

Technical Bulletin

Consistent Lot-to-Lot Performance in EX-CELL™ 420 Serum-Free Medium for Insect Cells

Introduction

EX-CELL™ 420 is a serum-free insect medium developed in 1997 by SAFC Biosciences. This media was formulated and optimized for the culture of Sf9 and Sf21 cells, but has also shown value in growing *Drosophila* S2 and *expresSF+* insect cells^{1,2}. Historically, within the commercial serum-free insect media market, there have been problematic issues with cell growth consistency between different lots of serum-free media. With more academic and pharmaceutical institutions exploring the utility of insect cells and the Baculovirus Expression Virus System (BEVS) to produce recombinant proteins and therapeutics, it is vitally important to have consistent lot-to-lot growth characteristics.

Since the development of EX-CELL™ 420, SAFC Biosciences has been committed to determine the key elements responsible for lot-to-lot consistency in our insect media. During this time, we have re-evaluated raw materials and manufacturing processes, and, reviewed the results of quality control growth promotion assays from more than 90 different cGMP lots of EX-CELL™ 420. This approach has helped us recognize that there are critical combinations of raw materials responsible for growth, including several raw materials that act synergistically within the medium.

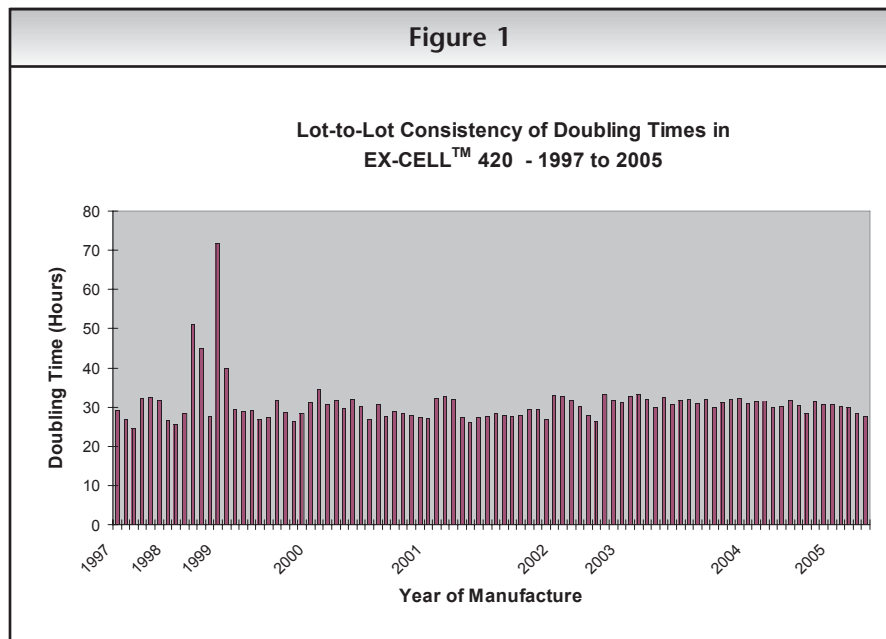


Table 1: Improvement in Doubling Time and Cell Density Consistency in EX-CELL™ 420

Year of Manufacture	Doubling Time (Hours)	Average Doubling Time Hours
1997 to 1999	32.6 ± 10.7	4.1 ± 1.6
2000 to 2005	30.1 ± 2.0	4.1 ± 0.8

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Yeast extract (the autolysate of Baker's Yeast), also known as Yeastolate, is widely used in insect serum-free media as a source of nutrients and B-complex vitamins. Because yeast is a living organism, and variable by nature, dried powder yeast extract can be inconsistent in its vitamin and amino acid concentrations between different lots. Recognizing this, SAFC Biosciences has greatly increased the stringency of our raw material screening process for yeast extract. We have also determined a synergistic relationship between yeast extract and other nutrients in EX-CELL™ 420. SAFC Biosciences determined that these components must be carefully screened together for quality of growth promotion prior to formulation of a complete lot. Concomitantly, SAFC Biosciences enhanced our proprietary manufacturing processes to ensure consistent, stable incorporation of critical components within the medium.

The results of these endeavors have led to more consistent lot-to-lot performance of EX-CELL™ 420. As can be seen in Figure 1, the early years of production (1997-1999) yielded several lots of EX-CELL™ 420 that were variable in performance. During 1999 however, raw material and manufacturing improvements were implemented; the same figure shows the dramatic improvement in lot-to-lot consistency after these improvements. Table 1 shows the average doubling times and cell densities in lots manufactured between 1997-1999, and between 2000 and 2005. Overall, there has been a slight reduction in doubling time to approximately 30 hours, with improvement in the standard deviation to approximately two hours. These improvements have led to extremely consistent performance in EX-CELL™ 420.

Media development is a constantly evolving science, and, as time progresses and better raw materials and screening methods become known and available, SAFC Biosciences will continue to evaluate and improve our media so that it performs to the highest of our customers' expectations.

References

1. EX-CELL™ 420 Serum-Free Medium for the Growth of Spodopteran (Sf9 and Sf21) Insect Cells, SAFC Biosciences, Literature No. R015.
2. Growth Characteristics of the *expresSF+*® Serum-Free Insect Cell Line in EX-CELL™ 420, SAFC Biosciences, Literature No. T066.

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