Volume 2 Issue 1

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Sustainability by Design

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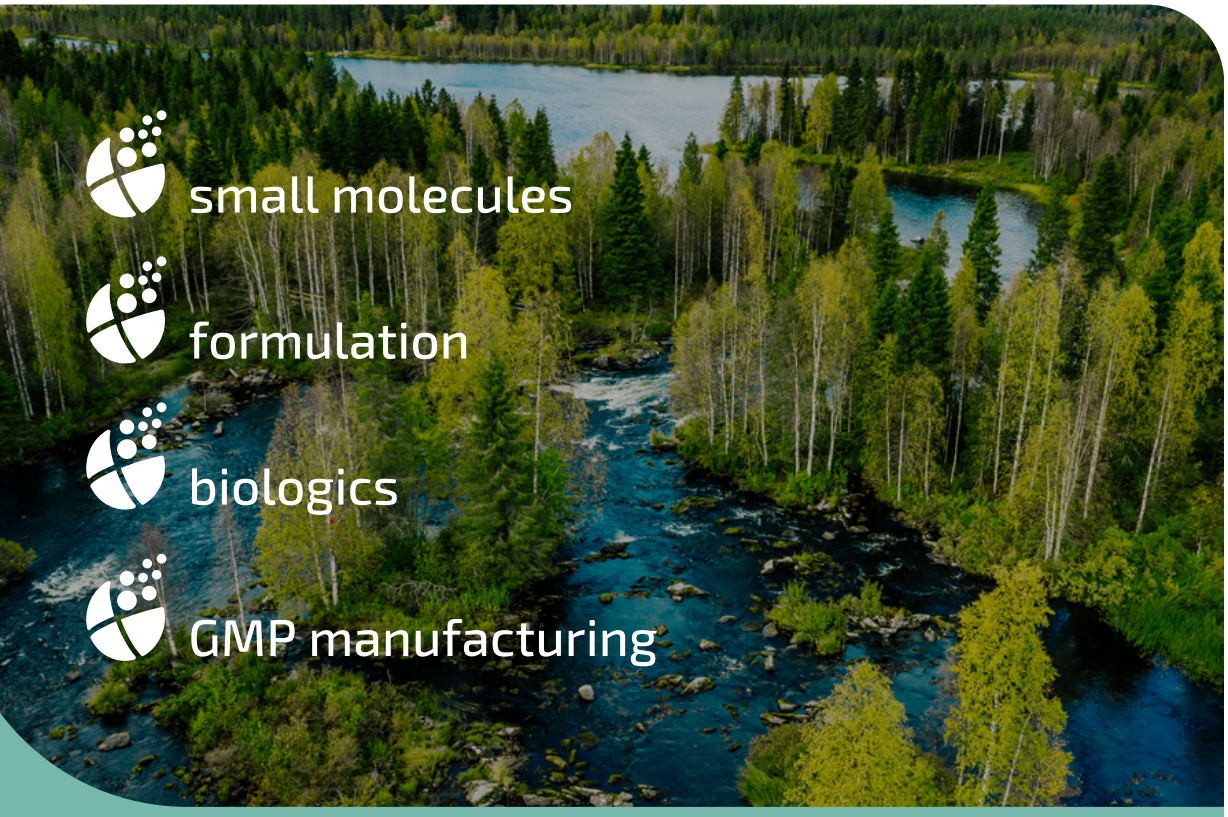

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Step-by-step Sustainability:

How Nanoform is Shaping a Greener Future for Pharma

Pharmaceutical companies are working to drive more positive outcomes for patients, but to truly benefit patients and the world, it is critical for the industry to examine and improve the environmental impact of their medicine's value chain. A 2019 study[1] estimates that the pharmaceutical industry emits 48.6 CO_2e (carbon dioxide equivalent) per million dollars. The impacts of climate change will pose a significant threat to global health,[2] bringing about additional deaths from malnutrition, malaria, and heat stress; as such, it is the industry's responsibility to safeguard human health and well-being by adopting a planet-centric approach to drug development and manufacturing. Many businesses within the sector have already begun working to increase the sustainability of their operations, with major pharmaceutical companies such as Merck[3] and AstraZeneca[4] adopting ambitious carbon neutrality targets for 2025 and 2030, respectively. When accelerating sustainability efforts across the pharmaceutical value chain, innovative technologies may hold the key to unlocking a greener future for the industry.

Sustainability in Pharmaceuticals

As with nearly every sector, the pharmaceutical industry is under significant pressure to manage sustainability risks.[5] A range of issues face the sector including global greenhouse gas emissions and proper disposal of drugs and pharmaceutical waste. Therefore, the solutions must target every step of the product lifecycle.[6] These include:

- Research and development methods
- Manufacturing processes
- Logistical operations
- End-use patient administration and disposal

Compared to other, more "industrial" sectors (such as mining or energy), the environmental impact of the pharmaceutical and healthcare sectors has received relatively little attention. Studies[1] have specifically pointed out the "dearth of peer-reviewed literature on pharma emissions". This has often led to the incorrect assumption that the sector is a green one. In actuality, the data that exist show that the pharmaceutical industry has a 55% higher emission intensity than the automotive industry.[1] Altogether, the healthcare sector accounts for nearly 5% of global greenhouse gas emissions – the equivalent of a small country.[7]

Business leaders have recognised the need to build a more sustainable pharmaceutical industry as well. According to Global Data, 43% of respondents to a poll of stakeholders within pharma cited the environment as the segment of ESG (environmental, social, and governance) that needs addressing the most.[8]

Furthermore, government bodies have also begun implementing legislation designed to push the industry towards more sustainable practices. The European Commission's proposal for a new Urban Wastewater Treatment Directive is emblematic of this, as government bodies move to tackle the environmental impact of businesses alongside leaders.[9]

In addition to this, businesses are also facing a changing competitive landscape, as sustainability becomes a more important differentiator within the pharmaceutical sector.[10]

The signs are clear – sustainability will only grow in importance for pharmaceutical business leaders in the years to come. If the industry is to meet this challenge and help transform every step of the value chain to be greener, it must adopt the latest, cutting-edge technologies.

Improved Bioavailability for Greener Outcomes

Bioavailability is a cornerstone of a drug's therapeutic efficacy.[11] However, it also has a significant impact on the manufacturing and environmental footprint of any given drug. By enhancing the bioavailability of a drug, businesses can potentially reduce the dosage of an active pharmaceutical ingredient (API) required to achieve a therapeutic effect – and, by extension, the quantities involved in manufacturing each unit of drug product. This can have a cascading effect along the value chain, not only reducing the environmental impact of the transport and shipping of materials, but also the cost. Low bioavailability is also a major reason that drug candidates fail to reach the market,[12] with an estimated 70% of novel medications[13] suffering from poor

Measured surface area (BET) and SEM particle size of nanoformed APIs

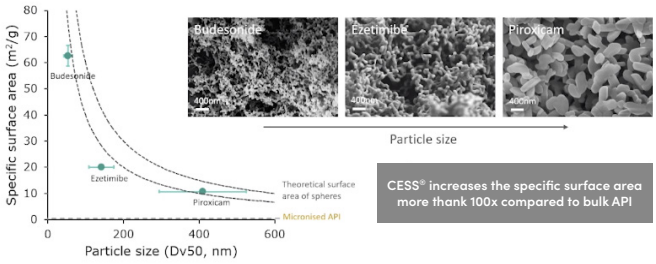


Figure 1 – Nanoform data illustrating the link between particle size and surface area

solubility, leading to poor bioavailability. This contributes to wasted time and resources.

A variety of methods to improve the bioavailability of APIs exist within the pharmaceutical development sector. Spray-drying of amorphous solid dispersions (ASDs) is one of the most common, however it can be environmentally harmful as it uses large quantities of environmentally damaging organic hydrocarbon solvents.[14] Research suggests that organic solvents make up 60% of mass consumption in the pharmaceutical industry,[15] highlighting the need to find alternative, less environmentally damaging methods.

Nanoform's proprietary Controlled Expansion of Supercritical Solutions (CESS®) is a cutting-edge nanoparticle engineering technology, which can increase the bioavailability of drug particles. It works by increasing the specific surface area of API particles, leading to significantly enhanced water solubility – and, by extension, increased bioavailability (see Figure 1). The technique uses GMP-grade CO_2 recycled from local industrial side streams instead of harmful organic solvents.

- The CESS® process begins in a pharma grade 40 m^3 CO_2 tank that sits outside of Nanoform's facility and feeds CO_2 into pressure vessels.
- Bulk API powder is dissolved in CO_2 in the pressure vessel at elevated pressure and temperature.
- This is then transferred through a pressure line where pressure is reduced slightly, by just enough to initiate nucleation and control the particle formation.
- Once the nano-nuclei suspension is produced, it is then atomised into a collection vessel. In this step, the droplets rapidly expand and instantly freeze around the API nanoparticle, preventing the particles from aggregating.
- The result is nanoparticles in dry ice in the collection chamber, which resembles snow. The process is then stopped, and the pressure is reduced, allowing the CO_2 to sublimate and leaving behind a dry nanoparticle powder. These particles can be utilised in dry formulations or wet formulations.

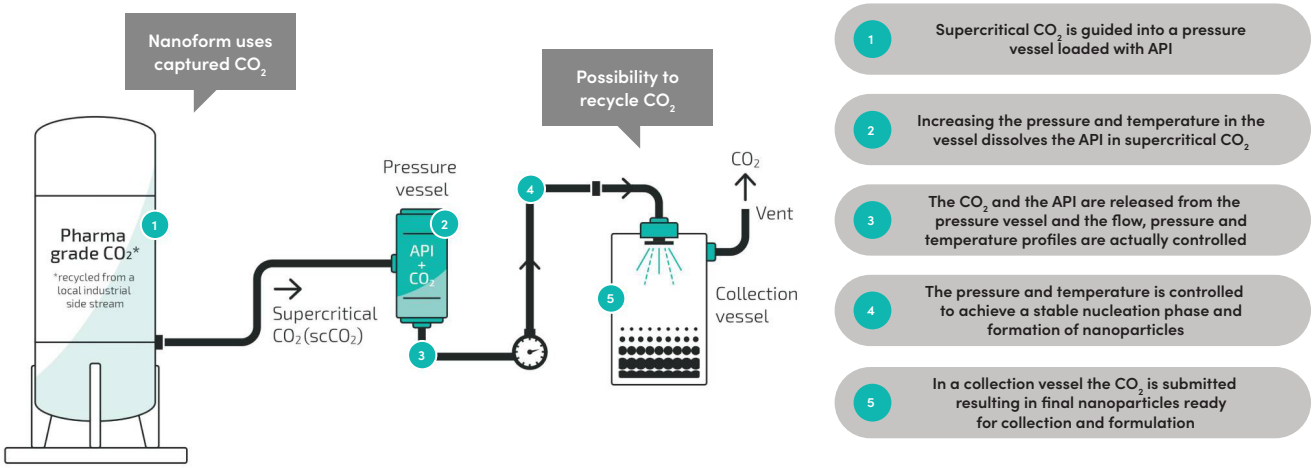
The process produces uniform nanoparticles that are tunable in size, shape, and morphology. This enables manufacturers to produce excipient-free, dry API nanoparticles directly from solution. Ultimately, the particles can achieve sizes as small as 10 nm, significantly increasing dissolution and therefore bioavailability.

How AI Can Enable More Sustainable R&D

By using technologies such as AI and digital twinning, manufacturers can drive more efficient R&D timelines as well as reduce waste and streamline drug discovery. Typically, companies test a number of drug design pathways to identify potential candidates in what is often a time-consuming, labour-intensive and wasteful process. But by informing decision-making processes with AI, pharmaceutical companies can carry out in silico experiments to rule out drug design pathways that would have proved unviable.

Nanoform leverages this concept in its STARMAP® online platform – the digital twin of its CESS® process – which can characterise a molecule based on its physicochemical properties and its chemical structure. STARMAP® utilises these to predict its solubility in CO_2, its propensity to crystallise, and whether it will produce an amorphous or crystalline end result. This information is then used to predict an API molecule's success with the CESS® process. The technology augments experimental results with detailed expert knowledge and the power of sparse-data AI to allow reliable predictions of nanoformability. STARMAP® is used alongside CESS® to identify the candidate molecules compatible with the process, thereby ensuring labs invest resources in the

The Controlled Expansion of Supercritical Solution – CESS®



Nanoform's CESS® is the only 'solution-to-particle' technology that can manufacture nanoparticles without organic hydrocarbon solvents, excipients and complex production processes.

Figure 2 – The CESS® process stepwise

drug candidates with the greatest chance of success – and minimise waste from an environmental perspective.

Targeting Waste Downstream

Unused and expired medicines can pose a significant public health risk. The US produces over 3.5 million tons of medical waste annually.[16] It has even been found that 11% of surveyed households possess residual medicines and 8% of medicine packs are partially or completely unused.[17]

Waste is often generated downstream when formulation and presentation routes do not align with patient preferences. Therefore, by aligning manufacturing processes with patient needs, pharma companies can create drugs that are both patient- and planet-centric. For example, one in six US adults report dysphagia,[18] or difficulty swallowing. CESS® can potentially facilitate smaller pill sizes by decreasing the amount of API needed to achieve a therapeutic effect, leading to improved compliance for the many patients suffering from dysphagia. This empowers more patients to finish their drug courses, resulting in fewer discarded medicines and less overall waste.

Another way that CESS® can help to improve patients' quality of life and adherence to treatment regimens is by facilitating alternative delivery routes. CESS® achieves this by producing API nanoparticles that are small enough to cross previously impassable biological barriers,[19] such as nasal membranes, the corneal layers in the eye, or even potentially the blood-brain barrier. Traversing these barriers enables access to local delivery routes that bypass systemic circulation, leading to reduced adverse side effects and further strengthening compliance for patients. CESS® may also be able to reduce the initial burst release for long-acting injectables in combination with other approaches, leading to enhanced sustained-release nanoparticle formulations. Opting for oral delivery and long-acting injectables instead of parenteral routes can also mean fewer hospital trips for patients, easing the process and resulting in better health outcomes for patients.

Alongside the enabling power of CESS®, the expertise of Nanoform's pharmaceutical development team in a wide range of delivery routes – including oral, inhaled, injectable and ophthalmic – is key to unlocking the full potential of nanoparticle formulations and enabling more patient-friendly therapeutics. By doing so, improved outcomes are possible from an environmental and global health standpoint.

Forging the Pharmaceutical Industry of the Future

The facts are unequivocal – the pharmaceutical industry requires a rapid shift towards a more sustainable value chain. A crucial component of the future of pharma, the call for more sustainable drug development will only get louder. It is the responsibility of the sector to answer this call and respond appropriately.

Nanoform's suite of proprietary offerings can help businesses with this transition, making every step of the value chain more sustainable. With Nanoform's game-changing technologies, pharma companies can find solutions to their complex drug development challenges, enabling a better future for both patients and the planet.

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Dr. Jamie Unwin

Dr. Jamie Unwin is the VP Strategic Insights at Nanoform, an innovative nanoparticle medicine-enabling company. Jamie's role is to help clients understand the value Nanoform's services and solutions can bring to their individual drug candidates, and portfolios as a whole. A twenty-year pharma industry veteran, Jamie and his teams have provided Insights to maximise patient, physician, and payer access to twenty three new drug launches. Jamie is a recognised opinion leader in the Business Insight world, and has held senior roles at GlaxoSmithKline, GE Healthcare, Janssen (Pharmaceutical Companies of Johnson and Johnson) and most recently was VP Enterprise Insights for Biocon Biologics. In addition to his role at Nanoform, Jamie is also a visiting lecturer at Imperial College Business School (London, UK) where he teaches classes on advanced analytics in healthcare.