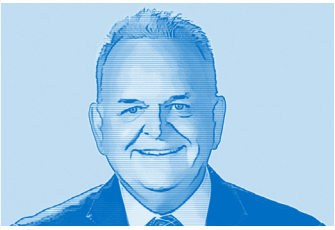


5 Biggest Trends of Oligonucleotide Manufacturing in 2022

Chris Rombach
Vice President of Sales and Marketing at Asahi Kasei Bioprocess America

Over his 30-year career Chris has focused on business development while holding various leadership roles at companies serving the biopharmaceutical industry. His background includes; filtration, separation, containment and material transfer. He was a founding member of the BPSA (Bio-Process Systems Alliance) and one of the early pioneers of single use systems. He holds a BS in Biology from Humboldt State University.

10% of new drug approvals by the FDA will be oligonucleotide-based

The rapidly growing market for Oligonucleotide manufacturing represents a lucrative opportunity for investors and pharmaceutical companies that wish to produce novel pharmaceutical products and therapies. So far, synthetic oligonucleotides have been studied and used extensively in the creation of new pharmaceuticals and at least ten oligonucleotide drugs have already been approved by the Food and Drug Administration (FDA).

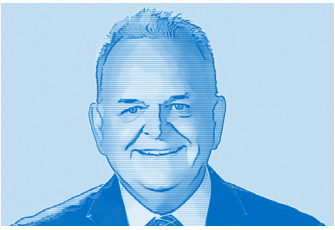
While Pfizer's drug Macugen is the best-known oligonucleotide drug on the market today, there are about 250 programs under development for new drug approvals. Industry insiders, such as Neil McKenna Ph.D., predict that roughly 10% of new drug approvals by the FDA will be oligonucleotide-based. The projection further emphasizes this industry niche's potential for exponential developments.

Given the excitement from investors and big pharma around oligonucleotide drugs, industry professionals scrutinize how oligonucleotide manufacturing can be scaled, including the price of raw materials, cost-effectiveness, reproducibility, and quality assurance concerns. With the abundance of opportunities this class of drug represents, let's explore what exactly oligonucleotides are and the five biggest trends in oligonucleotide manufacturing in 2022.

1. Scaling

Without a doubt, a high priority focus and breakout 2022 trend for this growing industry is scaling up the manufacturing process. The sector is already showing performance growth with the surging popularity of organic data storage and we're seeing developments in therapeutics such as CRISPR. In 2020, the novel coronavirus evolved into a global pandemic which exponentially increased not only the popularity but the necessity of mRNA vaccines. So much so that the market, which was valued at 6.3 billion as of 2021, is on-trend to hit over 14.1 billion by 2026.

In order to meet demand, manufacturers, which are traditionally smaller operations, have to scale up. Priorities within the scaling process include modernizing facilities, optimizing machinery, and innovating more efficient synthetic processes. Lateral to this trend, companies are looking to acquire small operations and build advanced new processing plants to expand their company's overall output capacity.



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2. Sustainability

Sustainability is a key focus across a plethora of industries and the Oligonucleotide sector is no stranger to its influences. In 2022 we'll be seeing a strong trending presence of sustainability as industry professionals strive to implement a greener mindset and eco-friendly approach to the division's operations. With Oligonucleotide manufacturing, in particular, finding ways to waste less and use more environmentally friendly materials is not only vital for the bettering of the planet we reside in but is also optimal for the cost and efficiency of its production.

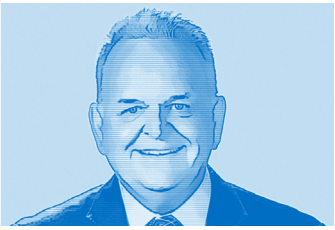
Currently, the synthesis process uses thousands of liters of harsh, flammable solvent per kilogram of the final product. Innovating and implementing new chemicals to complete certain processes, especially during the upscaling process, will lead to less waste, equipment corrosion, and a safer working environment.

Some of the most commonly proposed, sometimes implemented and often examined ways to make the overall manufacturing process more environmentally friendly include minimizing diafiltration volumes, AEX chromatography, HIC replacing RP-HPLC, diastereoselective synthesis of phosphorothioate oligonucleotides, LPOS (Liquid-Phase Oligonucleotide Synthesis), and enzyme-based technology (for examples Ligation and TdT). These help to reduce the overall waste and byproducts produced by the manufacturing process.

3. Improved machinery

Precise machinery works with human ingenuity and state-of-the-art chemistry in order to synthesize oligonucleotides. It is only logical that improving the equipment will improve the overall efficiency resulting in less waste and higher batch yields as well as increasing the ability for manufacturers to more easily scale.

Two of the most important considerations for advancements in this area are to develop and normalize equipment that can stand harsh chemicals more effectively and have machines that are easy to maintain.



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2022 will revolve around eco-efficiency, scaling up production, and updating the technology to suit a "smart factory" future.

4. Digitalization

Digitalization and automation go hand-in-hand for the advancement of scaleable oligonucleotide manufacturing. It is highlighted in the Pharma Initiatives 4.0 as a guide into the modernization of these processes and is important for all the machines and systems to integrate into one centralized platform (DCS), which will enable manufacturers to capture and analyze a complete set of data in real-time. Having these insights will allow workers to see exactly what's happening so they can maintain production, make systemic improvements, and fix any arising issues with greater speed and accuracy.

5. Striving towards Ideal Synthesis

Of course, a major goal of manufactures is to overcome the hurdles presented in the synthesizing of oligonucleotides and ultimately to strive towards a higher coupling efficiency.

There are several major issues when trying to synthesize oligonucleotides. These problems cause a massive waste of material, loss of yield, more impurities, less quality end products, as well as many other roadblocks. The ideal environment to carry out the synthesis process would be in a dry, closed system with no production of 'dead volume' (dead volume can include flushing agents, capping elements, and amidite) that can usually transfer over multiple steps in the operation.

The solutions mentioned above aim to tackle these problems head-on, along with evolving the design of factory systems and procedures.

It's clear that the manufacturing process of oligonucleotides is multifaceted and complex. The swelling acclaim of this niche industry is highlighting the need for rapid evolution. A majority of the trends we're likely to see in the industry in 2022 will revolve around eco-efficiency, scaling up production, and updating the technology to suit a "smart factory" future.

Questions?
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