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Trends in Biopharma 2022

How Technology Is Impacting Biopharma Today and What the Future Holds

With COVID-19 dominating the biopharma headlines over the past two years, it might be easy to overlook other important trends happening in the industry. The top issues and ideas most impacting biopharma today range from emerging modalities to refinement and adoption of innovative methodologies.

Some trends encompass clinical influences, like the pandemic, and are massive and dramatic, whereas others, like antimicrobial resistance (AMR), can be equally massive but are more insidious. We see trends related to business conditions – like the widespread arrival of biosimilars – and to manufacturing technology advances (such as those grouped under Biopharma 4.0), as well as the emergence of breakthrough therapies.

Computational methods are widely proving rapid successes in biological related problems, including diagnosis and treatment of diseases. [2]

Top Biopharma Trends of 2022

A key area of regulatory focus continues to be toward using data analytics and advanced manufacturing techniques for process intensification, automation, modularization, rapid scale-up and quality control.

All of them promise to advance, change, and impact the way biopharma companies prepare for the future. A common element among the trends we examine here is being able to understand which will bring disruptions in the way work is done today, and which represent a slow evolution of technology and processes that will gradually make biopharma development and manufacturing more resilient, profitable, and helpful to humankind.

Some of the most impactful issues and technologies affecting the biopharma industry today include:

1. COVID-19
2. Monoclonal Antibodies (mAbs)
3. Biosimilars
4. New Therapeutic Approaches
5. Advanced Analytical Techniques
6. Bioprocessing 4.0
7. Antimicrobial Resistance (AMR)

1. COVID-19

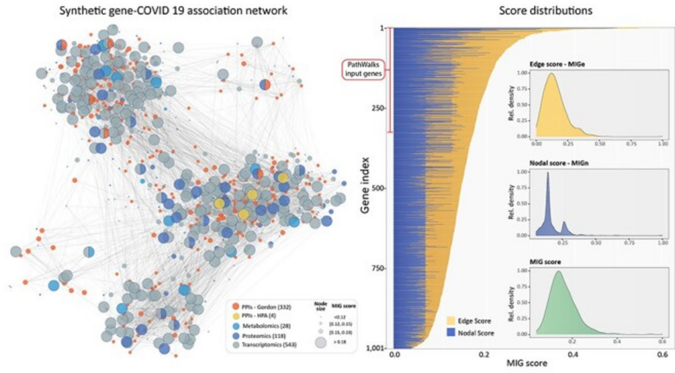
The world was shocked by the arrival of SARS-CoV-2. On the positive side, the biopharma industry responded quickly with vaccines, including ones based on viral vectors and mRNA. It seems that the door for nucleic acid-based therapeutics has blown open. Will this lead to many novel approaches to treat cancers and other challenging diseases? Time will tell, but it does seem likely that more nucleic acid (NA)-based treatments will join classic protein and peptide biotherapeutics.

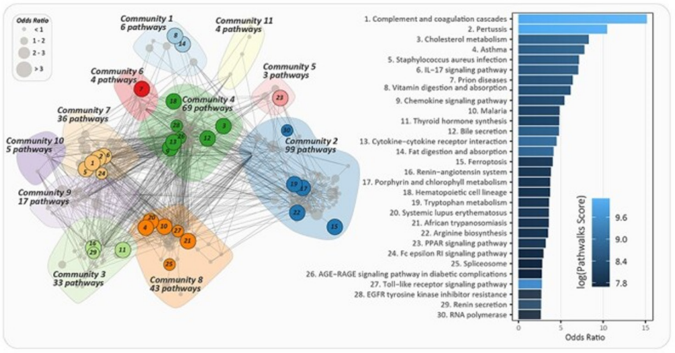
From the bioprocessing side we have witnessed an incredibly fast process development and ramp-up to meet the global demand for COVID vaccines. If NA biotherapeutics, based on similar molecules and delivery strategies, are successful then platform processes can be established by the major players, and specialized CDMOs will probably emerge as a cornerstone of this part of biopharma. It is likely that production methods will have a more modern touch than those used for proteins and peptides and include at least some of the Biopharma 4.0 tools. [1]

A large number of articles in the medical literature show how AI and various computational algorithms were used to find potential drug candidates and create vaccine trials quickly. Data analytics methods played a key role in this process.

In one report related to COVID-19, for example, researchers combined large amounts of data from numerous sources regarding virus and patient genomics and proteomics (multi-omics), with information about existing drug mechanisms of action to discover and prioritize existing drugs that might either prevent viral infection or reduce the effects of infection. The proposed candidates for "drug repurposing" (DR) included compounds that were recently found to generate promising results in clinical trials, as well as some that were presented for the first time as potential COVID-19 therapeutics. Such a multiplex approach, focusing on DR, can offer a fast first round defense against future viral infections until vaccines enable mass immunization and/or novel antiviral agents are developed. [3]

Quality by Design is "a systematic approach to development that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management." [7]



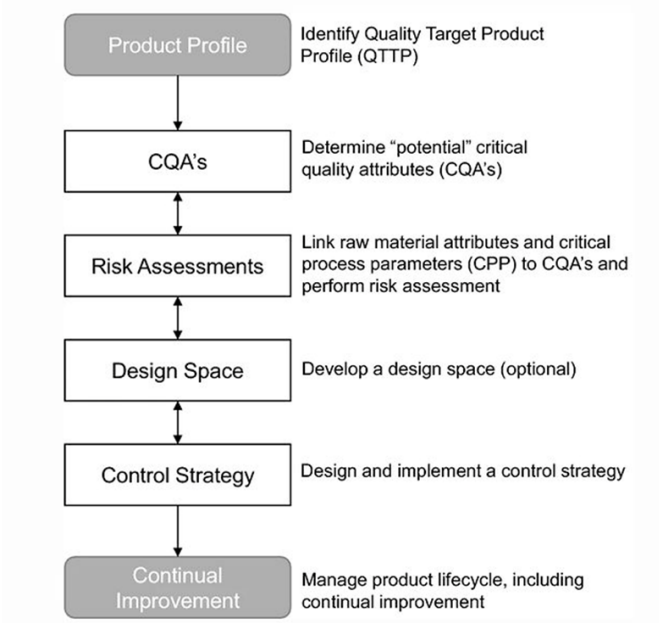


2. Monoclonal Antibodies (mAbs)

Despite the dramatic arrival of NA-based vaccines, there is no doubt that mAbs will continue to be the dominant class of biopharmaceuticals for the foreseeable future. Some estimates indicate that they could represent 80% of the future biologicals market.[4,5] According to the Pharmaceutical Research and Manufacturers of America (PhRMA), 20% of projects in the world-wide clinical pipeline use mAbs or conjugated mAbs. [6]

The molecular similarity of different mAbs has led to rapid maturation of production methods. The arrival of successful mAbs coincided with enthusiasm from regulatory agencies to promote QbD approaches and this in turn has led to platform production processes that operate in so-called design spaces defined by control parameters. The introduction of mAb biosimilars encourages competition to improve yields, flexibility, robustness, and process economy. Together with the several-decade long success of mAbs, this is leading to the bolder application of new technologies. QbD differs from past approaches to product development by building quality into every step of the process, rather than relying on testing to achieve quality. In essence, QbD is a statistical approach to development that focuses on process understanding and control by assessing variables that may impact quality. That means a QbD approach hinges on being able to analyze a broad set of data effectively.

QbD involves the use of Design of Experiments (DOE) to establish a Design space that is broad enough to allow flexibility in the process (or raw materials) but narrow enough to ensure critical quality attributes (CQAs) are met.



Around 9% of over 12, 600 projects in clinical development, globally, relate to these genetic approaches according to the PhRMA [14]

3. Biosimilars

The biosimilar market had an estimated value of US$ 13.0 Billion in 2021 and is expected to reach US$ 60.8 Billion by 2027, indicating a CAGR of 26% over 2022-2027 [8]

Biosimilars have been approved and applied successfully for 15 years in the European Union (EU) and have been shown to reduce healthcare costs and increase access to important biological medicines [9, 10] Market penetration of biosimilars in the United States has been somewhat slower, but the increased availability and utilization of biosimilars is projected to save up to USD$100 billion in drug costs over the first 5 years of this decade. [11, 12]

Also important is the improved access to advanced biopharmaceuticals globally, due to regional manufacturing of biosimilars. India, China, South Korea, and Singapore are at the forefront of biotherapeutic development and production outside of Europe and North America. Whether to build new or outsource production is a frequent question in the battle to reach new markets. [13]

The success of biosimilars is fundamentally based on them having lower development and production costs. This can be achieved through fleet-footed facilities that apply more modern technologies than those used by the originator, cloned facilities by an originator who can apply experience from many years of production, and intensified unit operations that are possible in a new facility.

The increased competition due to biosimilars means that innovators need to gain market share asap, before the patents run out, and biosimilar manufacturers need to be better than the originators, as well as beating other biosimilar manufacturers, to deliver a cheaper but just as good product. Flexibility is an additional demand due to the fierce competition and the need to change production output rapidly to meet changing demand from a dynamic market.

Ensuring a biosimilar meets the critical quality attributes (CQA) of the original biologic is a major challenge. Optimizing production at full scale is impractical, which makes a quality by design (QbD) approach using a reliable scale down model of the process an attractive alternative. An acceptable method in line with with ICH Q9, Q10, Q11 guidelines is to create a scale-down model using multivariate data analysis (MVDA) and Design of Experiments (DOE).

4. New Therapeutic Approaches

We've already mentioned NA-based therapies, but other developments can be expected, e.g., in cell therapy, gene therapy, and gene editing. Furthermore, packaging and delivering therapies, e.g., using viral vectors, nanoparticles, or vesicles such as exosomes, will probably gain importance as novel therapies increase in complexity.

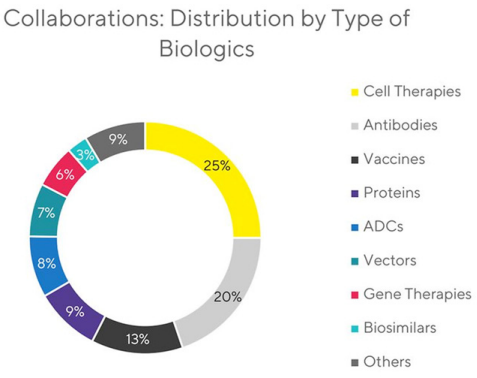
Cell therapy is a form of treatment that infuses or transplants whole cells into a patient for the treatment of an disease, like cancer. . A variety of different cells can be used in cell therapy, including stem cells, lymphocytes, dendritic cells, and pancreatic islet cells. In one example, CAR-T, cells are genetically modified before being returned to the patient.

Closely related to this example, gene therapy uses modified or new genes with the goal of treating, preventing, or potentially curing a disease. Gene editing involves the alteration of genes to correct mutations, to introduce new genetic information, or to remove specific DNA sequences e.g., using CRISPR-Cas9 technology. In gene editing, DNA

By 2025, the US FDA expects to be approving 10 to 20 cell and gene therapy products a year. [17]

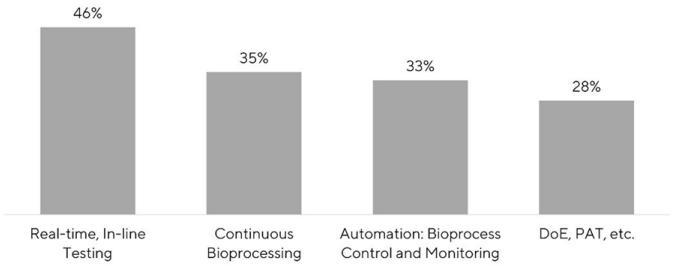
sections are inserted, replaced, removed, or modified at particular locations in the human genome in order to treat a specific disease.

Any new therapeutic approach comes along with development and manufacturing challenges. Big pharma may well choose to outsource rather than building its own capabilities when it comes to manufacturing novel therapeutics. CDMOs, in turn, will compete for business based on track record, competencies, and the use of technologies that can avoid batch failures and deliver according to regulatory requirements. Novel methods are open to the application of the latest industrial technologies, including the use of Design of Experiments (DOE) and Process Analytical Technologies (PAT) for rapid process parameter optimization and development of clear process controls that allow for development of robust, scalable processes, and continuous manufacturing.



Cell therapies and antibodies are presently the most popular (in terms of several associated deals) types of biologics in this field, representing 25% and 20% of the total number of instances, respectively. [15]

PAT and other types of advanced models for process control are pivotal to support the industry trend towards continuous manufacturing. In a 2020 survey by BioPlan Associates [1], CDMOS rated real-time and inline testing, continuous bioprocessing, automation for bioprocess control and monitoring, and PAT/DOE tools as the top new product development areas needed.



Source: 17th Annual Report and Survey of Biopharmaceutical Manufacturing Capacity and Production, BioPlan Associates, Inc., April 2020. [16]

Collaborations between cell and gene therapy manufacturers and CDMOs partners are increasing. The number of active collaborations grew ten-fold in five years, from 42 in 2013 to more than 444 in 2018.

Across all industries, 70% of companies either have a digital transformation strategy in place or are working on one, according to a Tech Pro Research survey [21]

5. Advanced Analytical Techniques

One constraint in biopharma development and manufacturing is the lack of information-rich/useful measurements. Temperature, pH, ionic strength, UV absorbance and a few other analyses are, typically, all we have online.

Multivariate Data Analysis (MVDA) can expose complex, often unexpected, relationships between these simple parameters and manufacturing performance, but there is a hunger for more advanced process analytical technologies that directly relate to a product's critical quality attributes (CQAs). Raman spectroscopy is perhaps the obvious candidate for this type of sophisticated in-process monitoring of a product's CQAs.

Raman spectrometers collect huge amounts of information in the form of spectral data. It is not possible to measure the concentration of the target molecules in spectral data alone, but requires a reference analysis of the target molecules, such as glucose, lactate, or other metabolites. Advanced data analytics tools are needed to make sense of the information. If the data analysis can be incorporated into the process automatically, it opens to the door to process automation.

Using Raman spectroscopy in biomanufacturing is an effective way to apply Process Analytical Technology (PAT) and monitor bioreactor analyte concentrations, like glucose, lactate, glutamate, and glutamine in a sample. PAT tools can become even more effective when the analyzers themselves are integrated within the bioreactor system. Integrated PAT makes sampling, sample analysis, data collection, and consolidation an automated process, making walk-away Raman spectroscopy analysis a reality.

6. Bioprocessing 4.0: Automation, AI, and Data Analytics

Whether it's embracing the principles of Quality by Design (QbD), incorporating process analytical technology (PAT) or optimizing your supply chain, data analytics plays a significant role in fostering digital transformation in the biopharma, healthcare and life science industries.

Consider these statistics:

- Companies use only 4% of the data they have available. [18]
- Only 20% of biopharma companies are digitally mature, whereas 80% are in the early stages or still developing. [19]
- The IDC estimates that by 2024 over 50% of all IT spending will go toward digital transformation. [20]
- Across all industries, 70% of companies either have a digital transformation strategy in place or are working on one, according to a Tech Pro Research survey [21]
- The 2020 State of Tech Spend report 22 showed that digital transformation was expected to be the top budget item for IT expenditures in 2020.

Create More Efficient Processes

Digital transformation offers a mechanism for companies to revise their business models, to improve production processes, and even to design and discover innovative drugs and treatments faster by using artificial intelligence to screen compounds. From process automation to using data analytics in clinical trials, leveraging digital transformation helps to create more efficient processes as well create services that fully engage and provide value to key stakeholders.

Prevent future process deviations. Another area where digital transformation helps biopharma companies improve manufacturing is using the vast quantities of data

generated from bioprocessing to help predict (and prevent) future process deviations. By using advanced data analytics to create accurate models of cause and effect from past production runs or batches, companies can create models for how future batches should operate, predict outcomes based on key performance indicators and set process parameters.

Adopt continuous process manufacturing. From quality by design (QbD) to continuous process manufacturing, regulatory agencies have shown their support and indeed promotion for the benefits of digital transformation in the pharma and biopharma space. The FDA encourages manufacturers to adopt continuous manufacturing using advanced multivariate data models, because it improves process control, reduces variability, and improves product quality and consistency.

From a business perspective, continuous manufacturing promises to reduce costs and help products get to market faster. Better control means improved product quality and more standardization, making it easier, for example, to develop and manufacture biosimilars. It also becomes the foundation for a robust quality by design (QbD) strategy.

7. Antimicrobial Resistance (AMR)

Drug-resistant infections by bacteria and fungi in particular, that were formerly routinely treatable, have emerged as an urgent public health threat. AMR is a natural evolutionary process accelerated through overuse of antibiotics in medical care and animal husbandry. AMR may also have been exacerbated during the COVID-19 pandemic, as doctors use large amounts of antibiotics to treat hospitalized patients with weakened immune systems at risk of secondary infections.

Clearly, there is an urgent and ever-increasing need to develop new and effective treatments to combat AMR, and to avoid turning back the clock on the progress made since the mid-20th century. Medicines in the clinical development pipeline are not only antibiotics. They include non-traditional antibacterial agents, such as bacteriophage products, live therapeutic products, and monoclonal antibodies. Also, effective preventive vaccines indirectly decrease the need for antimicrobial use. Today, 89 medicines are currently in development related to AMR. [23]

Some Predictions for the Future

If we look at where this is heading in the future, we expect that:

- Accelerated regulatory approvals will lead to a growth in demand for cell and gene therapy products.
- The increase in demand and need for quick scale-up will lead to more cell and gene therapy developers looking to outsource.
- Outsourcing to CDMOs will continue to grow, and the selection criteria may come down to portfolio breadth, ability to incorporate advanced data analytics, regulatory compliance and cost.
- As development phases accelerate (as with COVID-19 vaccines and treatment), being ready for full-scale manufacturing and commercialization means creating scale-ready processes from the start.
- Quality by design using DOE and MVDA will become integral to all PAT technologies, and essential for rapid scale up.

Conclusions

Major trends in the biopharmaceutical industry are the result of changing healthcare demands and evolving technological capabilities.

Although not addressed here, healthcare demands include demographic-related effects, such as the widespread increase in diseases like cancer, more common in aging populations. As described, COVID-19 continues to have an impact, and AMR is an increasingly important concern.

The biopharmaceutical pipeline contains 12 680 projects in clinical phases and 14 750 projects in preclinical development. [6]

The emergence of NA-based therapies, the continued success of mAbs, future gene-related therapies and other novel therapeutic approaches, and the continued success of biosimilars, all put pressure on the industry to use agile, reliable, quality-assured technologies. QbD is a good foundation, but more data and better use of data are fundamental to enable the biopharma industry to cope with future challenges.

As regulatory agencies and competition continue to stress the need for advanced manufacturing processes that rely on data analytics, the future will embrace important methods like automation, digitalization and modularity in manufacturing. Improvement in the application of AI to manufacturing will increase the accuracy of predictive modeling, enable efficient automation of medical devices and manufacturing processes, leverage knowledge management resources to improve regulatory review, and focus and improve post-market surveillance methodologies using machine learning (ML).

Although biopharma development and production are traditionally cautious activities and characterized by risk-avoidance, artificial intelligence, the internet of things, machine learning, and a battery of digital approaches referred to under the Biopharma 4.0 banner are waiting to be let in once the data analytics platform is in place.

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