

LONG[®]R³IGF-I: An Insulin Alternative Exclusively for Cell Culture Applications

SAFC Biosciences™
Accelerate Success™

LONG[®]R³IGF-I is a recombinant analog of human insulin-like growth factor-I (IGF-I) that has been specifically engineered for the enhancement of cell culture performance. LONG[®]R³IGF-I is more biologically potent in vitro than either insulin or native IGF-I and has been shown to significantly increase recombinant protein production. It is ideal for both research and large-scale culture systems using serum-free or low-level serum applications.

All cells with Type-I IGF receptors have the potential to respond to LONG[®]R³IGF-I. Studies using this growth factor as a supplement in cell culture have shown that it can result in performance that is equivalent to or better than recombinant insulin in numerous cell types, including Chinese hamster ovary (CHO), baby hamster kidney (BHK), human embryonic kidney (HEK 293), Vero, PER.C6[®], Madin Darby canine kidney (MDCK), hybridomas, and fibroblasts.

LONG[®]R³IGF-I is manufactured using a patented *E. coli* expression system that is free of animal-derived components. This product is specifically designed and manufactured exclusively for the industrial cell culture market for distribution by SAFC Biosciences — a secure supply of a dedicated animal-component free (ACF) CGMP critical raw material.

**LONG[®]R³IGF-I:
NOW AVAILABLE AS A LIQUID**
Now available in a liquid format, liquid LONG[®]R³IGF-I provides the following additional benefits:

- Easy to use, stable solution at 1 mg/mL in 100 mM acetic acid
- Convenient packaging: 5-mL vial or 100-mL bottle
- Stable at 4–8 °C: No thawing required, use directly from the refrigerator
- Equivalent performance to lyophilized LONG[®]R³IGF-I

In addition, there are no differences in the manufacturing process for liquid and lyophilized powder LONG[®]R³IGF-I, ensuring consistent product.

ADAPTATION FROM INSULIN

To adapt cells from insulin to LONG[®]R³IGF-I, a titration should be performed for each different application

because the optimum concentration needed may vary depending upon the cell type used and other components present in the medium. The recommended final concentration range of LONG[®]R³IGF-I is 10 to 100 µg/L. Because LONG[®]R³IGF-I and insulin may compete for the same cell receptors, the effectiveness of LONG[®]R³IGF-I will be masked if it is added in conjunction with commonly used concentrations of insulin (1–10 mg/L). However, inclusion of lower concentrations of insulin (<1 mg/L) in cell culture medium containing the recommended levels of LONG[®]R³IGF-I can result in beneficial synergistic effects in certain applications.

There are two basic methodologies for adapting cells to medium containing LONG[®]R³IGF-I: *direct substitution* and *gradual weaning*. Direct substitution involves the transfer of cells from an insulin-containing medium to an alternative insulin-free medium containing an appropriate quantity of LONG[®]R³IGF-I (10–100 µg/L, recommended starting at 50 µg/L). Gradual weaning allows the

incremental removal of insulin from the media (halving the concentration on each passage) while maintaining LONG[®]R³IGF-I at a fixed concentration (as above). As the cells become adapted to lower concentrations of insulin (<1.25 mg/L), the clone can be periodically screened for the ability to grow in medium without insulin (e.g., medium containing only LONG[®]R³IGF-I). The point at which insulin can be fully removed from the medium will vary with each cell line.

SUMMARY

LONG[®]R³IGF-I is a CGMP, ACF alternative to insulin for use in cell culture applications. Now available as a liquid, it provides an easy-to-use, ACF solution, that can be directly used in multiple cell culture applications without the need for reconstitution or thawing. Convenience and performance make it a superior alternative to insulin.

LONG[®] is a registered trademark of Novozymes GroPep Limited. Composition covered by US Patent No. 5,330,971 and foreign patents assigned to GroPep Limited. PER.C6[®] is a registered trademark of Crucell N.V.

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Comparative effect of LONG[®]R³IGF-I and insulin on CHO cell number, viability, and recombinant protein production. **A)** CHO cell number in serum-free media containing LONG[®]R³IGF-I or insulin; **B)** viability of CHO cells in serum-free media containing LONG[®]R³IGF-I or insulin; **C)** cumulative recombinant protein production in CHO cells

