

Optimized for Commercial Manufacturing: BioBLU® HNQ

Stefan Schlößer, Christoph van Eickels, David Solbach
 Eppendorf SE, Bioprocess Center, Juelich, Germany
 Contact: bioprocess-experts@eppendorf.com

Executive Summary

The emergence of cell and gene therapies has revolutionized the way to treat hitherto incurable diseases. However, it also changes the way how we look at the curative agent which, as opposed to traditional therapeutic approaches, is often the cell itself. Therefore, it is more vital than ever to ensure a healthy cell culture by controllable and reproducible culture conditions,

minimized contamination risks, and scalability for R&D as well as clinical and commercial manufacturing purposes. Eppendorf BioBLU HNQ Single-Use Bioreactors are optimized for these purposes. Together with strong bioprocess controller and software offerings, they provide the documentation to support your work in clinical and commercial manufacturing.

The dawning age of cell and gene therapies

The field of cell and gene therapies (CGT) offers great potential to cure hitherto incurable disease. Treatments like adeno-associated viral vector therapy against inherited blindness or chimeric antigen receptor (CAR)-T cell therapy against blood cancer are already approved by authorities and helped many patients worldwide [1-3], while new developments like stem cell-derived therapies are constantly emerging.

In terms of cell-derived therapies, two methods are commonly used for treating patients: autologous and allogeneic [4].

In the autologous approach, the cells in question are isolated from patients and engineered outside of the body to tackle certain diseases before being re-introduced into the same patient. This procedure ensures an apposite treatment with less side-effects due to personalization to a

single patient. However, the concomitant production in small batches makes it difficult to offer the curing possibility to larger patient groups [5, 6].

Allogeneic therapy on the other hand allows more patients to benefit by using cells from an external, healthy donor. This enables production of more doses for storage as an off-the-shelf treatment for patients. The difficulty here lies in the necessity for large and consistent high-quality batches, as well as storage conditions to prevent impairment of the cells' integrity [7].

Tackling the challenges: stirred-tank bioreactors for R&D and commercial manufacturing

Despite these pros and cons, both autologous and allogeneic have their 'raison d'être' as complementary approaches to offer the optimal treatment for each patient. In relation to

that and as opposed to traditional therapeutic approaches like antibody therapy, the final product of CGT is often the cell itself. Thus, it is more important than ever to minimize contamination risks both from a cell culture perspective, but also from the vessels the culture is grown in. At the same time, these vessels need to ensure controllable and reproducible culture conditions, while enabling scale-up, scale-down, and scale-out options for both R&D and manufacturing.

In that sense, stirred-tank single-use bioreactors are a valuable tool to develop and produce the therapies of tomorrow. With their easy handling, out-of-the-box usability, minimal cleaning effort, and consistent scalability options, they enable scientists to generate robust processes for batch control and thus minimize risks for patients. Furthermore, they provide much higher cell numbers where more traditional 2D culture methods reach their limit, and, with the fitting impeller type, can be used even for sensitive cell types.

To provide this power of single-use bioreactors to the CGT field, documentation packages are needed, attesting the bioreactor material certain properties. These documents are important for the users to help qualify their systems for use in clinical and commercial manufacturing, as well as helping them during audits and for maintaining.

Examples for such documents are summarized in Table 1.

Table 1: Examples for bioreactor documentation requirements.

All polymeric materials, as well as the assembly process can be declared as either ADI free or compliant with the EMA410/01 guideline
Testing for cytotoxicity
Absence of certain food allergens
Endotoxin levels of <0.100 endotoxic units (EU)/mL
Sterility assurance level of 10^{-6}
Biocompatibility

Introducing the BioBLU HNQ Single-Use Bioreactor

In order to provide this level of documentation for the user, Eppendorf introduces the BioBLU HNQ Single-Use Bioreactor, the bioreactor optimized for clinical and commercial manufacturing.

The BioBLU HNQ Single-Use Bioreactor comes with a product-specific validation guide along with manufacturing site certifications, quality assurance statement, dimensions and drawings, as well as materials of construction. Together with the system-specific product documentation package containing batch/lot/serial numbers, system specific test results like sterility and endotoxin levels of <0.100 endotoxic units (EU)/mL, material test reports,



Fig. 1: Various models of the BioBLU HNQ Single-Use Bioreactors are available and optimized to support your clinical and commercial manufacturing.



Find more information and product features here:
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certificate of conformity etc., the validation guide constitutes the documentation package and provides the information to qualify your systems for use in clinical and commercial manufacturing. Reach out to us for more information on the Eppendorf products and documentation for work in clinical and commercial manufacturing: bioprocess-info@eppendorf.de.

Furthermore, Eppendorf provides IQ and OQ services. These are essential for documenting that your equipment is installed and operating according to specific parameters, which further supports your qualification efforts.

Bioprocess controllers and software for work in clinical and commercial manufacturing

Besides having a reliable bioreactor documentation, the necessity for process validation by the user does not stop there. When it comes to regulating the cells' growth conditions for clinical and commercial manufacturing, a documentation package is also necessary for the bioprocess controllers attached to the bioreactor. Also, the software to operate the bioprocess controller must fulfil certain requirements for the use in clinical and commercial manufacturing.

Examples of these software requirements are summarized in Table 2.

Table 2: Examples for software documentation requirements.

Computer generated, timestamped audit trail of who (unique identifier, signature) did what, when and why in the manufacturing of a batch, in changing relevant systems settings or any other electronic records
Ensuring authenticity and prevention of forgery and manipulation by permanently linking electronic signatures to the corresponding records
Access control designed to support role-based user rights (segregation of duty) to ensure only authorized individuals can access and perform tasks according to their role, as well as the possibility to record unauthorized/failed access attempts
Ensuring data integrity by providing backup and recovery features, accuracy check features to discern altered records and providing exact copies of electronic records in human readable form
Software development and maintenance (e.g., updates and patches)

End-to-end solutions for clinical and commercial manufacturing

With its portfolio, Eppendorf covers the whole bioprocessing journey from R&D to clinical and commercial manufacturing:

- > The BioBLU HNQ Single-Use Bioreactors with working volumes of 1 L, 3 L, 10 L, 40 L, providing unmatched scalability
- > The BioFlo® 320 bioprocess control station, providing seamless transition of your process from 0.4 L to 40 L on a single platform
- > The DASware® control plus SCADA software, offering extensive embedded process automation features and intelligent recipe management

In conclusion, the combination of BioBLU HNQ Single-Use Bioreactors, BioFlo 320 control station, and the DASware control plus SCADA software, along with the detailed validation guides offer an end-to-end solution for customers working in clinical and commercial manufacturing.

With an unmatched 400-fold scalability factor on a single platform, BioBLU HNQ Single-Use Bioreactors deliver robust and reliable cell culture performance and cover all the scales necessary for success, from small-scale research to commercial manufacturing. The BioFlo 320 control station controlled by the DASware control plus SCADA software ensure a well-controlled growth environment and the validation guides help qualifying the user's systems for clinical and commercial manufacturing. Thus, you and your lab are equipped to go the whole CGT journey with our Eppendorf experts by your side to support you. Let's bioprocess together.

References

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