Comparison of N-1 seed train performance in HyPerforma Rocker BioProcess Containers using Renolit 9101 and Aegis5-14 films

Introduction

Rocking-style bioreactors have been present in the bioprocessing industry since the 1990s [1] and have been commonly used as part of the seed train for production processes. The Thermo Scientific™ HyPerforma™ Rocker Bioreactor utilizes HyPerforma™ BioProcess Containers (BPCs), the HyPerforma™ G3Lab™ Bioprocess Controller, and Thermo Scientific™ TruBio™ software, powered by the DeltaV™ Distributed Control Platform from Emerson, providing a complete, ready-to-use solution for bioprocessing applications.

The initial film selected for use with the HyPerforma Rocker BPC was Renolit™ 9101 film (an LDPE film), which has been used successfully with the product for several years. We have recently added Thermo Scientific™ Aegis™ 5-14 film as an option for the HyPerforma Rocker BPC after numerous customer requests, to provide a consistent film for those using the Thermo Scientific™ HyPerforma™ Single-Use Bioreactor (S.U.B.).

This application note shows the performance of CHO-S cells grown in N-1 reactor conditions in both Renolit 9101 and Aegis5-14 films. In an effort to benchmark biocompatibility of the two films, a working volume of 5 L in the 50 L HyPerforma Rocker BPC was chosen for the purpose of confirming acceptable growth performance, using practical worst-case growth promotion conditions of container contact surface area to culture liquid volume. Results confirmed equivalency of the two film types, giving confidence to using the HyPerforma Rocker BPC with Aegis5-14 film for seed train applications, in place of the original HyPerforma Rocker BPC with Renolit 9101 film. This option enables film consistency through the seed train and production vessels.

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Materials and methods

CHO-S cells were maintained in Gibco™ Dynamis™ Advanced Granulation Technology™ (AGT™) Medium throughout the scale-up and culture process in the single-use HyPerforma Rocker BPCs. Materials used in this study are described in Table 1.

Cell culture preparation and monitoring

Dynamis AGT Medium was reconstituted per product instructions using Thermo Scientific™ HyPerforma™ Single-Use Mixer (S.U.M.) systems. The medium was supplemented with 8 mM Gibco™ L-glutamine and 1 mL/L Gibco™ Anti-Clumping Agent, then sterile-filtered. Samples were taken daily to assess cell health and growth using the BioProfile™ FLEX2™ Automated Cell Culture Analyzer (Nova Biomedical) and Vi-CELL™ XR Cell Viability Analyzer (Beckman Coulter).

Bioreactor cultivation

CHO-S cells were cultured in Thermo Scientific™ Nalgene™ single-use PETG Erlenmeyer flasks through scale-up and then were inoculated into each of the HyPerforma Rocker BPCs at a working volume of 5 L, and a Nalgene single-use PETG Erlenmeyer flask at a working volume of 35 mL. Dissolved oxygen (DO) and pH were not controlled in this study. Cells were grown for 4 days in batch mode to show typical growth performance in an N-1 reactor. Agitation and gassing parameters for the run are outlined in Table 2.

Table 1. Cells and culture components.

Component	Description
Cell line	CHO-S
Medium composition	Dynamis AGT Medium with 8 mM L-glutamine and 1 mL/L Anti-Clumping Agent
Shake flasks	Nalgene single-use PETG Erlenmeyer flasks with plain bottom, 125 mL
S.U.B. hardware	HyPerforma Rocker Bioreactor
Single-use BPCs	HyPerforma Rocker BPC, 50 L (Renolit 9101 film), Cat. No. F100-2546-001 HyPerforma Rocker BPC, 50 L (Aegis5-14 film), Cat. No. SH31187.03

Table 2. Conditions for HyPerforma Rocker BPCs and Nalgene single-use PETG Erlenmeyer flask.

Component	50 L HyPerforma Rocker BPC	125 mL Nalgene Erlenmeyer flask
Working volume	5 L	35 mL
Temperature	36.5°C	36.5°C
pH	Not controlled, CO_2 manually added at 8% of air flow (40 mL/min)	Not controlled, utilized CO_2 incubator with setting at 8%
Rocker rate and angle of agitation	20 rpm, 7 degrees	110 rpm
DO	Not controlled, air manually added at 0.5 L/min through overlay sparge	Not controlled
Target seeding density	2 x 10^5 cells/mL	2 x 10^5 cells/mL

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Results

Figure 1 shows the comparative results for the two film types of the 50 L HyPerforma Rocker BPC, along with the cells grown in the 125 mL Nalgene Erlenmeyer flask. VCD for all three conditions was within 10% of each other and reached expected values. Viability for all three conditions was within 1% of each other.

Conclusion

The results confirm equivalent growth using the two film types, and perhaps most importantly, demonstrate fitness for use. These confirmation data will help enable end users to confidently transition to Aegis5-14 film when using the HyPerforma Rocker Bioreactor. This latest film option best supports cell culture process development and scale-up operation needs by offering the utmost speed, confidence, quality, and assurance of supply, as these qualities are inherent and well-proven benefits of the Aegis5-14 film architecture, matching those used in other flagship S.U.B. products.

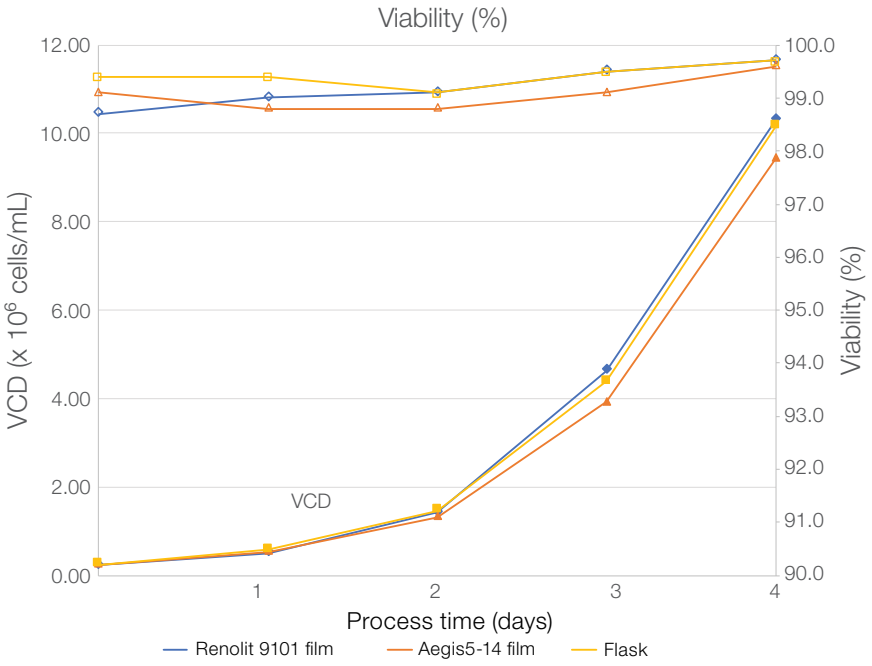

Figure 1. VCD and viability of cells grown in 50 L HyPerforma Rocker BPCs with different film types, and cells grown in a Nalgene Erlenmeyer flask. Viability is shown with the lines with open symbols; viable cell density (VCD) is shown with the lines with filled symbols.

Reference

1. Singh V (1999) Disposable bioreactor for cell culture using wave-induced agitation. *Cytotechnology* 30:149–158.

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