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2021Sustainability in Pharma Packaging, Devices and Manufacturing Report

A starting point to address a big issue, hear from three pharma leaders on paving the way for sustainability in pharma.

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Contents

In this short report, Informa presents a call to action from its sustainability lead, three contributions from CPhI sustainability experts, as well as a short review of the recent CPhI Sustainability Index.

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Pharmapack recyclability podcast:
https://player.captivate.fm/episode/5c3c4cdf-6511-4948-b14f-818d8df5ab4d

A trend report on sustainability in collaboration with Aspen:
https://www.cphi-online.com/trend-report-sustainability-in-pharma-news112773.html

Sustainability webinar with Pfizer:
https://www.cphi-online.com/strong-this-webinar-originally-aired-as-part-of-file117059.html

Learn more about sustainability at Informa:
https://www.cphi-online.com/dev/2021/sustainability.html

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Introduction: A message from the Informa Pharma Team

We want to work with you to help ensure pharma is renowned as an industry leading the charge on sustainability, ethics, and diversity

The pharma industry has many incredible achievements to celebrate from the last two years and is now well on its way to overcoming the single biggest challenge we have ever faced in Covid-19. But, as a global civilization, this is not the only existential threat we currently face. And, undoubtedly, climate change and sustainability will be with us long after the memories of Covid fade. This is why in the next few years at CPhI Worldwide we are calling on the industry to come together – individually, collectively and through ourselves – to find new ways, both big and small, to meet the challenge.

At Informa, sustainability has long been a core of our business, and we are always looking at ways to make our events more sustainable and reduce their environmental impact. Undoubtedly, the pharma industry collectively shares our commitment for this cause, and in the last few years, we have seen a swathe of exciting developments in pharma packaging, recycling, and new approaches to process improvements.

In terms of our events, we are constantly evolving with initiatives like the Shell scheme, 'Better Stands', who are working with our venue partners to utilise renewable energy sources (whenever possible) and viewing all aspects of our events from a more sustainable standpoint. For example, we use recycled carpets, have a digital first approach to printing, and source food locally. We even offer carbon offsetting and intelligent power use so that we maximise the impact of every KW used.

However, we want to go further the next few years and make sustainability not only a central tenet of our events, but integral to how we interact with our pharma partners globally.

As a first step, in this short sustainability report, we will look at a smattering of issues that we can address, thus, exploring how we begin the bigger conversation about building a more sustainable pharma industry. We will look at new areas that have gone under the radar of pharma's current environmental agenda – where great strides have already been made in making drug devices more sustainable and in the recycling of packaging and patient adherence. Moving forward, for example, we can study how we can reduce the e-number in pharma processes

and make the manufacture of complex chemicals and drug therapies more environmentally friendly.

Taking this further, we will also be discussing and promoting case studies of good corporate governance in the industry, everything from working conditions and supplier contracts, to pay and diversity.

These can also include, but is not limited to; biocatalytic methods, green chemistries, and improved process development. But of course, all of this must be achieved without slowing development or reducing our ability to make these vital, life-saving medicines. As an organisation that brings the pharma community together, this will continue to be a focus in everything we do – from our agendas and our onsite initiatives to our awards for companies that are making a real-world difference in the sustainability of the pharma industry.

This report is just the beginning of our plans to use our role within the industry to debate how we can improve our practices, and to help deliver improvements to the sustainable discovery, development, supply and production of pharmaceuticals. Taking this further, we will also be discussing and promoting case studies of good corporate governance in the industry, everything from working conditions and supplier contracts, to pay and diversity. The modern consumer is now looking for far more from its corporations; they want not just excellent products and safety, but they also to know and trust they are using companies that add value to society beyond profits and products. What I love about this industry is that it is already undertaking an invaluable contribution to society, and I am interested in seeing the role we can play in promoting the wider impacts that many pharma companies have in building better societies locally, regionally, and globally.

In fact, over the next 12-months, in addition to a bigger focus on the onsite seminars, roundtables and sessions, we will also be releasing regular reports, case studies, and introducing a global panel of leaders who will lead the debate and promote further positive change in the industry. This means that we will be inviting every attendee and exhibitor to reach out to us to take part, and we will be launching a series of working groups to ask the big questions and to promote improvements. These working groups will discuss everything from 'process improvements', 'device and packaging sustainability' to areas like 'waste reduction and recycling', 'renewable energy and plant efficiency' and what makes a great 'corporate citizen'.

We don't take on this commitment lightly, but as an industry, pharma has shown what we can achieve when we collaborate – and I cannot wait to work with our partners to make a difference.

Pharmapack Sustainability Index: Europe leads on pharma packaging and device sustainability, well ahead of the United States

Overview

Launched for the first time in 2021, Pharmapack and CPhI Worldwide have introduced a new sustainability index[1] for the major Pharma economies. Below we summarize the key findings of the index as well as industry opinions on the growth in green R&D, and the role the competing interest of patient centric device design is playing:

Introduction

There has been a raft of changes across the pharmaceutical drug device delivery and packaging sector in the past few years, with a continued drive by drug delivery device and packaging manufacturers towards patient centricity. The aim is to improve the patient experience, but also, to increase patient compliance and reduce attrition rates. Yet with smart packaging and devices proliferating these goals have often worked against the industry's other main trend, namely, to improve sustainability.

Answering the concerns around the rising number of non-degradable plastic waste, drug delivery device and packaging companies have sought out greener, more sustainable solutions including the use of bioplastics and blister packaging.

This index will explore how far long each country is in terms of achieving optimal sustainability of pharma devices and medicines.

1. Commissioned in late summer 2021 the index summarises the scores and opinions of more than 50 companies from across global pharma on how the industry is doing in terms of sustainability

The Drive Towards Sustainability

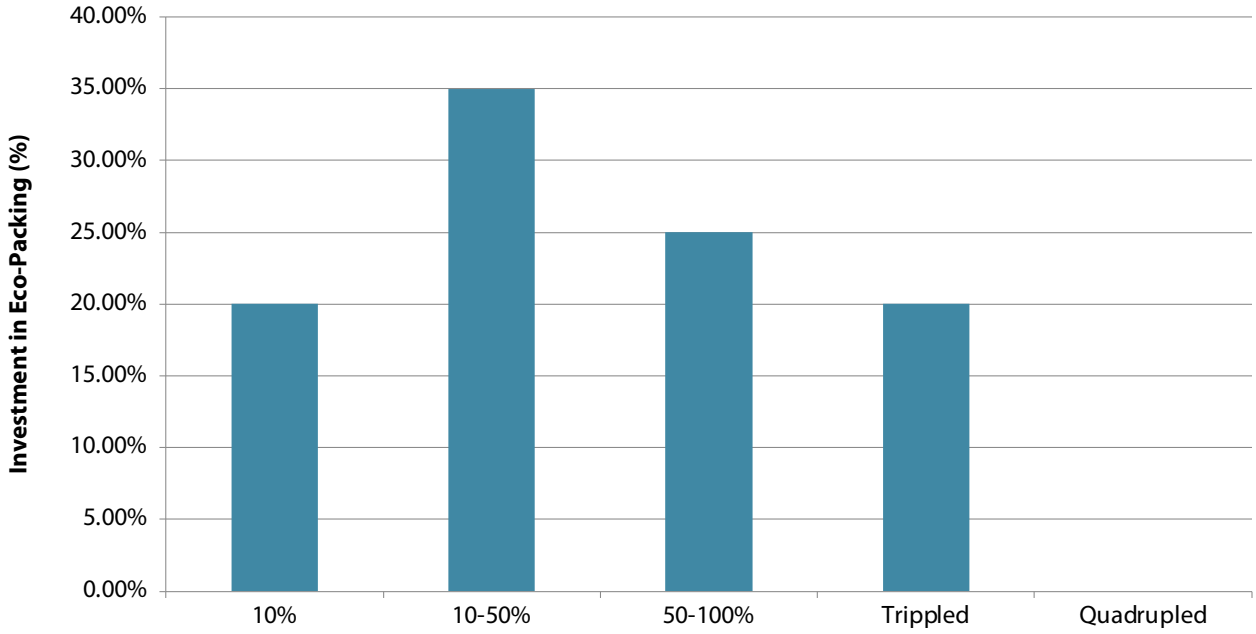
While the COVID-19 pandemic has captured the attention of the world, including the pharma industry, there is also another looming issue on the horizon, in the form of climate change. Pharma has seen a drive towards sustainability in the last five years, with an increasing number of companies looking to reduce their carbon footprint, reduce waste, minimize greenhouse emissions and remove plastics. One major sector that has come into focus is packaging, and while packaging in pharma is used less than in industries such as food and FMCG, most medical packaging is derived from polymers, with the majority of medical waste disposed of via landfill. Governments are creating wider sustainability strategies across many industries and pharma is no different, with a recent drive towards green chemistry initiatives to reduce the use of solvents in API manufacturing just one example.

Pharma has seen a drive towards sustainability in the last five years, with an increasing number of companies looking to reduce their carbon footprint

Almost half of the respondents believe that investment in eco-packaging will increase by at least 50% within the next two to three years, and this will be largely driven by

companies looking to lower their carbon footprint in line with the global goals in the 2030 agenda, as set out by the United Nations. Pharmapack expert Gregor Anderson, believes that there should be more done in terms of creating a sustainability index as it's usually measured as a CO_{2eq} value: *"With the wide range of medicinal packaging platforms available there is a large choice for patients and each platform has its own inherent sustainability index. The sustainability index is usually measured as a CO_{2eq} value and today there is no clear guidance on what standards the Pharma industry should meet when it comes to sustainability. Healthcare providers and customers are increasingly asking about metrics regarding the global footprint of medical devices, medicines and packaging and this especially ties into the former's own sustainability initiatives."*

Figure 1: In the next five years by how much will investment in eco-packaging increase business confidence



How does the industry think different countries compare for pharma sustainability?

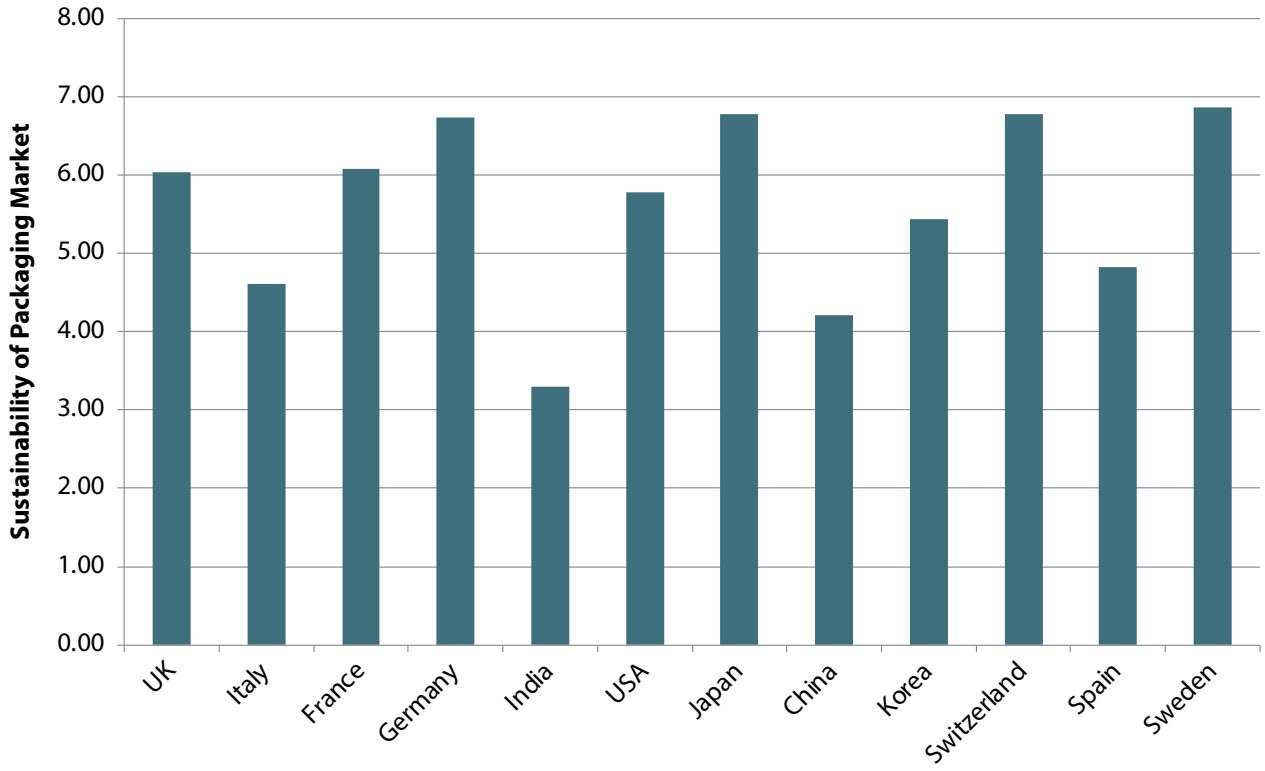
Pharmapack's new *Sustainability* Index (scored out of ten) – is created to gauge the perception of how much is being done by each country in terms of plastic use, waste reduction, device recycling and which country has the most progressed approach to sustainability – assessing how far long each country is in terms of achieving optimal sustainability of pharma devices and medicines among its population.

Leading the Index in its inaugural year is Sweden (6.87), whose adoption of a strategy for a circular economy in 2020[3] has been key in their drive towards a more sustainable approach to packaging. To give just one example, Svensk Plaståtervinning has invested in building the world's largest plastic recycling facility, 'Site Zero'.[4] The UK (6.04), who have implemented a tax on virgin plastic materials in disposable packaging, Germany (6.74), Switzerland (6.78) and France (6.09) are also all perceived by the industry to be leading Europe's efforts in sustainability.

While both the governments of India and China have made sizable efforts at reducing their respective pharma industry's carbon and environmental impact, the market has yet to be convinced, with India (3.30) and China (4.22) having the lowest perception scores by some distance, and significantly this is the only [CPhI/Pharmapack] metric where the United States ranks lower than the majority of European nations. We surmise this is more likely due to the United States' weaker government commitments rather than a reflection of the relative commitment to sustainability of drug device companies from the USA.

2. https://www.government.se/press-releases/2020/07/sweden-transitioning-to-a-circular-economy/
3. https://www.packagingnews.co.uk/news/environment/recycling/swedens-site-zero-become-worlds-largest-plastic-recycling-plant-02-09-2021

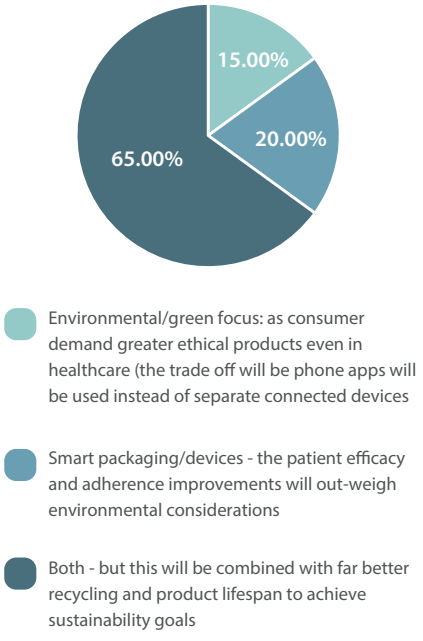
Figure 2: Packaging Sustainability Index 2021 – scores by county out of 10



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

However, the two dominant trends 'smart packaging' and 'green packaging' are often diametrically opposed in practicality – as smart devices tend to be less recyclable – but encouragingly 65% of our respondents believe that both can coexist. The majority of the industry believes 'a shift towards better recycling and improved product lifespan' will help integrate sustainability goals without compromising device adoption over the next three years. However, 15% believe that consumer demands will take precedence, demanding greater ethical products to be used, while 20% believe that smart packaging will prevail as patient efficacy and adherence improvements will out-weigh environmental considerations for now.

Figure 7: The two dominant trends 'smart packaging/devices' and 'environmental/green packaging' are often diametrically opposed *(It's hard to achieve both simultaneously)*. Which do you think will have the biggest bearing on product development over the next 3-years ?



Conclusion

One of the interesting aspects of the Pandemic is that novel drug delivery device innovation – other than novel injectors – was temporarily slowed and as the industry return to normality, we can expect a rise in new devices throughout 2022. Significantly, future covid vaccines will further increase the need to injectable devices and the pandemic has also clearly shown the benefit of both connected and self-use devices – so we anticipate this will continue to advance at rapid pace and that device manufacturers and pharma will increasingly collaborate to use them in conjunction with other digital assets (apps, phone, computer). Ultimately, this will bring the patient into far greater control of their own care and its management. In the medium term we anticipate these efforts to start aligning with recycling schemes so that patient adherence (which is inherently green, since it seeks to optimize use of medicines) so that overall impact and sustainability gains be made alongside therapeutic improvements.

In an industry so use to US leadership, sustainability is in the view of the industry currently being driven forward by European nations. The EU's block-wide ability to regulate, is pressing the industry to investigate the materials it uses, but also, how post-use – when virgin materials are often required – we can then reliably collect and recycle these devices.

Significantly, future covid vaccines will further increase the need to injectable devices and the pandemic has also clearly shown the benefit of both connected and self-use devices

Over the next few years, we expect medicine delivery to be more efficient as the patient gains greater digital tools. Yet in sustainability may also see these very same digital tools being used to empower the patients to be smart of the solution – using remainders, maps and instructions on how, when and where to responsibly dispose of packaging waste and devices – we are, after all, regularly told we are all in it together.

Sustainable Pharma Packaging -future challenges, threats and opportunities

Authors: Gregor Anderson, MANAGING DIRECTOR Pharmacentric Solutions Ltd.

Introduction

With world leaders meeting at the UN Climate Change Conference this year and North America and Africa having their hottest June on record in 2021 we are all now increasingly aware about the pressures the planet is under. This includes global warming and as greenhouse gases gradually push the mean temperatures up by at least 1° the planet is creeping further to the edge. The effect from the consequences of global warming (from for example poor air quality), and with the potential for further pandemics, these factors will undoubtedly increase the use of medicines across the globe. All medicines require packaging, from simple blisters, pouches and bottles to more complex combination devices (such as inhalers, pumps, vials and injectors). The packaging used on medicines is vital to ensure the medicine's stability through a guaranteed shelf life, protection during distribution, ease of dispensing and all of these attributes enabled through high volume manufacture at an affordable cost. Additional features such as anti-counterfeiting marking, and a child resistant/senior friendly capability add to the value the medicines packaging brings to the end customer, the patient.

With medicines packaging in focus, there are challenges ahead. The packaging market for medicines is substantial. With an estimated 2021 value of approx. USD 95B (possibly more now due to COVID?) the volume of materials used is substantial. Although it is much less than other areas where packaging is used such as food and FMCG. Most medicine packaging formats are derived from polymers but can also use materials including glass, aluminium laminates, cartonboard, etc. All primary and secondary packaging materials used are of premium quality with full provenance known as part of well-established and mandated quality requirements. At present used medicine packaging is typically disposed of via landfill (for example if medicines are taken/disposed of 'at home' in the domestic waste steam) or incineration (more commonly seen in hospitals & primary/community care). There is a future set of challenges that the whole Pharma industry must consider as far as packaging post use is concerned and also real opportunities to reduce the potential for packaging impact on the environment and reduce medicine waste.

All medicines require packaging, from simple blisters, pouches and bottles to more complex combination devices

There is no doubt that global warming will affect us all if we keep behaving as we are today. Governments and industries are well aware of the threats and challenges of climate change and although they are primarily being driven from the Western world there are initiatives underway that are designed to start to change how we currently behave (e.g., The UK has implemented a tax on virgin plastic materials used in disposable packaging – Pharma primary pack materials are exempt, at present). As Governments create wider sustainability strategies across many industries each is setting out its own roadmap (e.g. automotive) to meet long term net zero targets. The Pharma industry will be impacted by these strategies too and packaging will be an obvious area for challenge, and

this can even be seen now with some customers (e.g. NHS in the UK /Aarus University Hospital in Denmark) asking for reduced packaging in tenders and setting targets for CO_{2eq} reduction. The time needed to deliver improved sustainable efficiencies will be longer with Pharma as there is no one simple solution to medicines packaging CO_{2eq} reduction. Any change needs to be fully understood and proven as it must not compromise the safety of the patient or increase the risk of delivery failures. Another important factor is the whole Pharma industry has to work together as an aligned partnership for solutions to be viable. This is because no single Pharma company can tackle the bigger opportunities such as recycling and standardisation of packaging materials and pack formats. These are only two examples where landfill or incineration for medicines packaging can be reduced. With a joined-up industry roadmap real change can be implemented and this will need all stakeholders on board too. Green solutions should ultimately be a competitive advantage for all.

Pharma packaging components and formulations have evolved over time to be manufactured with more and more efficient processing. This includes minimising waste and there has been a focus on reducing, for example the use of solvents in active pharmaceutical ingredient (API) manufacture, through green chemistry initiatives. The packaging that the API is packed in (and the delivery devices that dispense some APIs) have evolved over the decades to offer enhanced performance, reliability, and patient centric benefits. Primary packaging materials such as PVC and aluminium laminates have been used in tablet and capsule blisters and HDPE in bottles. Glass is still used extensively in syringes and vials. As mentioned, what these materials have in common is that they are well understood, they perform appropriately, they have robust supply chains, they run efficiently on established production lines and are cost effective. However, the disposability of 'used' combination devices and other medicine packaging formats is an ongoing uncomfortable question. The devices are engineered to be robust, easy to use and perform with absolute reliability. The primary packaging materials are as mentioned developed and specified to offer appropriate protection to the medicine. They all use virgin contact materials (because they are mandated too) and typically derive from a portfolio of high-quality materials, each chosen for their specific characteristics.

With these formats an issue with medicine pack and device recycling is one of contamination (biological and medicinal). Collecting and effectively removing these contaminants will need resolving as will ensuring enough volume of used (and sometimes unfortunately, unused medicines) packaging is available to make recycling a viable proposition. Reverse logistics will need to be controlled and sorting materials made effective and safe. This is the reason the industry must work in partnership, and with packaging suppliers and healthcare providers (including pharmacies). Patients need to be part of the solution too and clear, frequent and simple messaging is needed to make sure used packaging collection is easy.

Any change needs to be fully understood and proven as it must not compromise the safety of the patient or increase the risk of delivery failures.

As well as being informed about 'take back' schemes how patients take their medicines needs to be improved, especially with more complex combination devices. These devices vary on how they operate and as can cause poor adherence, which is obviously wasteful. Solutions for this must be considered when developing devices (and new packaging) and effective training -where necessary- is an effective initiative to improve adherence. There has been an advance in the development of some 'smart' packaging and devices, and these certainly have a place (such as in clinical trials) but they have the challenge of often incorporating electronics and batteries and these are not easily recyclable. Any additional 'smart' solutions have to be carefully evaluated for their real added value to the patient (and the healthcare professional) and there needs to be a full understanding of how data will be managed from these devices plus other patient centric challenges such as refilling/replacing primary packs -and even replacing batteries-.

With the wide range of medicinal packaging platforms available there is a large choice for patients and each platform has its own inherent sustainability index. The sustainability index is usually measured as a CO_{2eq} value and today there is no clear guidance on what standards the Pharma industry should meet when it comes to sustainability. Healthcare providers and customers are

increasingly asking about metrics regarding the global footprint of medical devices, medicines and packaging and this especially ties into the former's own sustainability initiatives.

Consistent CO_{2eq} measurement methods ensure sustainability decisions can be made with a degree of accuracy. Having independent specialists (such as the Carbon Trust) undertake these Life Cycle Analysis (LCA) to build a clear data set for inhalation manufacturers to help them understand where the greatest impact comes from and which specific areas to focus on. These include:

- API (the active pharmaceutical ingredient can often account for much of an inhalers CO_{2eq})
- Use (such as recommendations regarding cleaning refillable devices, as 'total use' must be considered)
- Device/packaging (primary/secondary materials, energy to mould, waste, transportation)
- Production (including tertiary packaging materials, energy, waste, transportation)

Understanding the LCA data and sharing it with suppliers is key as these suppliers are often the device or packaging manufacturer (and even the API manufacturer as the market moves more into CMOs) and they themselves can be incentivised to be part of the total sustainability solution. As an aside, cost reduction initiatives are common within the industry and a typical default of CO_{2eq} reduction is usually an output when there has been a cost reduction program implemented. Having LCA baselines for all products and processes will be a future requirement for medicine manufacturers and these data driven metrics are going to become part of competitive tenders and this is already beginning to happen.

Designing packaging and combination devices for enhanced sustainability as core criteria of the medicines development process is another strategy that Pharma companies and their packaging suppliers need to consider as part of the 'toolbox' available to the industry. There is more use of Green Packaging Guides in companies that share/describe best practice and they now extend these principles to packaging and devices. Green Guides set out a series of 'rules' that ensure (and challenge) the design specifications of devices and related packaging. These Green Guides should be shared with suppliers, and they should also be revised regularly to ensure that the latest advances regarding Design for Sustainability are included. Alignment with suppliers' own sustainability initiatives should also be encouraged and awareness of these is imperative (such as the New plastics economy global commitment from the Ellen MacArthur Foundation).

Cost reduction initiatives are common within the industry and a typical default of CO_{2eq} reduction is usually an output when there has been a cost reduction program implemented.

In conclusion without doubt climate change is the world's greatest current threat. Every individual, every government, every organisation and every company must take accountability to reduce their CO_{2eq} output. As such, healthcare, healthcare suppliers and healthcare providers need to have clearly aligned and defined strategies to reduce the CO_{2eq} of their medicines and associated packaging/devices that they prescribe, produce, and dispense. The challenges and the threats are mounting for all manufacturing sectors and this extends to the Pharma industry. There is no single specific 'magic bullet' that will optimise the sustainability of what is made and consumed regarding medicine packaging platforms. It is only through a series of prioritised initiatives that packaging platform manufacturers and stakeholders can turn these threats and challenges into opportunities. This will require the whole industry (and again stakeholders) to be more aligned and take more accountability for future strategies for the short, medium and long term. Diseases will only increase as the impact of climate change reaches all parts of the globe and there is the imminent threat from pandemics as we have recently seen. Making and supplying affordable and sustainable medicines must be an ongoing target and as such the industry must leverage optimised materials, design devices using sustainable 'design guidelines', use the lowest GWP materials, improve adherence, measure LCA and share recycling investments. There is a 'toolbox' available, it just needs to be implemented.

Active Pharmaceutical Ingredient Manufacturing and Formulation Drive to a NET ZERO?

Author: Girish Malhotra, President, EPCOT International

Active Pharmaceutical Ingredient Manufacturing (API) and Formulation Drive to NET ZERO (Carbon Neutral)?

"Net Zero"[1] [emissions produced = emissions removed] is in vogue. It has significant value and will have huge impact on the planet if we do nothing. Speculated target dates to achieve the goal are 2025, 2045, 2050 or thereafter. There will be a firm date soon.

For the pharmaceutical industry "thereafter" might be the target to meet. This is based on magnitude of E Factor (environmental factor) from 2017 illustrated in Table 1[2]. It is difficult to say how much effort to date has been put in to reduce this factor. Based on the current status and the following analysis, it is most likely pharma has not done much. Thus the task is going to be formidable.

High "E-Factor" numbers[2] present an excellent opportunity to reduce emissions and waste quickly. Effort will be needed. This is my perspective. There is no financial or any other obligation with any educational/commercial or regulatory body.

	Tonnes per year	E Factor (Kg waste/kg product)	Total Annual Waste Tonnage
Oil Refining	106-108	<0.1	10,000,000
Bulk Chemicals	104-106	<1-5	5,000,000
Fine Chemicals	102-104	5-50	500,000
Pharmaceuticals	10-103	25->100	100,000

Table 1: "E Factor" in the Chemical Industry[2]

Reasons for Pharma's High E-Factor

To get to "Net Zero" in pharmaceuticals, which has the highest "E-Factor", we need to understand the reasons. They will facilitate in implementing the right solution/s.

Pharmaceuticals have two distinct components API (active pharmaceutical ingredients) and their finished dose form (FDF) that are produced by blending API with inert excipients. Discussion here is focused on small molecule drugs that like fine/specialty chemicals, are similarly synthesized. Pharma's highest "E-Factor" is due to its manufacturing practices. Improved manufacturing will lower the "E-Factor" and drive to "Net Zero".

One interesting fact for the pharmaceutical industry which has been least understood by the world at large is that a small quantity of API is needed to produce large number of tablets. Table 2 is an illustration of the relationship between API needed and the produced tablets per year.

Patients	Milligrams	# of Tablets/person/yr.	API, Kilograms/year	Tablets/yr.
50,000,000	1	365	18,250	18,250,000,000
50,000,000	50	365	912,500	18,250,000,000

Table 2: API and Tablets per year Relationship[3]

Using best estimates, annual global need of these three randomly three selected drugs are illustrated in Table 3. Based on annual need, each API can be produced at a single plant. Multiple formulation plants would be needed to convert this plant's output into solid dosage.

However, at present these API and finished dosages, are being produced at multiple API and formulation plants [4]. Processes for each drug most likely are not the most efficient and have a high "E Factor".

	Omeprazole	Metoprolol	Modafinil
Population	7,800,000,000	7,800,000,000	7,800,000,000
Global need, %	14	1	0.06
# people	1,092,000,000	78,000,000	4,680,000
mg needed/day	40	50	200
Tablets used # days/yr.	50	365	365
Total mg needed/day	43,680,000,000	3,900,000,000	936,000,000
API need Kg/Yr.	2,184,000	1,423,500	341,640
Current Number of API Sites	94	29	51
Current Number of FDF Sites	768	70	338

Table 3: Annual API Need for the illustrated drugs

Why are so many sites are producing the same API and their formulations? There has to be some rationale. The only explanation can be combination of high profitability of each producer, no external pressure to reduce their manufacturing related emissions, and regulatory requirements and hindrances.

The large number of plants for API production and their formulations[4] tell us that each lacks value of economies of scale. Lower number of plants will use better technologies and should have significantly reduced waste.

Fundamentals of chemical engineering teach that. Need to improve and lower pharma's "E-Factor" has been well recognized [5,6,7,8,9] but not much progress has been made to remedy the situation. Lack of progress suggests that the producer companies see ZERO or very low return in manufacturing technology innovation.

What is Needed to Lower Pharma's E-Factor

In reality, API manufacturing and formulator companies don't have to innovate much to lower their "E-Factor". They are practicing all of the necessary manufacturing technologies. They have to repurpose and re-invent these technologies, unit processes and unit operations[10] and the knowledge that has existed and been practiced since the beginning of the twentieth century. Pharmaceutical manufacturing has to relinquish its "mortar pestle" mode and proactively apply the principles of science and engineering differently. In this effort pharma cannot forgo and has to practice FDA's cGMP[11] requirements as their way of life.

Companies don't have to rely on the regulators and the equipment vendors leading them as to how and what to do to innovate and produce quality products. Actually the FDA have made innovation and continuous improvement more difficult by prolonged approval times[12,13] and meaninglessly suggesting what and how manufacturing should be done. Review and repurpose of the existing practices has to be the modus operandi. Nondestructive creativity is needed[14,15] if the companies want to repurpose and reinvent. Some of the methods[16,17] have been reviewed.

For the pharma to lower its "E-Factor" or achieve high "green chemistry" marks, they not only have to adopt "good chemistry" but also practice "good chemical engineering" as their way of life[8]. Pharma manufacturers have the command and the knowledge of their patient's needs and what is expected by the regulators. Pharma has to relinquish fitting different processes in the available equipment[18,19]. Many may not believe but fitting processes in the existing equipment requires use of excessive amount of solvent use, a major cause of high "E- Factor". Though recovered and re-used, it still is a major contributor to pharma's "E- Factor". Formulation practices have to reconsidered as the existing technology applied properly can lower "E-Factor" significantly.

Actually the FDA have made innovation and continuous improvement more difficult by prolonged approval times[12,13]

Each product illustrated in Table 3 can be produced using continuous synthesis[20] process. Thereby minimizing emissions from each synthesis plant. Solid dosage for these products can be similarly produced in minimum number of formulation plants. "E-Factor" from these continuous production plants would be magnitudes lower than over 1,350 plants currently being used.

If the waste numbers from Table 1 are applied to the three drugs in Table 3 and "E-Factor" from Table 1 are applied numbers illustrated in Table 4 would be the waste for each of the API. Actual emissions for these drugs may be different but the industry average are used to illustrate their impact. Bold numbers are the emission numbers if they were reduced.

E-Factor	Omeprazole	Metoprolol	Modafinil	Total Waste, Kilogram/yr.
Kg. Waste per Kg. Product	Waste for each drug at different levels, Kilogram/yr.			
100	218,400,000	142,350,000	34,164,000	394,914,000
50	109,200,000	71,175,000	17,082,000	197,457,000
25	54,600,000	35,587,500	8,541,000	98,728,500
E-Factor numbers if emissions are reduced.				
5	**10,920,000**	**7,117,500**	**1,708,200**	**19,475,700**

Table 4: Waste Generated for the APIs (Table 3) using Table 1 Waste numbers

Pharma has the tools and means[16,17]. Additional tools and means are reviewed in a manuscript under preparation[21].

Pharma while keeping its "market centricity" has to adopt "process centricity"[22] from the onset rather than believe that the manufacturing processes will be improved tomorrow. It would be like believing that tomorrow will come, if it ever will come. Any changes made in manufacturing processes after regulatory approval can influence the drug performance and are a major cause of lack of most process improvements.

Global effort is needed to lower pharma's "E-Factor". Adopting uniform global effluent standards[23] would significantly reduce "E-Factor". Regulators rather than becoming an encumbrance would have to actively change their "modus operandi" for reducing the approval time for brand and generic drugs[12,13]. Today the speculated ANDA (abbreviated new drug application) approval time is between 36-48 months as official approval times are not available. NDA (new drug application) approval time, unless emergency use authorization, are anyone's guess.

The overall task is not going to be easy. If it was, it would have been accomplished long time ago. In addition, there will be significant resistance from the involved businesses, regulators/governments and even patient communities.

Minimizing/reducing the "E-Factor" has multiple wins. They lower manufacturing costs, protect public health and the environment and also lower the drug costs to the public.

We need to ask ourselves "What would be our legacy for the generations to come?" Let us write it.

Adopting uniform global effluent standards[23] would significantly reduce "E-Factor"

Environmental Sustainability in Pharma: A view on Pharma's progress towards positive impact

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The pharmaceutical industry is no stranger to environmental regulation, often controlling emissions of air and water pollutants in order to minimise damage to the local environment from toxic and pharmaceutically active chemicals.

Over the past couple of decades, since the Kyoto protocol in 1997, a broader movement towards reducing the effects of climate change have been introduced by nations aimed at all industries. The latest evolution of this movement is the Paris agreement, ratified in 2015, that specifically aims to keep global warming at no more than 1.5°C of pre-industrial levels by 2050[24]. The EU is aiming to go a step further with its European Green deal, introduce in late 2019, where it has committed to become the first climate neutral continent by 2050 and has allocated over €1tn to its objectives. These initiatives aim to provide a cleaner environment, affordable renewable energy, resilient industry, longer lasting products and a better quality of life[25].

There is a strong argument that health systems as a whole should be frontrunners in limiting the impact of climate change, as it strikes at the heart of population health: a changing climate will drive poorer outcomes, increase mortality and health inequity. These can arise from multiple causes, among them severe weather, extreme heat, a changing ecology of disease vectors, increased allergens and geopolitical conflicts over scarce resources.

The reality, however, is that unlike high-emission industries such as transport, mining and energy, the healthcare sector has generally kept a low profile in the public eye when it comes to sustainability questions. This is evidenced by the lack of research activity on quantifying the impact of the industry on the environment; one of the very few studies in circulation suggests healthcare contributed 4.4% of the world's carbon footprint in 2014[26] and likely to have increased since. When it comes to pharma, a study suggests that it is smaller in revenue, yet more polluting than the automotive industry, which may come as a surprise to many. The findings also suggest that there are large variations of CO2 emissions between different companies of a similar revenue size[27]. Note that they did not control for the disease area focus of these companies – a primary care specialist will have different logistical and manufacturing challenges than a company focused on rare diseases.

In addition, climate change will affect the pharma industry through various internal and external factors, some of which are listed in *Figure 1*. Broadly, these factors can be split into upstream and downstream effects that will either affect pharma or those where pharma can influence. These factors are not mutually exclusive and pharma will have a varying degree of influence over its ability to control these challenges, for example minimising effluents in water and air pollution at manufacturing sites are easier to control than shifts in burden of disease or cultural attitudes towards health.

Pharma companies are subject to a country's regulations regarding sustainability and the environment, for example they must comply with legislation regarding clean air and water standards, such as the EPA's Management of Hazardous Waste Pharmaceuticals regulations in the US.

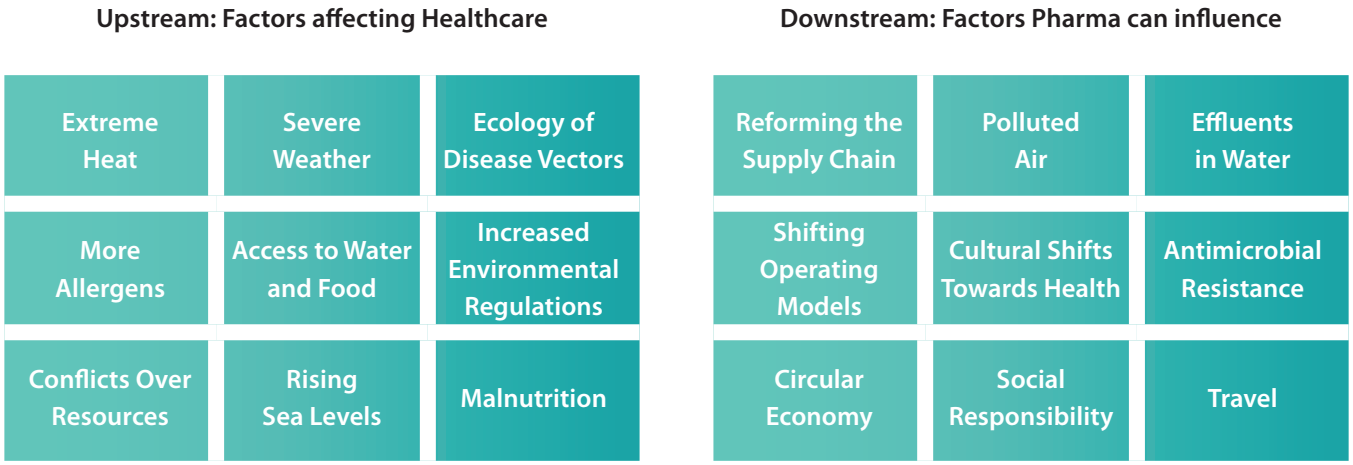


Figure 1: Upstream and Downstream Environmental Factors • **Source:** IQVIA European Thought Leadership

However, there are few regulations that directly target the pharma industry on areas such as reductions in greenhouse gas emissions and conservation of water.

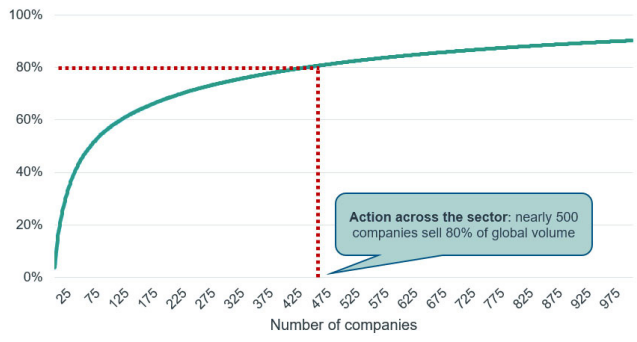
Instead, the pharma industry has been looking to produce its own guidelines and take action proactively through industry bodies and think-tanks. The European Federation of Pharmaceutical Industries and Associations (EFPIA) recently released a white paper on climate change[28] outlining its members commitments to climate change. Several larger pharma companies have also come together to release the Biopharma Investor ESG Communications Guidance 2.0[29], which highlights areas of Environmental, Social and Corporate Governance (ESG) that pharma companies should prioritise.

These guidelines contain forward looking commitments to sustainability and incorporate standardised metrics to track commitments. However more needs to be done from industry bodies to advance guidelines into concrete action points that can be adopted by specific sub-sectors, such as companies operating within biotech, large pharma, generics, API, FDF, CDMOs, CROs, MedTech, packaging, amongst others.

Major public pharma companies have already shown leadership in these activities: Sanofi reduced its CO_2 emissions from refrigerants by 40% since 2015 levels, Pfizer being the first in the industry to approve Science Based Targets in 2015, Roche and Novartis historically running long-standing programmes dedicated sustainability.

This is a good start, and expected from industry leaders, yet more needs to be done to increase awareness and action in smaller, private companies based in emerging economies as they frequently have a small molecule generics business model: manufacturing with low margins, but with a global reach. As of June 2021, 20% of all prescription medicine volume sold globally came from 10 companies and 30% from 20 (IQVIA MIDAS MAT Q2 2021, Rx-only). To achieve significant change impacting 80% or more of the supply chain, around 500 companies need to come together to drive change (*Figure 2*). Of these 500, 40% of them are headquartered in India or China, 30% in Europe and 20% in the US which offers the possibility for cooperation from major jurisdictions. Further compounding the complexity is that these manufacturers often rely on multiple partners to manufacture their API intermediates, excipients and raw materials; this is why supply chain transparency is such an important area to tackle this problem.

Figure 2: Global Rx Volume share per company *(Standard Units, 2021)*



Source: IQVIA European Thought Leadership; IQVIA MIDAS MAT Q2 2021; Rx-only

The top 5 areas that we have identified as key challenges (*Figure 3*) that pharmaceutical companies need to address in the near future are:

1. **Environmental, Social, and Corporate Governance.** A greater shareholder expectation of accountability. There needs to be increased awareness and incentives to engage smaller companies and generics manufacturers

2. **Water Use and Quality.** A Reduction in use of fresh water and greater scrutiny on toxic and active effluents

3. **Circular Economy**. Reduce waste and design products that are greener and more benign

4. **Reforming the Supply Chain.** Introduce greater transparency to track emissions and improve procurement

5. I**ncreased Environmental Regulation.** Enforcement of regulations will likely increase, and pharma must be ready to proactively engage regulators

These factors will inevitably affect the internal and external pressures on a pharmaceutical company. Externally, investors will scrutinise how board members are selected and demand greater transparency and action. Regulators will force processes and that will affect operations from R&D through to manufacturing. Internally, Environmental, Social and Corporate Governance officers will be assigned to oversee initiatives and work with COOs to drive change within the company. To ensure this happens in time, strong vision and leadership is required coupled with accountability from all employees across the entire value chain; companies need to communicate effects from higher-order collaboration derived from individual actions.

One of the key tools to drive change from supply partners is to implement sustainable criteria for procurement functions. Public purchasing in healthcare systems has a strong part to play in initiating the cascade of action. The movement towards greater sustainable criteria in tenders began with the Nordic countries, but is quickly gaining traction in other western nations. A study in 2019 using 80,000+ Most Economically Advantageous Tender (MEAT) lots from IQVIA's THOR database across Northern Europe showed that MEAT tenders containing "Environmental" criteria peaked in 2016 and declined to 10% of all MEAT lots by 2019 (*Figure 4*). The weight of Environmental criteria broadly stabilised around 5%. Note that other related criteria such as sustainability, recycling, social responsibility, lifecycle cost were excluded from this chart, and these will have increased in proportion. As we look ahead, criteria that address environmental matters will increase in the near future and will begin to be adopted by smaller countries as stakeholders align to modernise tender practises.

As the industry reacts to pressure from social and environmental concerns, it needs to find ways to align profitability with greener operations. Recycling and purchasing renewable energy are proven methods of reducing waste and emissions, yet more focus is needed

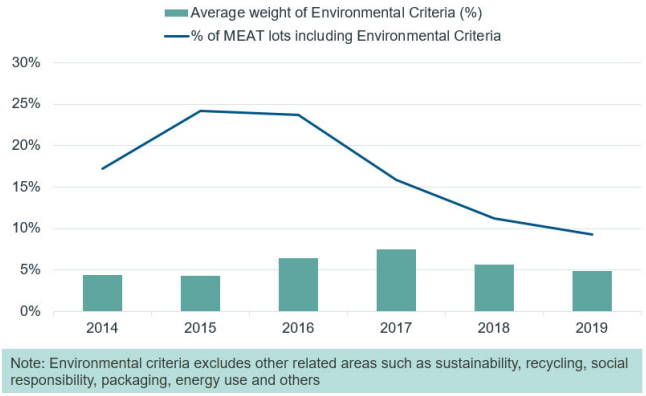
Figure 3: Five Key Priority Areas for Pharma • **Source:** IQVIA European Thought Leadership

to design better medicines from the ground up. These might include greener synthetic routes, lower API use through novel formulations, or reusable devices. A green shift in early product design would be a real win for the industry as it attempts to align environmental sustainability with commercial success. Combined with value chain transparency and lifecycle analysis, this could pave the way for an industry-wide certification system with a sustainability score linked to medicine batches.

Currently, pilot projects and green devices show great promise, but their uses are confined to miniscule volumes compared to global medicines provision. More needs to be done by the industry to set ambitious science-based targets and influence supply partners to collectively bring environmental concerns into the mainstream.

For more information on green products or other environmental topics, please reach out to aurelio.arias@iqvia.com

Figure 4: "Environmental" Criteria use in tenders
(Denmark, Norway, France, Spain, and the UK 2021)



Note: Environmental criteria excludes other related areas such as sustainability, recycling, social responsibility, packaging, energy use and others

Source: IQVIA European Thought Leadership; IQVIA THOR

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For news, reports, webinars and other resources on sustainability in Pharma, please visit https://www.cphi-online.com/dev/2021/sustainability.html

Interested in getting involved in our sustainability mission?
Please reach out to Silvia.Forrova@informa.com