

# Technical Bulletin

## LONG®R<sup>3</sup>IGF-I Storage, Stability and Specifications

### Format and Storage

LONG®R<sup>3</sup>IGF-I is available as a lyophilized powder, Catalog No. 85580C, or a 1 mg/mL liquid formulation in 100 mM acetic acid, Catalog No. 91590C. Both formats are shipped at ambient temperature and stored at 2 to 8 C.

	Format	Available Sizes	Storage
85580C	Lyophilized	1, 5, 10, 20 and 50 mg	2 to 8 C
91590C	Liquid (1 mg/mL)	5 mL, 100 mL	2 to 8 C

After reconstituting a solution of lyophilized LONG®R<sup>3</sup>IGF-I as prepared below, or after opening a vial of liquid LONG®R<sup>3</sup>IGF-I, the product should be stored re-capped in the original vial at 2 to 8 C. It is imperative that the vial is re-capped properly to form an airtight seal, as the volatile nature of the acetic acid solution can result in evaporation and consequentially a concentration of the LONG®R<sup>3</sup>IGF-I in solution.

### Stability — Long-Term

Formal ICH Q7A compliant stability studies are used to assess the long-term stability of LONG®R<sup>3</sup>IGF-I when stored at 2 to 8 C. These studies are ongoing with the current shelf-life for each formulation indicated in the table below.

	Format	Shelf-life (2 to 8 C storage)
85580C	Lyophilized	3 years
91590C	Liquid (1 mg/mL)	18 months (ongoing)

The following assays are performed to assess the stability of the liquid and lyophilized LONG®R<sup>3</sup>IGF-I formulations throughout the formal stability studies.

Assay	
Protein Synthesis	Clarity of Solution
Endotoxin	Bioburden
Gel Electrophoresis	Mass Spectroscopy
Reverse Phase HPLC	N-Terminal Sequencing
Appearance	Particle Content

### Stability — Transport

The stability of LONG®R<sup>3</sup>IGF-I during transport at ambient temperatures has been investigated for both formulations. Samples were sent from Novozymes Biopharma Australia to SAFC Biosciences™ in Lenexa, Kansas, USA and returned to Novozymes Biopharma Australia with temperature loggers to record the temperature range during transit.

	Format	Range recorded	Total transit time
85580C	Lyophilized	10 to 30 C	9 days
91590C	Liquid (1 mg/mL)	6 to 30 C	20 days

The following assays were performed to assess the stability of LONG®R<sup>3</sup>IGF-I following transport at uncontrolled ambient temperatures.

Assay	
Protein Synthesis	Clarity of Solution
Endotoxin	Bioburden
Gel Electrophoresis	N-Terminal Sequencing
Reverse Phase HPLC	Particle Content
Appearance	

Specifications for all tests were within limits, demonstrating that both LONG®R<sup>3</sup>IGF-I formulations remain stable during transport at uncontrolled ambient temperature.

### Final Product Specification

Final product specifications for both formats of LONG®R<sup>3</sup>IGF-I can be found on the reverse side of this publication.

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## Final Product Specification

### Catalog No. 85580C, Lyophilized LONG<sup>®</sup>R<sup>3</sup>IGF-I

Test	Specification
Appearance	White/creamy crystalline deposit
Biological Activity: by stimulation of protein synthesis	ED <sub>50</sub> < 10 ng/mL
Bacterial Endotoxin: by chromogenic LAL assay	< 0.10 EU/μg protein
Identity (A): by reverse phase HPLC	Conforms to reference standard by retention time and chromatographic profile
Identity (B): by N-terminal sequence analysis	MPFAMPLSSSLFVNGPRTL
Molecular Weight: by mass spectrometry	9108 - 9112 daltons
Purity: by NuPage Bis-Tris gel electrophoresis	≥ 95% single band between 6000 and 14400 daltons

## Final Product Specification

### Catalog No. 91590C, Liquid LONG<sup>®</sup>R<sup>3</sup>IGF-I

Test	Specification
Appearance	Clear liquid
Biological Activity: by stimulation of protein synthesis in rat L6 myoblast cell line	ED <sub>50</sub> < 10 ng/mL
Bacterial Endotoxin: by chromogenic LAL assay	< 0.10 EU/μg of protein
Identity (A): by reverse phase HPLC	Microheterogeneous mixture of LONG <sup>®</sup> R <sup>3</sup> IGF-I, typically 4 peaks with the major peak > 60% of total peak area
Identity (B): by amino acid sequence analysis of N-terminal 18 amino acids	MFPAMPLSSSLFVNGPRTL
Purity: by SDS-polyacrylamide gel electrophoresis under reducing conditions	A single band ≥ 95% with the same electrophoretic mobility as LONG <sup>®</sup> R <sup>3</sup> IGF-I reference standard. No additional individual band ≥ 5%. Total of additional individual bands < 5%.
Concentration: by reverse phase HPLC as used in Identity (A)	0.9 - 1.1 mg/mL
Bioburden	Total Viable Aerobic Count ≤ 100CFU/mL. Enterobacteriaceae and gram negatives absent in 1 mL. <i>Pseudomonas aeruginosa</i> , <i>Staphylococcus aureus</i> absent in 1 mL.

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