

A Q&A

Parallel Control and Powerful Software Solutions – Important Tools for Efficient Vaccine Development



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RNA and DNA vaccines require less volume than traditional microbial and cell cultivation production.

Many companies are working to advance the development of a vaccine in the context of the current COVID-19 crisis. New bioprocess technologies, such as single-use equipment and process automation, open up possibilities for quality control and validation. This is especially important in GMP-regulated environments, such as in the development and manufacturing of new influenza vaccines. When facing a pandemic outbreak, the need to smoothly develop new processes and quickly scale up to clinical production volumes is key to efficiently develop new vaccinations.

BioPharm International recently spoke with Dr. Jörg Schwinde, Key Segment Manager for Vaccines and Monoclonal Antibodies at the Bioprocess Center of Eppendorf, about the typical developmental process of new vaccines and how the COVID-19 pandemic influences the global vaccine developmental landscape.

BioPharm: Can you describe the vaccine market and what is driving the market?

Schwinde: The global vaccine market is at a value of approximately \$50 billion. About 80% are human vaccines and 20% are veterinary vaccines. Of the human vaccines, 90% can be considered as prophylactic and around 10% are therapeutic, such as treatments against cancer. It is remarkable that the market is dominated by five multinational companies. The Serum Institute of India should be highlighted as a leading company by vaccine doses per year.

The drivers are attributed to two factors: costs and yield. The cost per doses should be decreased, while the yield during production should be increased. Further, external pressure on pricing and funding are important, especially for developing countries.

BioPharm: What can we observe during this COVID-19 crisis?

Schwinde: First, it is remarkable that there are currently more than 125 COVID-19-related projects in the pipeline, according to the World Health Organization (WHO). About 15 of these are in clinical trial Phase I or II, and the first candidates did just recently enter the clinical phase III. Another observation is that competitors in the vaccine market cooperate with each other and big players join forces with comparatively younger companies. Finally, in addition to traditional platform technologies, RNA and DNA platforms are up and coming.

BioPharm: Are there specific effects resulting from these relatively new RNA and DNA techniques?

Schwinde: Yes, the volumes needed for producing DNA or RNA vaccines can be reduced tremendously compared

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to traditional microbial and cell cultivation production processes, while providing sufficient vaccine doses for the global demand. Despite the production volume, RNA platforms can be run even in cell-free systems. This opens new production possibilities.

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The product range is completed by Eppendorf freezers, centrifuges, and automation devices.

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BioPharm: The COVID-19 pandemic has shown us that time plays a major role in getting a vaccine developed. Assuming that human and animal cells or microbial strains are involved, can you describe the development process?

Schwinde: The speed to clinic or market plays a role in vaccine development. But time aside, safety and flexibility are also important factors. There is a good reason why it takes quite a while for a new vaccine to be developed and approved for the market. Everything starts with the selection of a cell line or a strain. The selection of a strain and the cultivation media are relevant initial factors that have many starting points for optimization. Once a strain is selected, all the process parameters like nutrient composition, pH, feeding rates, temperature, and so on need to be optimized. Parallel bioreactor systems that can monitor the effect of different parameter changes are efficient tools to optimize process conditions before a technology transfer to scale up and subsequent downstream processes follow. These processes are accompanied and improved by continuous data analytics in the frame of the process analytical technology (PAT) initiative. For example, cell densities and metabolic conditions can be continuously measured and controlled to achieve as much data as possible. By this I mean that the characterization of the process happens early in development, which supports the regulatory environment. Design-of-experiment (DoE) software tools play an important role in accelerating process development.

BioPharm: What do you see as positive influencers for the future?

Schwinde: Research and development will be accelerated by the efficient usage of data, parallel control of processes, and automation processes. Aside from reusable bioreactors and fermenters, single-use technologies have almost an equal market share. Additionally, modular manufacturing suites allow flexibility to increase and decrease production volume. The intensification of manufacturing processes will lead to smaller volumes and comparable yields. Last—but not least—powerful downstream techniques are being continuously developed because all efforts to optimize the upstream area should not get lost downstream.

BioPharm: What do you see as Eppendorf's role within this context?

Schwinde: Eppendorf bioprocess is the specialist in the upstream area. Cell line and strain selection, as well as cultivation media selection, are conducted with highly parallel and small-scale cultivation platforms with operation volumes from 50 mL to 3.7 L. Up to 24 vessels can be controlled by one process computer, which enables the user to characterize the maximum of process parameters in one experimental setup. The small-scale technique is followed by the controlled benchtop reactors, with operation volumes from 500 mL to 40 L per vessel. And by volume, this range is finalized by pilot and production bioreactors and fermenters with operation volumes of up to 1200 L. The majority of the vessel types are available as reusable and single-use.

On the bench, Eppendorf provides the largest range of single-use, stirred-tank, rigid-walled bioreactors and fermenters. In the near future, controlled and stirred cultivation bags for pilot and production purposes will be supplied up to 250 L operation volumes, at least initially. The software platforms of the process control are flexible enough to be combined with third-party analytic instruments like Raman technology, cell counters, or mass spectrometers. The product range is completed by Eppendorf freezers, centrifuges, and automation devices. These devices, accompanied by the precise liquid handling technique, enable efficiency in the lab to complete benchtop activities.

Located in Juelich, Germany, the Eppendorf Bioprocess Center Europe consists of a team of specialists focused on bioprocessing.