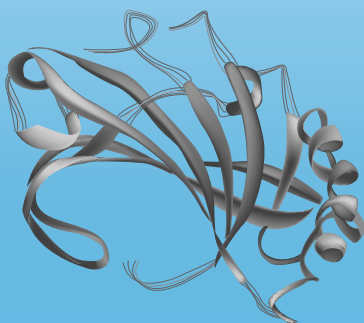
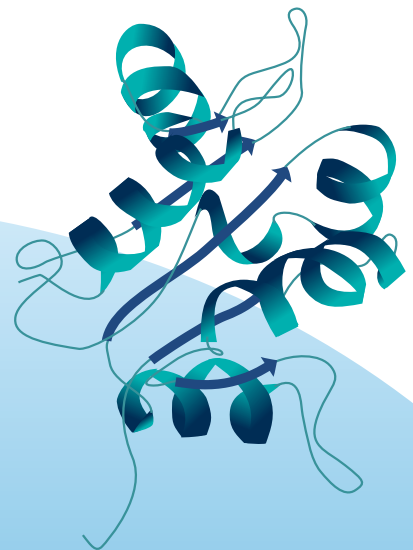
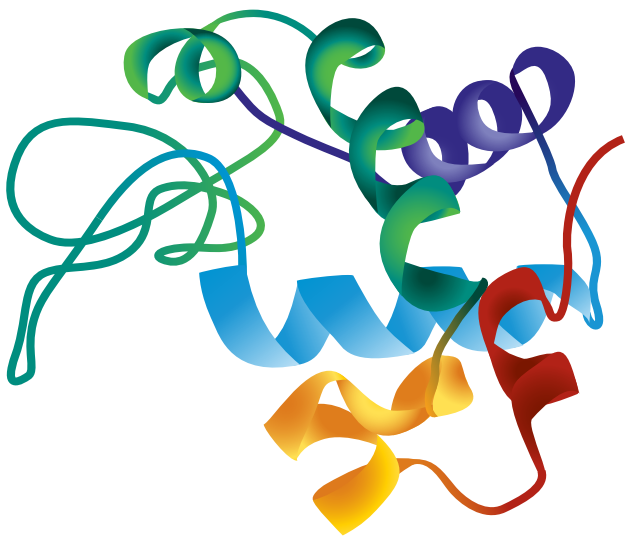


**biotechne®**

# GMP Cytokines and Growth Factors for Therapeutic Manufacturing





## R&D Systems™ GMP\* Proteins for Therapeutic Manufacturing

Immune cell therapies, stem cell therapies, and regenerative medicine, often grouped into the category of advanced therapy medicinal products (ATMPs), offer some of the most revolutionary and exciting new approaches for treating human disease. Because they utilize living cells or tissues as the therapeutic, the manufacturing process is vastly more complex than those of more traditional treatment methods. The use of high-quality media supplements such as growth factors and cytokines is paramount to ensuring safety, efficacy, and minimizing batch-to-batch variability.

R&D Systems has a rich history of producing the most widely used proteins in the world. Our expertise in protein development and manufacturing, combined with stringent quality control and experienced regulatory support, allows us to offer industry-leading GMP proteins for cell therapy manufacturing.



### Ensuring Consistency

#### Regulatory Certifications, Support, and Supply Chain Continuity:

- GMP products manufactured, tested, and released under an ISO 9001:2015 and ISO 13485:2016-certified quality management system
- A full Quality Assurance (QA) review of all batch and bottling records is done before any material is shipped
- Individual specification sheets with all testing results are reviewed by both our Quality Control (QC) and QA departments.
- Documented processes and QA control of documentation and process changes
- Personnel training program
- Raw material testing, tracing, and vendor qualification/monitoring
- Fully validated equipment, processes, and test methods
- Equipment calibration schedules using a computerized calibration program
- Facility maintenance and safety programs
- Material review board for variances
- Monitoring of stability over product shelf-life
- Product change notifications
- Investment in a new, state of the art manufacturing facility



\*R&D Systems GMP proteins are intended for use as ancillary materials in GMP manufacturing of investigational or marketed clinical products, such as cell therapy, gene therapy, tissue-engineered products, combination products, or other Advanced Therapy Medicinal Products. They are not therapeutic products or excipients, and are not suitable for direct administration to humans.



## Ensuring Safety and Efficacy

### Guidelines and Quality Control:

- USP Chapter <1043>, Ancillary Materials for Cell, Gene, and Tissue-Engineered Product
- Ph. Eur. General Chapter 5.2.12, Raw Materials of Biological Origin for the Production of Cell-based and Gene Therapy Medicinal Products
- Lot-specific Certificate of Analysis
- Certificates of Origin
- Animal-free capabilities
- Defined endotoxin specifications
- N-terminal sequencing for first 10 amino acids
- Defined purity specifications
- Mycoplasma testing
- Host cell protein and DNA testing
- Bioburden/Sterility testing in accordance to USP
- Validated activity testing
- Formal stability testing program



## Combining Purity, Bioactivity, and Consistency

As growth factors and cytokines are produced in biological systems, they are inherently susceptible to variability. To maximize efficacy and safety, a supplier should have a quality management system in place to ensure lot-to-lot consistency and highly-purified formulations. A highly potent cytokine or growth factor can also lower the amount needed for use and in turn lower costs.

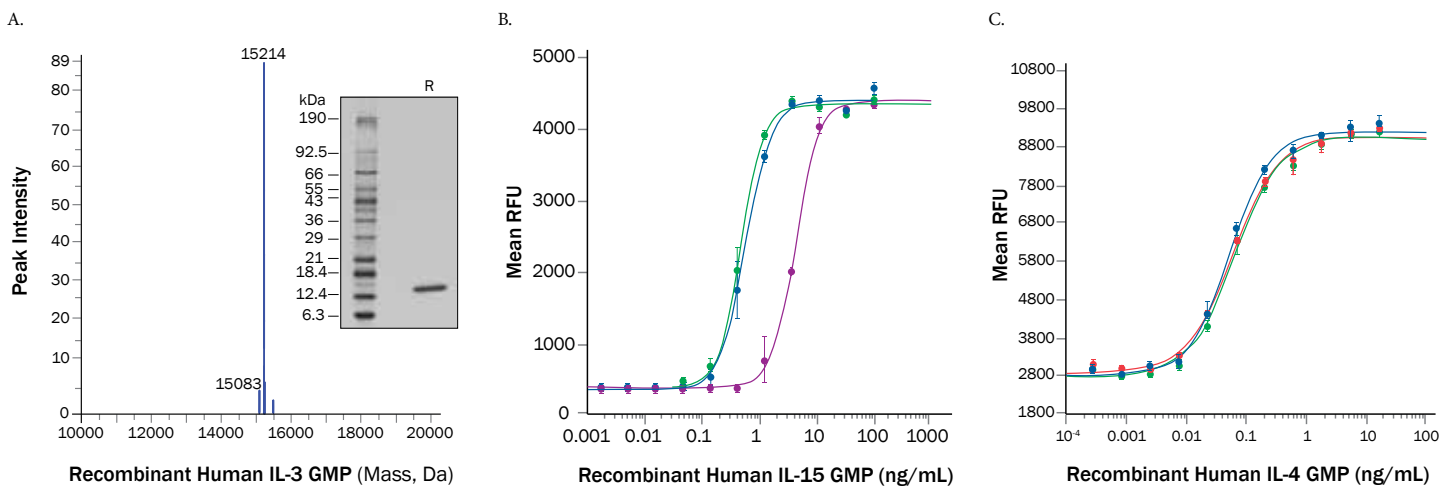


Figure 1. Characterization of Purity, Bioactive Potency and Lot-to-Lot Consistency. A. Electrospray Ionization mass spectrometry (ESI-MS) analysis of GMP Recombinant Human IL-3 (Catalog # 203-GMP). The labeled peaks at 15214 Da and 15083 Da correspond to the calculated molecular mass with the N-terminal Met, and without the N-terminal Met, respectively. Greater than 97% purity is also seen using SDS-PAGE under reducing (R) conditions (inset). B. Two lots of GMP Recombinant Human IL-15 (Catalog # 247-GMP; green and blue) exhibit 10-fold greater activity in a proliferation assay using M07e human megakaryocytic leukemic cells than the equivalent cytokine from another supplier (magenta). C. GMP Recombinant Human IL-4 (Catalog # 204-GMP) stimulates the proliferation of TF-1 human erythroleukemic cells. Overlapping curves highlight reproducible bioactivity over three different lots. The specific activity of recombinant human IL-4 is  $\sim 2.9 \times 10^4$  IU/ $\mu$ g, calibrated against human IL-4 WHO International Standard (NIBSC code: 88/656).



## Unparalleled Combination of Protein and Regulatory Experience

- Developing and manufacturing proteins since 1985
- Clients from countries around the world
- R&D Systems® GMP products are used in numerous clinical trials
- Regular client audits of our facilities
- Confidentiality assured
- More than 100 protein scientists dedicated to development and manufacturing
- More than 90 employees in quality and regulatory roles

## Other On-Site Capabilities for Enhanced QC Testing: Meeting Additional Customer Needs

- High Resolution Mass Spectrometry: Intact mass, post-translational modifications, protein identification
- Gel permeation chromatography/size exclusion chromatography (GPC/SEC): Aggregation assessment
- Reverse phase HPLC: Purity assessment can reveal truncations, mixed disulfide patterns, and more
- Light scattering analysis (SLS, DLS): Aggregation, oligomer analysis, and molecular weight determination when used in tandem with analytical sizing aggregation, oligomer analysis, and molecular weight determination
- Advanced HPLC testing: Homogeneity
- Surface plasmon resonance: Binding kinetics
- Differential scanning fluorimetry (DSF): Protein stability and protein-ligand interactions





## Animal-Free Manufacturing

Animal-free proteins are particularly important to researchers concerned with experimental variables caused by trace animal components or mammalian pathogens. When possible, R&D Systems® GMP proteins are made in an entirely animal-free process.

### Animal-free Laboratory

The facility and all equipment are maintained as an animal-free environment. No animal-containing materials have been inside the facility or in contact with the laboratory equipment. The facility is constructed to ensure there is no exposure of the product to contamination by animal-containing components and there is clear segregation of all labware, such as plasticware, tubing, gloves, pipette tips, and instruments.

**All proteins labeled animal-free are made in an E. coli expression system, in a dedicated animal-free area, with no animal-containing manufacturing components.**

### Animal-free Raw Materials, Instrumentation, and Equipment

- Animal-free Certificates of Origin from raw material suppliers
- Fermentation and purification processes follow approved SOPs
- All raw materials are traceable through batch records
- Bacteria and Sf9 cells are grown in animal-free media
- Dedicated animal-free fermentors
- Validated equipment cleaning procedures
- Dedicated product-specific, animal-free columns
- Column cleaning validated for animal-free manufacturing.
- Animal-free labware
- Proteins filtered using certified animal-free filters.
- Animal-free containers and dedicated cold storage room.
- Classified vialing clean room and dedicated animal-free lyophilizer
- Animal-free vials, stoppers, and crimp caps



## GMP Proteins Available from R&D Systems

GMP Protein	Catalog #	Animal Free
Activin A	338-GMP	
BDNF	248-GMP	
BMP-2	355-GMP	
BMP-4	314-GMP	
BMP-7	354-GMP	
Dkk-1	5439-GMP	
EGF	236-GMP	✓
FGF basic (146 aa)	233-GMP	✓
FGF basic (145 aa)	3718-GMP	✓
Fibronectin	4305B-GMP	
Flt-3 Ligand	308E-GMP	✓
GDF-8/Myostatin	788-GMP	
GDF-11	1958-GMP	
GDNF	212-GMP	
GM-CSF	215-GMP	✓
HGF	294-GMP	
IFN-g	285-GMP	✓

GMP Protein	Catalog #	Animal Free
IGF-I	291-GMP	✓
IL-1b	201-GMP	✓
IL-2	202-GMP	✓
IL-3	203-GMP	✓
IL-4	204-GMP	✓
IL-6	206-GMP	✓
IL-7	207-GMP	✓
IL-11	218-GMP	
IL-12	219-GMP	
IL-15	247-GMP	✓
IL-21	8879-GMP	✓
KGF/FGF-7	251-GMP	
LR3 IGF-I	8335D-GMP	✓
M-CSF	216-GMP	✓
NRG1-b1	396-GMP	
Noggin Fc Tag	3344-GMP	
Noggin	6057-GMP	

GMP Protein	Catalog #	Animal Free
NT-3	267-GMP	
PDGF-AA	221-GMP	✓
PDGF-BB	220-GMP	✓
SCF/c-kit Ligand	255B-GMP	✓
Sonic Hedgehog/ Shh, (C24II) N-Terminus	1845-GMP	✓
Sonic Hedgehog/ Shh, N-Terminus	1314-GMP	✓
TGF-b1	240-GMP	
	240AF-GMP	
TGF-b3	243-GMP	
Thrombopoietin/ TPO	288E-GMP	✓
TNF-a	210-GMP	✓
VEGF 165	293-GMP	
Wnt-3a	5036-GMP	

## GMP ProDots<sup>®</sup> Proteins

Welcome to the future of GMP cytokines and growth factors for cell and gene therapy manufacturing!

GMP ProDots Proteins are pre-aliquoted, lyophilized, and instantly dissolvable spheres of animal-free GMP cytokines or growth factors that are conveniently packaged into single-use bags for easy incorporation into closed-system manufacturing workflows.



What are GMP ProDots Proteins?

- Manufactured under animal-free and GMP controlled conditions
- Dissolve instantly in cell culture media or buffer
- Equivalent bioactivity as standard lyophilized GMP proteins
- Aseptically packaged into single-use bags and tested to USP <71> guidelines
- Each bag contains a pre-aliquoted amount of GMP protein
- Bags contain weldable tubing for sterile docking and a syringe port

GMP Protein	Catalog #	Animal Free	Source	Description#
IL-2	PRD202-GMP	✓	<i>E. coli</i>	20 µg of GMP IL-2 packaged into single-use bags.
IL-7	PRD207-GMP	✓	<i>E. coli</i>	10 µg of GMP IL-7 packaged into single-use bags.
IL-15	PRD247-GMP	✓	<i>E. coli</i>	5 µg of GMP IL-15 packaged into single-use bags.
IL-21	Coming Soon	✓	<i>E. coli</i>	10 µg of GMP IL-21 packaged into single-use bags.

Learn more | [randsystems.com/gmpprodots](https://randsystems.com/gmpprodots)



## Custom Manufacturing

At times raw materials needed for therapeutic manufacturing are only available for research use. In addition, pack sizes that would ease your manufacturing burden might not be available. We can help you navigate these hurdles by custom manufacturing proteins using GMP guidelines.

Our custom development teams include dedicated project managers, regulatory experts, and world class protein scientists to ensure the materials meet your specifications and facilitate the transition from pre-clinical to clinical applications.



## Partnering with you to meet your regulatory requirements

As the demand for biopharmaceuticals and the promise of cellular therapies grow, so does the need for high-quality growth factors and cytokines used for cell culture. Our experienced Quality and Manufacturing teams will partner with you to ensure we meet all of the requirements necessary to instill confidence as your reagent supplier.

Learn more | [rndsistemas.com/gmp](http://rndsistemas.com/gmp)

**R&D** SYSTEMS

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BIOLOGICALS

**TOCRIS**

protein**simple**

**ACD**

**bio-techne**

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