

Conference Report

Sustainability Across the Pharmaceutical Value Chain

How Switzerland Could Take a Leading Role in Promoting a Greener Approach

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Abstract: The sustainability of the pharmaceutical industry has aroused interest from various sectors and disciplines, including chemistry, biology and engineering. Given the Swiss drug sector's innovative engine and enormous economic importance, a Swiss Biotech Day panel discussion was held in May 2022 in Basel to address the question of how “sustainability across the pharmaceutical value chain” can be edged forward in Switzerland. Roche, Lonza, Pheida, ETH, the Swiss Academy of Engineering Sciences (SATW), and a newly established collaborative, Circular Carbon for Chemistry (ccLoop) joined forces and agreed that sustainability must become a key strategic goal for the industry in Switzerland. The panel looked at the sustainability challenge, at how a green transition can be achieved faster, and at how industrial biotechnology applications can improve industry's performance, energy efficiency and product value while yielding viable sustainable solutions to protect our environment. Switzerland is a leader in drug development and manufacturing. By placing greater energy and resources on the sustainability equation, we ensure continued leadership and a greener world. ‘Swissness’ will increasingly have to denote effective drugs produced sustainably.

Keywords: Biopharmaceutical supply chain sustainability · Energy efficiency · ESG metrics · Green drug manufacturing

Introduction

“Socialism collapsed because it did not allow prices to tell the economic truth. Capitalism may collapse because it does not allow prices to tell the ecological truth.” This is a 30-year-old statement from a Norwegian petrochemical executive, an industry which has been pilloried for over two decades and is still seen as the major environmental sinner.^[1]

A closer look, however, reveals that while the petrochemical sector's greenhouse emissions are centre stage, emission intensity measured in tons of CO₂ equivalent per million US dollars of revenue is higher in other industries.^[1] While emission comparisons must be treated with caution given the obscurity of many carbon and Environmental, Social, and Governance (ESG) metrics, it is evident that pharmaceutical production and supply chains are also significant contributors of CO₂ emission. This is probably because ESG is already high on the industry's agenda and also because the industry is a powerful force for good, driving innovation in the life science sector.

Despite this, there is a growing belief amongst Swiss experts that in the coming years, it should be possible for Switzerland's pharmaceutical and chemical sector to take leadership in improving its environmental credentials. In a position paper, the members of scienceindustries, representing the Swiss chemical and pharmaceutical industry, acknowledge the reality of climate change and describe the priorities and measures required to reach the goal of net zero by 2050.^[2] Encouragingly, their data indicates

that not only is the industry's fuel CO₂-intensity on target, but that since 2012, and even more so since 2018, actual values have been well below the target path (Fig. 1)

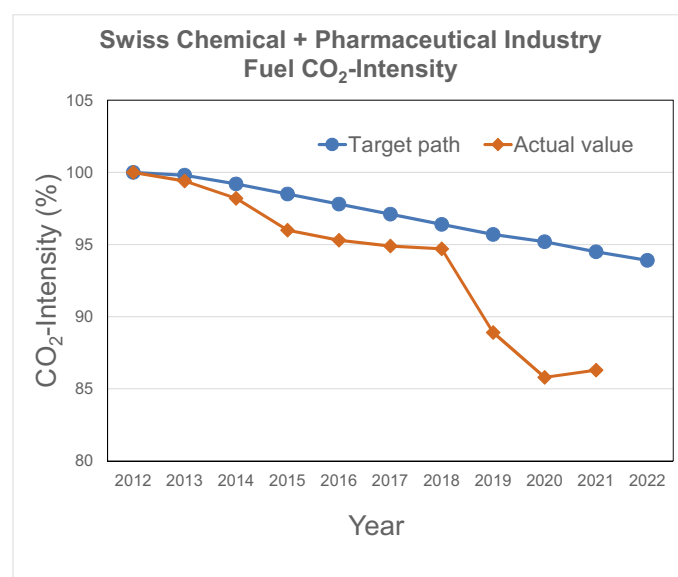


Fig. 1. CO₂ fuel intensity of major scienceindustries member companies (target agreements vs. actual values for 127 production sites). The Swiss association scienceindustries coordinates sustainability activities of about 250 member companies from the chemical, pharmaceutical and life sciences sectors. Data: Energy Agency of the Swiss Private Sector EnAW 2022.X

Following on from this success, next steps include strong emphasis on the environmental aspect of ESG, improving our ability to measure environmental performance, and investment in innovative green technologies and production methods in which Switzerland is or has the potential to become a world leader.

The Sustainability Challenge

Over the last decade, the drug industry has made enormous efforts to improve formulations, processes, and logistics. However, more could and should be done. Fortune/Deloitte's 2022 Life Science CEOs survey asked what supply chain actions CEOs expect to take in the next 12 months. Only 17% of CEOs said that they plan to expand sustainability/climate change initiatives, while 50% plan to expand the supply chain ecosystem with more partners.^[3]

The opportunities for sustainability are particularly significant in the small molecule pharma sector, which is still responsible for around 90% of global sales. The challenge here is the high E factors (ratio of kg waste/kg final product). As the complexity of optically active small molecule drugs increases, these E-values^[4] are reaching prohibitively high numbers with E-factors in excess of a thousand.^[5]

This is particularly relevant for Switzerland, given that 50% of our CHF 260 billion in exports is comprised of chemicals and pharmaceuticals.^[6] Embracing greener practices and processes

across the biopharmaceutical value chain is therefore an opportunity to maintain and develop Swiss leadership of the sector and, we argue, it must become a key strategic goal.

Swiss Biotech Day Panel Discussion and Participating Companies

This panel addressed the question of how ‘Sustainability across the pharmaceutical value chain’ can be edged forward in Switzerland and beyond.

While the topic ‘sustainability’ is anything but new, it rarely has priority in the industry’s congress agendas. The Swiss Biotech Association and the Swiss Academy of Engineering Sciences (SATW) organized a panel (Fig. 2) entitled ‘Sustainability across the pharmaceutical value chain’ during the 2022 Swiss Biotech Day in Basel to discuss how a green transition can be achieved faster and how industrial biotechnology applications can improve industry’s performance, energy efficiency and product value and thus yield viable sustainable solutions to protect our environment.



Fig. 2. The Swiss Biotech Day panel: from left to right: Martin Held, Sanna Fowler, David Hampton, Ulla Grauschopf.

Moderator: Hans-Peter Meyer – Expertinova AG, Swiss Academy of Engineering Sciences (SATW)

Panelists:

- Sanna Fowler, Head of Divisional Projects Biologics, Lonza
- Ulla Grauschopf, Head of Device & Packaging Development, F. Hoffmann-LaRoche
- David Hampton, Director, Pheida
- Martin Held, ETH Zurich, ccLoop – Circular Carbon for Chemistry Loop

The panelists represented an interdisciplinary group active in the large and small molecule industrial biotechnology.

Lonza (<https://www.lonza.com>) is a leading global Swiss CDMO (Contract Development and Manufacturing Organization) active in cell & gene therapy, biologics, antibody drug conjugates (ADCs) and small molecules. Last year, the company generated sales of CHF 5.4 billion with a workforce of over 16'000 employees worldwide.

F. Hoffmann-La Roche (<https://www.roche.com>) is the largest pharmaceutical company in the world and the leading provider of cancer treatments. In 2021, F. Hoffmann-La Roche ranked first in Rx sales output as well as well as R&D budget, and the company generated sales of CHF 63 billion, with nearly 98'000 employees worldwide.

Pheida (<https://www.pheida.com>) is a Swiss-based biotech company focused on deploying new biotechnologies at scale to accelerate the drive to Net Zero. It sees multiple opportunities

to use synthetic biology and advanced process engineering to reduce emissions of GHGs and other pollutants and to remediate contaminated land, especially for the energy, chemicals, mining and agricultural industries.

Circular Carbon for Chemistry or ccLoop (website under construction) is a new Swiss collaborative initiative spearheaded by ETH Zurich and Roche, which currently has five industry members with several others planning to join. ccLoop wants to promote the use of biobased materials and the de-fossilisation of organic chemicals and plastic materials supply in general.

Sustainability as a Competitive Asset

Item 12 of the United Nation’s goals for sustainable development focuses on ‘sustainable consumption and production’, and customers increasingly want to know whether processes are sustainably designed with sustainability goals in mind.

The panel found that sustainability can improve the competitive advantage of the Swiss biopharma business. Driving improvements, however, requires data clarity around market opportunities, costs, and margins. Modelling and life cycle analysis adapted to biopharma would allow the impact of new technologies and facilities to be quantified, making a clear case for entrepreneurs and investors. Agreement on how to measure environmental Cost of Goods Sold (E-COGS) would have an equally positive impact. The industry is well placed to manage change, the panel argues, and the earlier this is planned the better, as delayed changes will invariably have significant regulatory implications.

Committing to Change: A Multinational Developer’s Perspective

Biopharma is well established, highly regulated and contributes to the world’s health. Unsurprisingly, it generally ranks well with respect to ESG (Environmental, Social, Governance) as it is fully on board with social and governance objectives. The next step is indeed to focus on the environmental impact.

While analysts expect ESG to remain front and centre for the Life Science industry in 2022,^[3] only 25 of the top 200 global players consistently reported their direct and indirect greenhouse gas emissions in the past five years. This is, however, changing as biopharma companies, big and small, are setting ambitious targets for sustainability.

Roche has made a strategic commitment to half their environmental impact of its operations from 2019 to 2029, and to reduce green-house gas emissions to real zero by 2050. Ulla Grauschopf, panellist, emphasized that in 2021 Roche was among the top three most sustainable healthcare companies in the Dow Jones sustainability indices. Each business unit at Roche is tasked with analysing their own specific impact and footprint for the products they are developing. With respect to delivery devices and packaging for example, the issues are about non-sustainable materials, pack sizes, re-usability and/or re-cycling of components, energy savings, optimizing infrastructure, reduction of plastic waste, reduction of storage time temperatures and reduction of air travel as part of the development activities.

Product stewardship programs amended by cradle-to-grave/life cycle analysis have been applied since 2021 for thirty Roche products with the goal to increase the score of this 2021 baseline by 25% by 2025. Other pharma companies have adopted or plan to adopt similar strategies.

The bigger challenge is with the small innovative developers taking high risks with new molecules. Drug assets need to go from lab to clinic with a defined amount of investor money, and this is often in conflict with the sustainable manufacturing and delivery process objective. The drug development process is *per se* costly and peppered with uncertainties. Sustainable manufacturing is now an additional challenge but also an opportunity for innovative enterprises to differentiate them from the rest.

The Role of CDMOs

Today's contract development and manufacturing organizations (CDMOs) have a double mission. Lonza not only needs to reduce its footprint to meet its own targets but also ensure that it supports customers who are looking to reduce their scope 3 emissions – those that are the result of activities from assets not owned or controlled by the reporting organization, but that indirectly impact its value chain. As Lonza's Sanna Fowler confirmed, the company is focused on two main sustainability tracks.

First comes reducing the energy footprint of current operations with the ambition to source all electricity from carbon-neutral sources by 2025 and ultimately aim for net-zero greenhouse gas emissions by 2050. Lonza also plans to implement solvent recycling and wastewater reduction.

Second, Lonza has developed engineering guidelines to achieve the highest possible efficiency in new facilities. Design standards for HVAC, Steam and WFI (water for injection), cleaning processes and compressed air, for example, are in place, intended to reduce energy consumption and ensure assets are set up for the future. Increased CAPEX for green solutions will not only reduce environmental impact but has the potential to have a long-term, positive impact on OPEX. A worthwhile medium- and long-term investment.

The fastest growing area in the CDMO market are biologics and cell & gene therapies, which provide an opportunity for novel processes and standards. Yet our highly regulated industry can limit the scope for change whereby new methods and procedures take too long to be implemented. Take perfusion cell culture^[7] as an example. While perfusion allows much higher volumetric productivities, it is not yet frequently used. Nevertheless, infrastructure and process methods are key and must be increasingly geared and developed towards sustainability. Monitoring the impact of a given therapy using Process Mass Intensity^[8] (PMI), namely measuring total input requirements per API output is also recommended to consider how processes can be improved.

The Energy Opportunity

Compared to sustainability improvement with regulatory implications, energy efficiency is a low hanging fruit. In Switzerland for example, we can increasingly use 'green' energy sources. As Lonza's Anna Fowler emphasized, Swiss manufacturers are in the fortunate position of being able to utilize hydroelectric energy, which means that energy-intensive monoclonal antibody production in Switzerland using hydroelectric power is 'greener' than antibody production elsewhere. This is particularly relevant to the industry because 70% of biologicals sales are MAbs^[9] and in the UK, for example, 43% of electricity is still from fossil fuels.^[10]

Industrial manufacturing facilities are typically very large buildings with mostly flat rooftops, which implies an opportunity for photovoltaic installations. The use of energy for heating, cooling mechanical installations or pressurized systems must be reduced to a minimum using the best engineering principles. Last but not least, biopharmaceutical products typically require cold chains or even ultra-low temperature for transportation, which significantly impacts the overall eco-balance. Thus, improving product stability at higher temperatures must be a development criterion at a very early stage to save energy.

You Can't Do What You Can't Measure

While it is not always evident what specific technologies can do to reduce the environmental footprint, a changing appetite for sustainability is under way.

Life cycle analysis helps to pinpoint issues and enables corrective action along the value chain. Data clarity is relevant not only on processes, but on the market opportunities, costs and margins to make a clear case for today's and tomorrow's more ecologically conscious investors.

The industry needs modelling and life cycle analysis specifically adapted to biopharma to determine how best to evaluate the impact of new technologies and facilities and avoid the risk of 'stranded assets', namely when companies concentrate on a specific step which does not consider the complete value chain. The industry also needs common standards on how to measure environmental Cost of Goods Sold (E-COGS), panellists agreed.

In essence, driving sustainable change across the pharmaceutical value chain requires data clarity and adapted descriptive models. Certainly, we cannot do what we can't measure, especially in the era of big data and AI.

Leveraging Network Effects

While sustainability efforts made by leading biopharma developers and CDMOs are of paramount importance, action must not be limited to individual companies, the panel found.

Pheida's David Hampton emphasized that while there is significant interest in sustainable operations, there is often a focus on incremental improvements to the existing system that allows companies to continue 'business as usual'. Generally, people do not consider sustainability across a network, but focus on their own turf, failing to consider how an entire value chain can become more sustainable, which in turn will affect their business model. Critically, clear understanding of the value chain footprint and the changing economics of sustainability (*e.g.* carbon or other pollutant pricing) can create major changes in the competitiveness of different processes and, as Pheida has recognized, novel industrial biotech solutions can deliver big sustainability gains and substantial profits.

We must design, develop and model sustainability with respect to the entire value chain, rather than individual steps, the panel agreed. Moreover, the industry must be aware of progress outside their specific areas. Technologies that existed in the lab fifteen years ago but never made it into reality, may become financially viable as sustainability requirements take centre stage and relevant technologies improve. Pheida suspects that there are many interesting biotech and processing improvements languishing in the labs and IP records of major pharma and chemical companies that could now be of value given the opportunities to monetize improvements in sustainability.

The scope for joint action is clear. Even if many challenges are specific to the biopharma sector, the industry can learn to implement best practices from other sectors. There are important examples of coordinating initiatives here, such as the BioPhorum Operations Group (BPOG)^[11] working on single-use plastics.

The Carbon Loop for Chemistry (ccLoop) initiative is founded on the understanding that overlapping interests should lead to inter-company collaboration and deals between companies and sectors and include academia and governmental institutions, allowing industry players to join forces to generate sustainability opportunities at a profit. Solutions considered by the ccLoop initiative can and should be developed for more than one stakeholder, namely with the involvement of the entire community. In this respect, ETH's Martin Held emphasized, data which indicates the extent to which this could be achieved are not yet available and represent an important avenue for the future.

ccLoop will also work to realize opportunities in biobased materials. For example, in chemistry there is the potential to improve supply chain stability, rather than remaining dependent on volatile fossil feedstock markets. Another problem is that sustainability is calculated for single steps or products instead of considering the supply chain or asset life cycle. An intercompany platform would facilitate this type of analysis.

The panel also raised the question as to whether the pharmaceutical industry needs new solutions for solvents. There are high-level discussions to build a plant in Europe for the

conversion of wood to jet-fuel – why not produce solvents with a higher margin for the pharmaceutical companies instead? Pressure must come from the whole ecosystem, internally from the companies and externally from customers and regulators. The need to work together and join forces was repeatedly stressed.

Regulatory Directives Help

Regulatory directives are in place but many of these focus on the envelope and are not designed with bioproduction in mind. Moreover, they will (and should) vary significantly across geographies. For example, building standards are represented by BREEAM,^[12] Minergie, LEED^[13] and many other local standards. Switzerland is perhaps under-regulated compared to other countries, but regulations on sustainability are likely to be revised in the next ten or twenty years.

Most developed countries plan to enact laws for the regulation of CO₂ emissions in chemistry. It will be important to look at how these regulations will impact the competitiveness of Swiss manufacturers of chemical and pharmaceutical products outside their national markets. We need to consider the whole picture and the potential impact on the end users and ensure that ‘Swissness’ remains synonymous with fairness, precision, and reliability.

While regulatory pressure has a very significant role to play, investors and customers are key in driving change, the panel found. They are expected to drive the sense of urgency required to move forward. Don’t wait for regulations to change, take the lead by listening to what the market is saying.

The Role of Innovators

Switzerland is consistently among firsts across different innovation indexes. According to the Global Innovation Index 2021 (GII) for one, Switzerland remains the world leader in innovation for an eleventh consecutive year.^[14] Switzerland has also been named the most innovative country in Europe 2021 by the European Commission’s ‘European Innovation Scoreboard’, where the EC states that, “Switzerland’s strengths are in attractive research systems, human resources, and intellectual assets”.^[15]

Swiss innovation, whether developed at home or *via* international networks has the potential to increasingly revolutionize its vast biopharmaceutical sector. For this to happen, big pharma must look outside its own immediate area, connect the dots, and be open to innovative startups, SMEs and to multi-disciplinary groups.

For this innovation to take hold however, multinationals need to give innovators the opportunity to test their products and solutions at an early stage. As Stripe, McKinsey, and Meta found with their ‘Frontier Fund’ for nascent carbon removal techniques, early supply agreements encourage investors to pour money in risky new technologies.^[16] Sometimes it’s better for big industry to be early purchasers of nascent technologies rather than investors, McKinsey *et al.* found.

Conclusions and Take-home Message

Sustainability is like eating an elephant – it’s massive and we need to break it down. The danger is that we are so overwhelmed by the challenges that we do nothing and fail to set targets. Start anywhere you can with the elephant – it will take time, but the key is to get started. Table 1 provides a flavour of what can be done as has been suggested by our panel.

Ultimately, any endeavour is successful through the passion and ability of the people who execute it. Thus, the commitment starts with each of us as individuals, and we must do what is within our control. At the same time, we must think of sustainability as a whole, considering the entire value chain.

Certainly, the need to go to the clinic as soon as possible with a limited amount of cash will not go away – time and money are of the essence. Process changes made post-approval are difficult, especially for those requiring cell lines that are geared towards maximum productivity. Generally, an about-face to prioritize sustainability will be expensive.

While much innovation comes bottom-up from startups and SMEs, not all solutions are best developed by each company individually. There is considerable scope for cross-industry collaboration. There is a need for coordinated and innovative projects. Cooperation is needed along the value chain as well as across industries to avoid missing opportunities and to realize the benefits of scaling.

Nevertheless, and most importantly, sustainability should be seen as an opportunity to be more competitive, rather than a cost. The panel agreed with ETH’s Martin Held when he concluded that that ‘Swissness’ remains synonymous with fairness, precision, reliability, and increasingly sustainability. Indeed, if we play it right and focus our energies, ‘Swissness’ may serve as a new *pharma brand denoting effective drugs produced sustainably.*

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Table 1. Pharmaceutical value chain: Sustainability challenges and emerging solutions

Value Chain Step	Sustainability challenge	Solutions include
API Manufacturing	<ul style="list-style-type: none"> Energy and water consumption HVAC, purified water, WFI, cleaning processes, single use plastic and bioreactors Solvent requirements Reduce PMI and E-Factor to the maximum 	<ul style="list-style-type: none"> Green energy/photovoltaic roof tops New USP / DSP technologies Advanced monitoring and modelling, Process Mass Intensity (PMI), Digital Twins Digitalization Environmentally friendly solvents
Fill and finish	<ul style="list-style-type: none"> Energy and temperature control requirements Plastic packaging 	<ul style="list-style-type: none"> Green energy/photovoltaic roof tops Quality recyclable plastics Novel packaging technologies & materials
Transport & Logistics	<ul style="list-style-type: none"> (Ultra-low) Cold chain requirements for biologicals and vaccines 	<ul style="list-style-type: none"> Green energy Novel cold storage technologies Increased API stability & room temperature/2°–8°C drug product formations
Point of sale/ consumer	<ul style="list-style-type: none"> Cold storage Plastic and other medical waste disposal 	<ul style="list-style-type: none"> Green energy Novel cold storage technologies Recycling technologies Consumer education/behaviours change Apps
Across the value chain	<ul style="list-style-type: none"> Energy, storage, and plastic requirements Recycling of medical waste/possible environmental API pollution 	<ul style="list-style-type: none"> Life cycle analysis Monitoring and Modelling PMI Standards for environmental COGS Implement innovative sustainable solutions Industry 4.0 and IoT

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[4] E-factor: kg of waste produced for each kg of product produced.

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[7] Perfusion is a continuous manufacturing method, where cells grown in a bioreactor are retained (e.g. by filtration) and the culture medium containing the product collected after the bioreactor.

[8] Process Mass Intensity (PMI): The PMI for biologics is defined as the total mass input in kg of water, raw materials and consumables to make 1 kg of active pharmaceutical ingredient. This value is on average, 7'700 kg for monoclonal antibodies.

[9] <https://bioprocessintl.com/business/economics/the-market-for-therapeutic-mab-products/>

[10] 'UK Energy in Brief 2021', https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1032260/UK_Energy_in_Brief_2021.pdf.

[11] BPOG BioPhorum Operations Group of 90+ experts from biopharmaceutical end users, manufacturers and suppliers discussing challenges and trends in the industry. Founded in 2004 it is driven by the industry's increased use of Single Use Systems (SUS).

[12] BREEAM: Building Research Establishment Environmental Assessment Methodology.

[13] LEED: a certification provides a framework for green building design, construction, operation and performance.

[14] https://www.wipo.int/global_innovation_index/en/2021/, accessed on June 9, 2022.

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