

Technical Bulletin

LONG^{R3}IGF-I Frequently Asked Questions – Strategic Sourcing

Is LONG^{R3}IGF-I made to cGMP standards?

Yes; LONG^{R3}IGF-I is manufactured according to cGMP standards.

Is LONG^{R3}IGF-I used in the manufacture of other pharmaceutical products?

Yes; LONG^{R3}IGF-I is regulatory compliant and is used in the manufacture of biopharmaceuticals at all stages of development. It is currently used in the manufacture of several biopharmaceuticals approved by the FDA (United States), EMEA (Europe) and MHLW (Japan).

Are any animal-derived components used in the manufacture of LONG^{R3}IGF-I?

No; LONG^{R3}IGF-I manufactured using a process that is free of animal-derived components, confirmed by our regulatory group on request.

Can you describe the process by which LONG^{R3}IGF-I is prepared?

LONG^{R3}IGF-I is manufactured by Novozymes in a proprietary but conventional expression system. A frozen ampule of cells is taken from a validated working cell bank. The cells are fermented in a fed-batch system, in a fully defined media free of animal-derived components, to produce inclusion bodies which are harvested and dissolved. LONG^{R3}IGF-I is then refolded in redox buffer and purified by a four-stage chromatography step.

Four-stage downstream purification:

- Big beads Solid Phase (SP) cation exchange chromatography to capture LONG^{R3}IGF-I and remove host-cell impurities
- Reverse-phase chromatography (RPC 30) to remove host-cell contaminants and product-related impurities
- Fast flow SP cation exchange chromatography to further purify LONG^{R3}IGF-I
- Gel filtration (G25) using 100 mM acetic acid to remove urea and product-related impurities (aggregates)

The final step uses ultrafiltration to target the concentration range for dispensing and 5X diafiltration against 100 mM acetic acid to remove residual urea from the preceding gel filtration step. LONG^{R3}IGF-I is then dispensed and in the case of lyophilized Catalog No. 85580C, freeze dried.

Is LONG^{R3}IGF-I amenable to dry powder formulations?

Yes; SAFC Biosciences® has optimized the milling procedures for LONG^{R3}IGF-I and routinely manufactures dry powder media containing LONG^{R3}IGF-I.

What packaging sizes are available?

LONG R³IGF-I is available from SAFC Biosciences® as a freeze-dried powder in 5, 20 or 50 mg size vials, Catalog No. 85580C. A liquid formulation of LONG R³IGF-I in 100 mM acetic acid is available in 5 mL and 100 mL sizes at a concentration of 1 mg/mL, Catalog No. 91590C.

What type of documentation is provided?

All lots of LONG R³IGF-I are accompanied by a lot-specific Certificate of Analysis which includes product characteristics such as appearance, endotoxin, molecular weight, biological activity and purity.

Can you define the relationship between SAFC Biosciences and Novozymes?

The relationship between SAFC Biosciences and Novozymes is governed by a contractual agreement. SAFC Biosciences has exclusive rights to marketing and distributing LONG R³IGF-I for the industrial cell culture market. SAFC Biosciences also provides technical service for LONG R³IGF-I, including custom formulations into liquid or dry powder. Novozymes manufactures LONG R³IGF-I to cGMP standards as well as providing research and development and technical support as necessary.

Is the supply of LONG R³IGF-I secure and what is your risk management strategy?

LONG R³IGF-I is manufactured by Novozymes, the world's largest producer of recombinant proteins. Novozymes' manufacturing strategy is to protect its customer base by building capacity well ahead of forecast demand. Currently, Novozymes has the capacity to produce enough LONG R³IGF-I to supplement 80 - 160 million liters of serum-free media annually, with room to grow. As part of Novozymes' risk management strategy, an inventory safety surplus well ahead of one year's forecast demand is maintained in secured storage facilities around the globe. A Risk Management document is available upon request.

How often does SAFC Biosciences audit Novozymes LONG R³IGF-I manufacturing facility?

SAFC Biosciences audits the current Novozymes LONG R³IGF-I facility every three years.

Warranty, Limitation of Remedies

SAFC Biosciences warrants to the purchaser for a period of one year from date of delivery that this product conforms to its specifications. Other terms and conditions of this warranty are contained in SAFC Biosciences' written warranty, a copy of which is available upon request. ALL OTHER WARRANTIES, EXPRESSED OR IMPLIED, INCLUDING THE IMPLIED WARRANTY OF MERCHANTABILITY AND FITNESS FOR A PARTICULAR PURPOSE, ARE EXCLUDED. In no case will SAFC Biosciences be liable for any special, incidental, or consequential damages arising out of this product or the use of this product by the customer or any third party based upon breach of warranty, breach of contract, negligence, strict tort, or any other legal theory. SAFC Biosciences expressly disclaims any warranty against claims by any third party by way of infringement or the like. THIS PRODUCT IS INTENDED FOR PURPOSES DESCRIBED ONLY AND IS NOT INTENDED FOR ANY HUMAN OR THERAPEUTIC USE.

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