properties and accreditations, along with ISCC+ certification from the material suppliers, is reviewed against device material requirements and provides the evidence that the bio-based material is viable.

Whilst the bio-based materials are fundamentally identical to the conventional materials, and theoretically there should be no change in the risk profile to the device function or patient safety, according to guidance,[1] they could still be treated as a material change from a regulator perspective, and therefore the associated regulatory risks and impacts must be considered. Indeed, the risk here is invariably down to needing to satisfactorily evidence the identical properties of bio-based materials to a regulator as proof the change would not impact efficacy or safety, rather than necessarily proving it through experimentation. That being said, without suitable regulator engagement, this remains unproven.

All these risks, however, can be avoided by changing the device design definition to bio-based plastics before device verification and validation (V&V). For the OIC, as with most devices that are part of combination products, V&V includes bio-compatibility testing. with the target drug formulation and dosage, this sets material choices due to the cost and timescale of the tests. The Extractable and Leachable (E&L) of the bio-based materials are identical to the fossil materials, though either option would need assessing against any change in drug product, use, or posology. For OIC, this had not been started prior to the selection of bio-based materials. Subsequent proprietary projects using the OIC device platform with bio-based materials would only need to repeat V&V activities associated with a change of target drug.

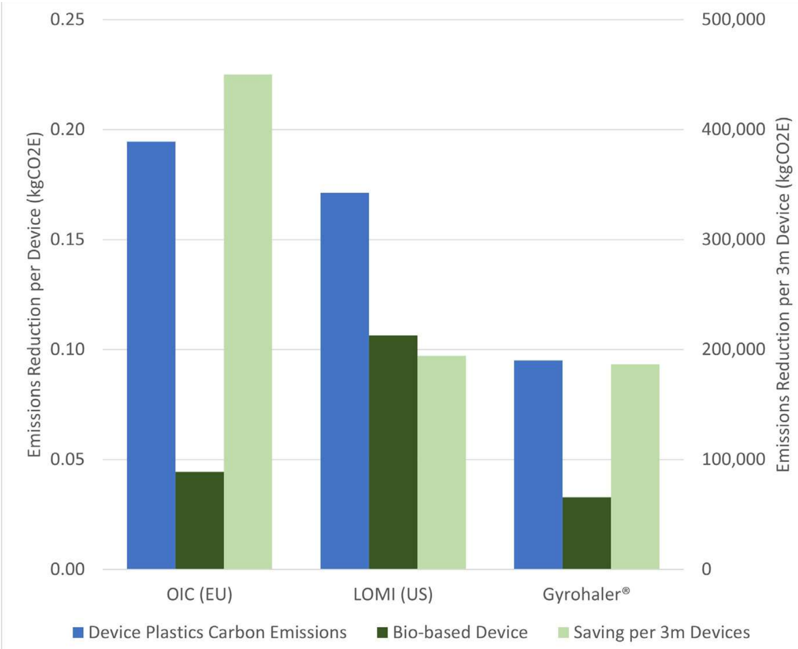
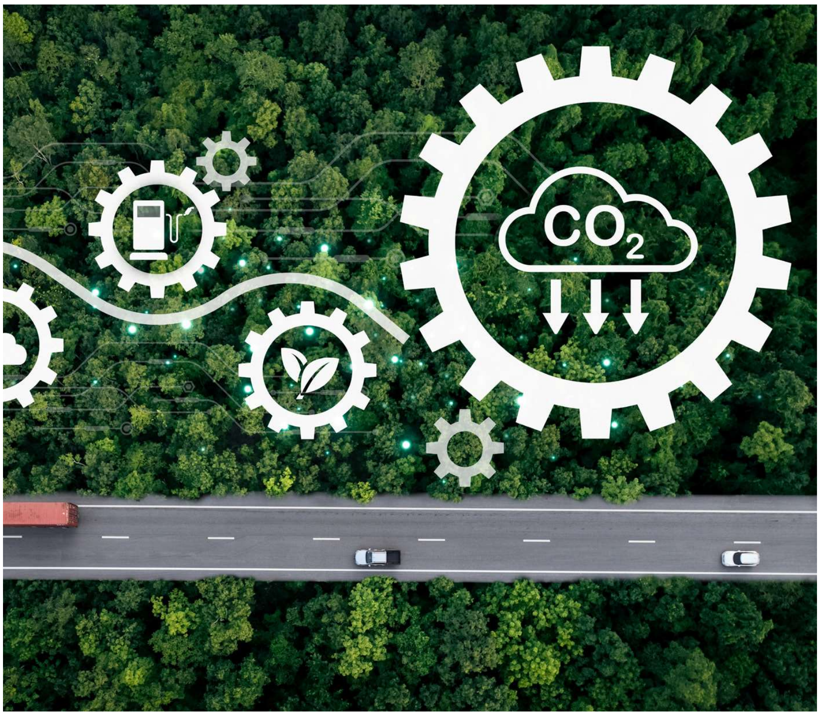


Figure 2: Estimated CO_2 reduction from using commercially available bio-based version of plastic grades for three bio-based Vectura devices. The LOMI and Gyrohaler® devices are both approved devices as part of combination products.

The Open Inhale Close, or OIC, device is a blister-based DPI designed for multi-dose applications. It has only 3 user steps: Open, Inhale and Close. It makes use of the versatility of injection moulding and Vectura's proprietary technologies to offer simplicity of design, low component count, intuitive user interface, digital connectivity readiness, generic device substitutability and low cost.

There is, invariably, a cost impact to the approach, and questions of supply chain resilience to consider. However, the cost impact is approximately one per cent at a product level, which is bearable given the large carbon footprint reduction. Similarly, supply chain risks are either identical to fossil grades due to co-production or improved by the distribution of feedstock production.



Conclusion and Next Steps

Short-term steps to improve the sustainability of medical devices can be taken now.

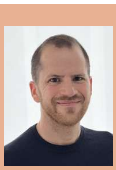
The implementation of bio-based plastics is best done at the early stages of development, but slot-in solutions, where available, allow bio-based material selection to be utilised at mould tool qualification, just prior to design verification and validation in the development cycle.

In theory, bio-based plastics can be applied to marketed and close-to-market products. The question of applicability to marketed devices is still an open one, and where some guidance in the approach to regulation is required. Understanding among all stakeholders is needed to allow the considerable impact of legacy plastics supply to be reduced using bio-based plastics.

Longer-term, a concerted effort is needed across the industry to drive change to minimise the impact of single-use plastics at end-of-life. This could be achieved by adopting fully circular design principles with better end-of-life management.

REFERENCES

1. FDA Guidance (2017): Guidance for Industry and Food and Drug Administration Staff. Deciding When to Submit a 510(k) for a Change to an Existing Device.



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Philip Smith is a Mechanical Engineer and Principal Engineer at Vectura Limited. Vectura is a leading specialist inhalation CDMO that provides innovative inhaled drug delivery solutions that enable customers to bring their medicines to market. With differentiated proprietary technology and pharmaceutical development expertise, Vectura has the device, formulation, and development capabilities to deliver a broad range of complex inhaled therapies. Vectura has contributed to the success of 13 inhaled medicines launched by our partners and licensees.