Interview: Taking Sustainability Beyond Compliance

In this exclusive interview, **Prof Hanns-Christian Mahler** of **ten23 health** engages in a wide-ranging discussion with ONdrugDelivery's Guy Furness about current challenges and trends in the drug delivery industry, particularly on the topic of sustainability – its advantages, difficulties and why companies should aim to do more than the bare minimum required by the regulation.

Q What do you think is the biggest misconception that biotech founders have about outsourcing development and manufacturing?

A When I specifically think about biotech startups, I think that there may not be a full appreciation of what is required to take a clinical R&D prototype to a full-scale commercial product. To take an example from my own experience, I once had a customer tell me that they didn't need a formulation for a sterile injectable, which put a smile on my face because every sterile medicine requires a formulation – you need to put it into some kind of formulation to be able to administer it to a patient.

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The question is only how much time and effort you want to put into your formulation development, depending on the stage of the development programme. Sometimes biotech founders don't intuitively appreciate how complex the whole process is, from defining a formulation to choosing primary packaging, and how those choices impact how the final product will be used – and whether you'll even be able to manufacture it in the first place.

Beyond the formulation, there are many other aspects that newer entrants to the pharma world might not have thought about. How do you make the product stable for storage? How do you actually administer it to patients? How do you manufacture and fill it at scale? Do you choose a cartridge, prefilled syringe or on-body injector (OBI)? Which needle size do you intend to use for the injection? I think that a lot of biotechs focus on the molecule first and foremost, and, while a molecule is the essence of a medicine, there is a lot more to getting that molecule to a patient in usable format – that's where pharmaceutical R&D really kicks in and where the expertise of CDMOs like ten23 becomes really valuable.

Q What do you think will be the key trends in pharmaceutical manufacturing in 2030 and beyond?

A If I look back at pharmaceutical manufacturing in the last decade or so, it was mostly about large-volume production – making the same product for everyone. It was a case of "Don't make it too complicated". Nowadays, however,

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we're seeing more segmented patient populations that require smaller batch sizes, especially in personalised medicines. In a nutshell, I expect that the market will move further towards differentiated solutions for patients, which is great from a patient perspective.

From a manufacturing perspective, this means that you will need smaller batches; you will need to have solutions that aren't one-size-fits-all. Achieving this may require capabilities that may or may not yet exist, even within larger corporations. I think we're going to see an increase in the number of specialist providers developing expertise in specific niches that are in demand in the wider market and seeing success with that approach.

Take OBIs as an example, which are a currently growing sector. OBIs are very effective for high-volume subcutaneous delivery, but we haven't built up the institutional knowledge for manufacturing and filling and assembling them yet – it requires speciality knowledge and assets. Currently, OBIs are manufactured in batch sizes on the order of 10,000 units, not the millions we are used to with traditional products.

Q Do you think that smaller batch sizes open the door to more innovative device solutions being given more of a chance?

A Yes, I think I'd agree with that – particularly in tandem with the greater prominence of CDMOs that can help pharma companies manage the risk where they might not have device-side expertise in-house. Let's consider subcutaneous delivery as an example; I remember being part of discussions in around 2007 or 2008 where I asked clinical colleagues what's the biggest volume we can deliver subcutaneously. Back then, I was told it was 0.5 mL by most, 1 mL by some and 2 mL by the really brave ones. Now, of course, we're delivering 10 mL. I recently read a paper where some colleagues at Eli Lilly performed a clinical study where they delivered up to 25 mL subcutaneously, also without permeation enhancers.

I've always been confronted with a lot of conservatism working in pharma, mostly driven by a fear of risk. It's understandable – we don't want to put the molecule or the patient at risk. Taking an exciting or innovative new approach is seen as inviting failure for the whole project because you're multiplying the uncertainties involved. Having said that, I think the industry struggles when it doesn't question its assumptions, such as how much we can deliver subcutaneously.

It's good to see the field evolving, although I think it could evolve much quicker. It's somewhere that CDMOs can really assist with speciality knowledge and capabilities. Let's say a pharma company needs to fill some cartridges for an in-development OBI – does it make sense for them to build their own specialist facility for only a few batches? Of course not. A CDMO, on the other hand, can have that specialist facility and use it for multiple projects with multiple partners. I think that's a healthy evolution.

Q Do you think sustainability is a competitive differentiator for pharma when selecting a CDMO?

A To start with, I believe pursuing sustainability is the right thing to do, regardless of any competitive advantages it might bring. That said, I do think that some have embarked on sustainability for that reason. Although, in the last few years, sustainability has become less of a priority for some companies, given the broader geopolitical perspective.

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For ten23 health, it's an important topic. In my opinion, sustainability should be a most important topic for everyone in the healthcare business, pharmaceutical manufacturers and CDMOS alike, because the health of the environment and human health are intrinsically linked; the more we adversely impact the environment, the more we adversely impact the health of patients. Asthma is a clear example of this, but it's far from the only one.

I have heard some argue that the industry is already doing enough good for the world by developing medicines, so why do we need to worry about greenhouse gas emissions or waste? To which I say, again, if you destroy the environment, you're damaging health as a secondary impact. There is absolutely no excuse for the pharma industry not to tackle sustainability. I always bring up the reference point that healthcare is responsible for 5% of global greenhouse gas emissions, which is comparable with the automotive industry.

There's a wonderful PhD thesis from the University of Oxford (UK) by Amy Booth. She analysed the approaches of multinational pharmaceutical companies with regards to climate action, and the interviewees said that it's secondary to patient wellbeing. They also said that sustainability depends on if it's affordable – it shouldn't impact profitability. As far as they were concerned, it's a question for the supply chain, regulators and policymakers. There's a lot of blame-shifting going on and, while a lot of companies are signed up to the Science Based Targets initiative (SBTi), only 16% are on track to meet the SBTi targets.

At ten23, we have an very open-book policy and are happy to share what

we're doing and how we evaluate our suppliers. Sustainability is not about putting up barriers – I'm always more fond of partnership rather than being competitive about things. We've been increasingly performing sustainability audits, though I'd still like to do more of them.

We've also achieved B Corp certification, which is a certification for sustainability, diversity and other considerations beyond being solely profit-focused. What I've found interesting is that I'm still frequently being asked what B Corp means. In practice, people outside of sustainability-focused roles don't really know a lot about the topic.

Q While sustainability as a topic tends to be dominated by CO_2, do you think that companies need to balance thinking about greenhouse gases with other concerns, such as water pollution and air quality?

A I cannot agree more; when I'm giving presentations about sustainability, one of my key slides is there to emphasise that "sustainability is more than decarbonisation". Pharma has a big impact on greenhouse gas emissions (CO_2 equivalents), but other considerations, such as waste or impact on biodiversity, are equally as important. Look at the number of disposables we produce from primary packaging alone, which all basically goes to waste. It's a question of resource use.

Then there's water, both from a withdrawal and wastewater perspective. On the wastewater front, we need to consider both contaminants that are produced during pharmaceutical manufacturing and disposal of the end products. For example, some people flush their medication down the toilet, and we need to take account of that.

Sustainable development goals can be really useful in situations where you have both a positive and a negative impact. They can help focus sustainability programmes on what we can do and how we can minimise our negative impact, such as waste. In practice, there will be unavoidable waste, unavoidable CO_2, so you have to think about how to do good beyond that, such as protecting forests that also add to biodiversity – which is something ten23 is working on in Pakistan with a fellow B Corp company. We also support an organisation called Seven Clean Seas, which removes plastic and other trash from the ocean.

I think that becoming too focused on decarbonisation is an overall negative for the industry. Instead, I think pharma needs to really expose itself to the topic, face up to the bad it's doing and think about the good it can do. It's about reducing and avoiding negative impacts – not only offsetting them – and taking overall responsibility as a business.

In truth, once you start paying attention to sustainability, it usually becomes a case of simply being more efficient and making better products – if you do things well, then they often become more sustainable. To go back to your earlier question, in practice, the real competitive advantage from embracing sustainability is that it is actually financially beneficial from an operational perspective. At the end of the day, there is nearly always a positive business case to be made for sustainable investments.

As an example, if you're buying photovoltaics for a facility, there's a big up-front investment to make, but it will offset operational costs in the long term. It can even offset operational risk because energy costs will probably go through the roof in the coming years. If you factor in your expected energy costs in 10 years from now, they will not be the same as today. You can go beyond that and think about batteries and energy storage, but even at the basic level it's a positive business case.

Q For sustainability, do you think that minimum compliance with regulations is enough or does pharma need to go beyond?

A In short, no, it's not enough. To use an analogy, think about it in terms of quality by design. If you don't follow good principles when you design a device and you manufacture it with tolerances that just scrape over the bare minimum, it will always be on the edge of failure – it won't take very much for it to break or just stop working. That's not a robust commercial product and the industry wouldn't accept it.

That said, in my view, I don't see a lot of people going beyond pure compliance with sustainability. For example, we're already seeing a lot of companies struggling to meet the EU's Corporate Sustainability Reporting Directive. At, ten23 we've opted into voluntary transparent reporting, but I'm not seeing that as a common approach. In fact, people ask me "Why are you doing this?" The simple answer is that we want to be transparent and that it's the right thing to do. I don't think that sustainability regulations are going to be enough to protect the planet, so we're going to have to do more than minimum compliance if we want to achieve meaningful results. But, ultimately, it's going to be a question for leadership to determine how far they want their companies to go.

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