ScaleReady

Recombinant Human IL-2 GMP

Catalog # BT-002-GMP

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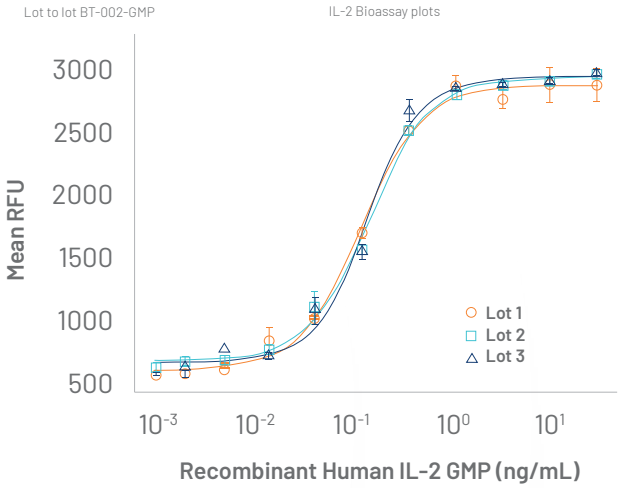
Recombinant IL-2 proteins are used by CGT researchers to promote the proliferation of CAR-T cells, TCR T cells, Tregs, TILs and NK and CIK cells in preclinical or clinical ex vivo use. Our GMP-grade cytokines boast robust reproducible bioactivity and confidence in RUO to GMP-grade translation that will accommodate closed-system requirements as you progress through clinical trials.

Our GMP-grade IL-2 contains the same cysteine to serine mutation found in Proleukin®. This mutation has been reported to prevent cysteine mispairing in E.coli which can lead to protein aggregation and makes our new GMP-grade IL-2 protein soluble in injectable-grade water.

GMP Recombinant Human IL-2 joins IL-7 and IL-15 produced within Bio-Techne's dedicated animal-free GMP facility located in St. Paul MN USA. The new facility has been optimized for scale to address these challenges so you can have confidence in your cytokines to meet the growing industry demand and the needs of your program from process development to commercialization.

- **Lot-to-lot consistency:** All new lots of GMP-grade IL-2 are rigorously tested to ensure consistency with previous lots and with a master lot, so you don't have to worry whether experiments will be reproducible over time
- **Reservable lots:** Entire lots can be reserved to accommodate your long term needs, preventing you from having to spend time and money requalifying lots
- **Manufactured in a state-of-the-art facility** dedicated solely to animal-free GMP proteins
- **Research-grade IL-2** (Catalog # BT-002-AFL) is also produced in the new animal-free facility using the same sequence and source as GMP-grade



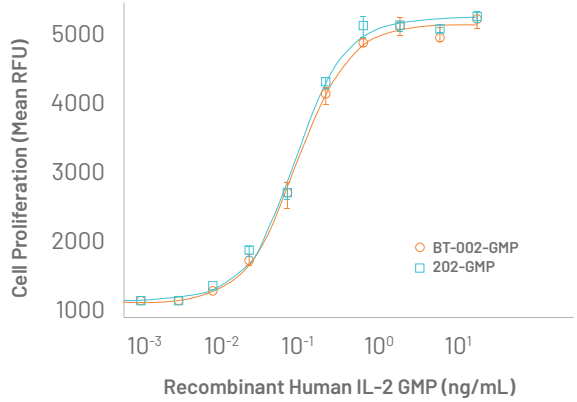
GMP-grade Recombinant Human IL-2 Produced in the New GMP Facility Displays Similar Bioactivity as the Original GMP-grade Recombinant Human IL-2 Protein. The bioactivity of GMP-grade Recombinant Human IL-2 (R&D Systems, Catalog # BT-002-GMP) manufactured in the new GMP facility was compared to the bioactivity of the original GMP-grade Recombinant Human IL-2 (R&D Systems, Catalog # 202-GMP) by testing the ability of the proteins to stimulate proliferation of the CTLL-2 mouse cytotoxic T cell line.

Comparison of the Original GMP-Grade IL-2 and the New GMP-Grade IL-2 Proteins

	Specification	202-GMP	BT-002-GMP
Manufacturing Site		Minneapolis, MN USA	St. Paul, MN USA
Sequence		Ala21-Thr153, with an N-terminal Met (Accession # P60568)	Ala21-Thr153 (C145S), with and without an N-terminal Met (Accession # P60568.1) - the same Cys to Ser substitution found in Proleukin®
Activity	Cell proliferation assay using CTLL-2 mouse cytotoxic T cells	The ED_{50} for this effect is 0.05-0.25 ng/mL.The specific activity of recombinant human IL-2 is >5.0 x 10^6 IU/mg, which is calibrated against the human IL-2 WHO International Standard (NIBSC code: 86/500).	The ED_{50} for this effect is 0.03-0.25 ng/mL. The specific activity of recombinant human IL-2 is >5.0 x 10^6 IU/mg, which is calibrated against the human IL-2 WHO International Standard (NIBSC code: 86/500).
Source	E. coli	X	X
Purity	>97%	X	X
N-terminal Sequence		Met-Ala21-Pro-Thr-Ser-Ser-Ser-Thr-Lys-Lys	Met-Ala21-Pro-Thr-Ser-Ser-Ser-Thr-Lys-Lys and Ala21-Pro-Thr-Ser-Ser Ser-Thr-Lys-Lys-Thr (low abundance)
Sterility Test	Tested per USP <71> guidelines	X	X
Mass Spectrometry		Dominant peak at 15549 Da	Dominant peak at 15521 Da (full length with Met)
Pack Sizes (µg)		50, 1000	50, 1000
Formulation		Lyophilized from a 0.2 µm filtered solution in acetonitrile and TFA	Lyophilized from a 0.2 µm filtered solution in sodium acetate with trehalose
Host Cell Protein	ELISA <0.5 ng/µg	X	X
Endotoxin	<0.01 EU per USP <85> guidelines	X	X
Mycoplasma	Ribosomal RNA hybridization assay: Negative	X	X
Reconstitution		Reconstitute at 100 µg/mL in 100 mM acetic acid	Reconstitute at 250–500 µg/mL in sterile deionized water
Facility	Animal-free	GMP facility located in Minneapolis, MN, USA	Dedicated animal-free GMP facility located in St. Paul, MN, USA

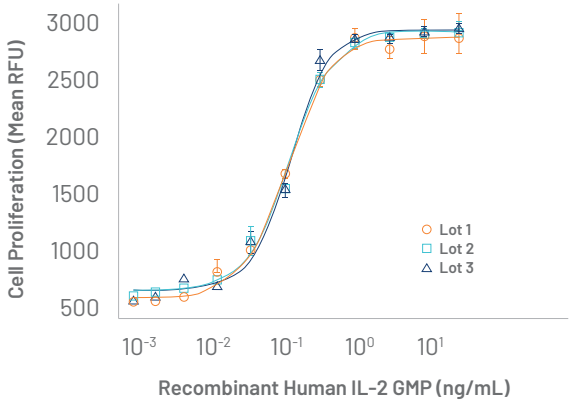
Proleukin® is a registered trademark of Clinigen Holdings Limited.

Bioactivity Comparison of Our New GMP IL-2 with Our Original GMP IL-2



New GMP IL-2 Displays Similar Bioactivity as the Original GMP IL-2. Our new **GMP-grade Recombinant Human IL-2** and our original **GMP-grade Recombinant Human IL-2** show equivalent ability to stimulate the proliferation of CTLL-2 cells.

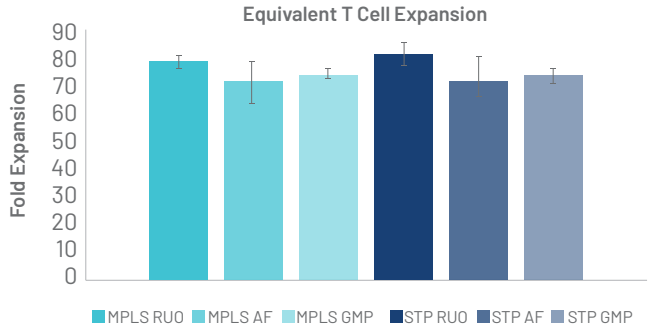
New GMP-grade Human IL-2 Displays High Lot-to-Lot Consistency

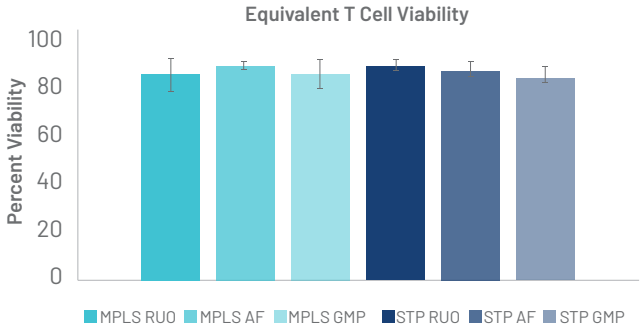


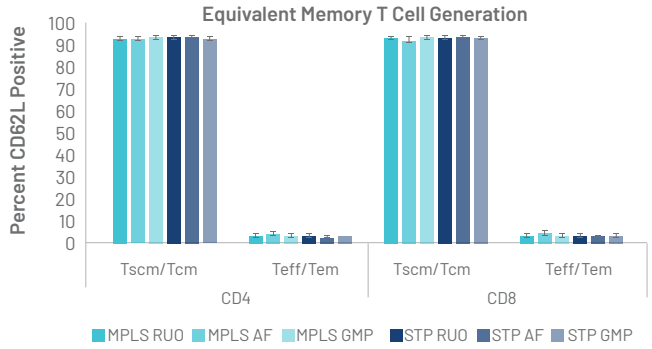
Analysis of the Lot-to-Lot Consistency GMP-grade Recombinant Human IL-2 Activity. Three independent lots of our new **GMP-grade Recombinant Human IL-2** were tested for their ability to stimulate proliferation of CTLL-2 cells. Each trace on the graph represents a different manufacturing run.

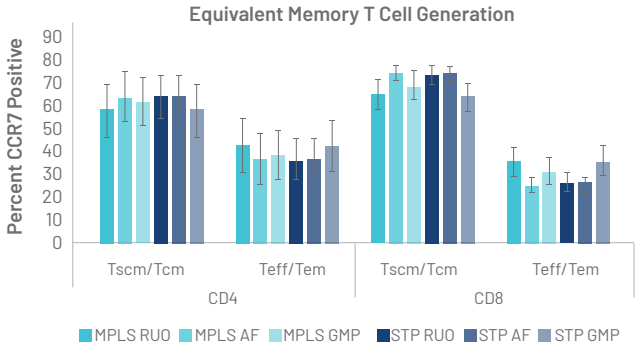
Performance of All Grades of IL-2 on Primary Human CD4+ and CD8+ T Cells

Easily and confidently transition your cell therapy program from research-grade IL-2 to our new animal-free GMP cytokine with minimal impact on T cell growth or phenotype. Each of our grades of human IL-2 perform equivalently as seen in this direct comparison between research use only, preclinical animal-free, and animal-free GMP IL-2, each produced at our Minneapolis or our new facility in St. Paul.









For these experiments, PBMCs were isolated from 3 donors with the Fresenius Kabi Lovo® Automated Cell Processing System followed by positive selection of CD4+ and CD8+ T cells. Cells were expanded in a Wilson Wolf G-Rex® 6M Well Plate supplemented with 200 IU/mL IL-2 for 3 days, followed by 10 – 11 additional days with fresh medium and IL-2. Expanded cultures were analyzed for c ell expansion (A), viability (B), and phenotype (C, D). Histogram bars represent the average of 3 donors.

For flow cytometry, cells were analyzed for either CD62L or CCR7 expression as alternate markers for T stem cell memory, T central memory, T effector, and T effector memory subtypes. In Panel C with CD62L staining, all grades of IL-2 induced the generation of nearly all Tscm and Tcm cells with very few Teff and Tem cells formed. In Panel D with CCR7 staining, all grades of IL-2 also performed equivalenty but they induced a more even distribution of the cell types.

Labeling in Graphs	Product Name	Catalog #
MPLS* RUO	Recombinant Human IL-2 Protein	202-IL
MPLS *AF	Recombinant Human IL-2 Protein, Animal-Free	AFL202
MPLS* GMP	Recombinant Human IL-2 GMP Protein	202-GMP
STP AF	Recombinant Human IL-2 Protein, Animal-Free	BT-002-AFL

Animal-Free Manufacturing Conditions

Our dedicated controlled-access animal-free laboratories ensure that at no point in production are the products exposed to potential contamination by animal components or byproducts. Every stage of manufacturing is conducted in compliance with R&D Systems' stringent Standard Operating Procedures (SOPs). Production and purification procedures use equipment and media that are confirmed animal-free.

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Contact us: info@scaleready.com

ScaleReady is a Joint Venture formed by Bio-Techne, Fresenius Kabi, and Wilson Wolf. Combining selected offerings from the three partners, the ScaleReady manufacturing platform combines tools and technologies for cell culture, cell activation and expansion, gene editing, and cell processing.

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