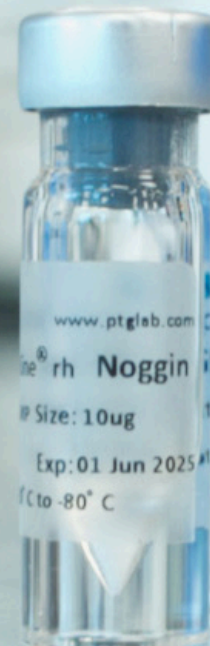
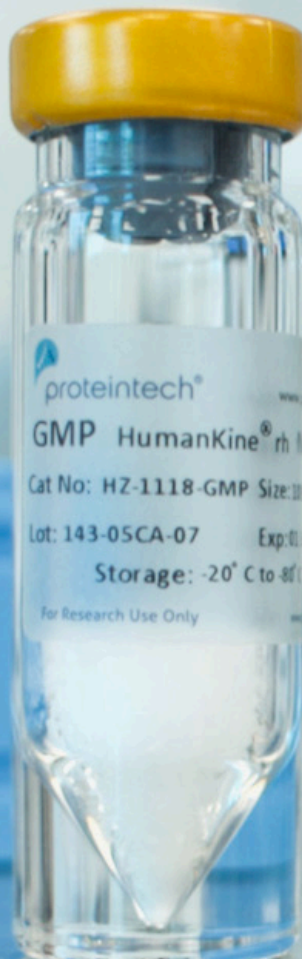


# GMP-GRADE HUMANKINE<sup>®</sup> CYTOKINES & RECOMBINANT PROTEINS

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# GMP-GRADE HUMANKINE<sup>®</sup> CYTOKINES & RECOMBINANT PROTEINS



# "FOR HUMANS...BY HUMAN CELLS"

Cytokines and growth factors are essential to advanced therapies. Unlike traditional pharmacologics, cell and gene therapies require the expansion and maintenance of living cells. These proteins coordinate and sustain these processes.

With the rise in clinical trials, there is a greater demand for safe, pure, and potent recombinant proteins. Besides being xeno-free and animal component-free, Proteintech's HumanKine® recombinant proteins are ISO 13485 certified and GMP-compliant, making them ideal for clinical applications. As these proteins are expressed and purified from HEK293 cells, they have native folding, glycosylation, and other post translational modifications. These properties result in higher bioactivity and stability than proteins produced using other mammalian or prokaryotic expression systems.

## Benefits of HumanKine® HEK293-expressed human proteins

1. Animal component, endotoxin, and xenobiotic free
2. Tag-free
3. Native folding and maturation
4. Authentic human glycosylation
5. High Activity

### Animal component, endotoxin, and xenobiotic free

Products derived from or by an animal are not used at any point during production.

#### Benefits of animal component free and xeno free proteins:

- The final product does not contain any constituent or components from non-human derivation.
- All the materials from procurement to final products are stored and handled in dedicated animal free facility.
- Final product or the process does not involve the use of materials or recombinant materials from non-human sources.
- Besides using a human expression system to minimize endotoxin levels, each lot is verified to be endotoxin free by LAL assay.

### Tag-free

HumanKine® products are expressed and purified without any tags.

#### Benefits of tag free proteins:

- Inclusion of a tag can often result in changes to the structure of the protein of interest.
- A tag may interfere with the active site of the protein resulting in altered biological activity.
- Presence of a tag can increase immunogenicity of some proteins, which makes a tag-free recombinant protein more desirable and reliable for in vivo applications.

## Native folding and maturation

Proper folding and maturation are crucial for optimal protein activity. Chinese Hamster Ovary (CHO) cells are widely used as a mammalian expression system for large-scale protein production, however they lack certain human-specific chaperones. Without these chaperone proteins to guide conformation, CHO cell-expressed recombinant proteins often are incorrectly folded and, in turn, have low activity. In contrast, Humankine® recombinant proteins are expressed in a human cell line, HEK293. This system has the optimal machinery for optimizing conformation and stability of human recombinant proteins. For example, Figure 1 demonstrates how this system generates more mature Activin A in comparison to the conventional CHO cell expression system.

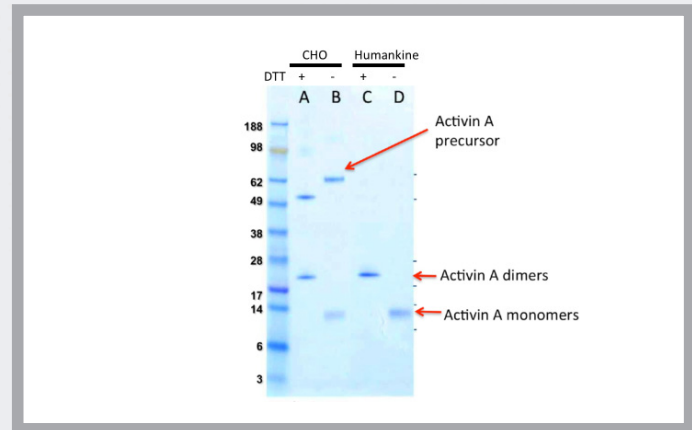


Figure 1 SDS-PAGE gel with Coomassie blue staining of purified Activin A from CHO cell and Humankine® systems, demonstrating the formation of mature Activin A dimers.

## Native human glycosylation

Glycosylation is an essential post-translational modification, which helps define protein structure, function, and stability. Previous research has established that substantial variations in glycostructures exist between recombinant proteins expressed in mammalian, yeast, and insect expression systems. Despite their extensive use in human recombinant protein production, non-human mammalian cells like CHO have different mechanisms for glycan addition. Consequently, glycoproteins produced in these cells may have lower activity than naturally expressed proteins and may even be immunogenic. To avoid these issues, Humankine® recombinant proteins are produced only in HEK293 cells. As a human cell line, this system generates glycoproteins that more closely resemble naturally occurring proteins, optimizing safety and potency. Figure 2 highlights the differences in glycan profiles of EPO recombinant protein expressed in CHO cells and HumanKine® human expression systems.

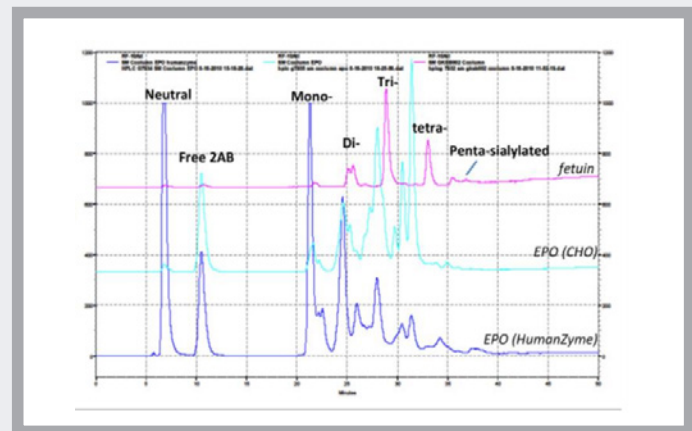


Figure 2 HPLC comparison of glycosylation of human cell expressed and CHO EPO, demonstrating significant differences in glycan composition. Fetuin was used as a positive control.

## High activity

Tag-free proteins expressed in HEK293 cells create proteins that tend to have higher activity than those produced in other expression systems. Figure 3 compares activity for multiple cytokines between different eukaryotic systems.

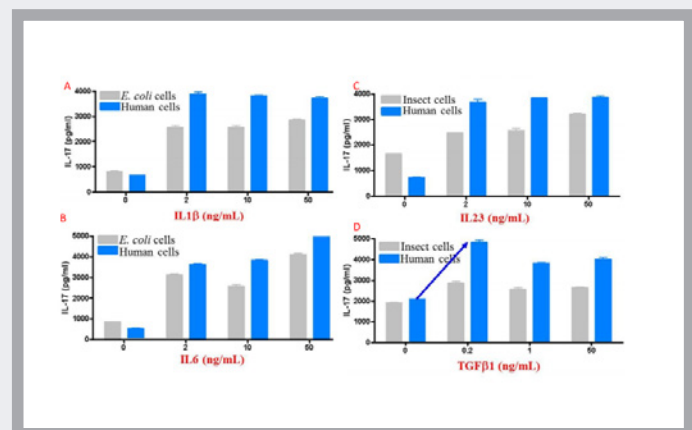


Figure 3 Comparison of activity of insect, human, and *E. coli* cell expressed cytokines (A, IL1β. B, IL6. C, IL23. D, TGFβ1), determined by Th17 differentiation of human CD4+ cells.

# GMP-GRADE PRODUCT MANUFACTURING

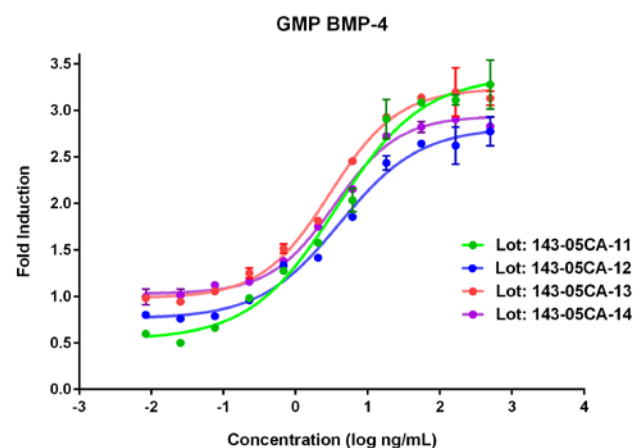
- Manufactured and validated in-house in compliance with ISO 13485 quality management system and appropriate GMP guidelines
- Extensive documentation of every lot's safety, purity, stability, and bioactivity
- Production in line with US Pharmacopeia 1043 guidelines
- Frequent equipment qualification and recalibration
- ISO class 6 cleanroom for production



## Rigorous quality control of batches

- In-process QC testing throughout production
- Every product goes through finished product QC test and QA manually ensures that it meets acceptance criteria before release

*(Figure 4) GMP-Grade Recombinant human BMP-4 (HZ-1045-GMP) stimulates dose-dependent induction of alkaline phosphatase production in the ATDC-5 mouse chondrogenic cell line. Alkaline phosphatase production was assessed using pNPP as a chromogenic substrate*



# MANUFACTURING PROCESS BENEFITS

## Mycoplasma and Endotoxin Free

- Mycoplasma testing of every lot
- Human cell expression system limits endotoxin levels and products are tested to confirm they're endotoxin-free
- Safety is procedure-oriented by trained personnel
- Detailed cleaning and gowning procedures
- Prior to purchasing, we ensure that raw material is free of animal components



## Facilitating the transition from pre-clinical to commercialization

To facilitate a seamless transition from pre-clinical studies to commercialization, both Research-Grade and GMP-Grade HumanKine® cytokines and growth factors are manufactured through the same production process, minimizing variability in performance between Research-Grade and GMP-Grade products.

Though Research-Grade and GMP-Grade products go through the same production process, GMP-Grade products have a more rigorous quality check and provide more extensive documentation support to ensure traceability and transparency for regulatory requirements.



# HUMANKINE® CYTOKINES AND GROWTH FACTORS

\*HumanKine® Research-Grade cytokines and growth factors are available GMP-Grade upon request.

Cat. No	Product name	Activity (ng/ml EC50)	Purity	Expression source	
HZ-1138	Activin A	≤5	>95%	HEK293	16
HZ-1222	beta NGF	≤3	>95%	HEK293	
HZ-1128	BMP-2	≤60	>95%	HEK293	21
HZ-1045	BMP-4	≤10	>95%	HEK293	41
HZ-1229	BMP-7	≤100	>95%	HEK293	7
HZ-1211	Cystatin C	≤5µM IC50	>95%	HEK293	
HZ-1168	EPO	≤2.5	>95%	HEK293	3
HZ-1285	FGF Basic TS	≤0.5	>95%	HEK293	9
HZ-1218	FGF-4	≤1.25	>95%	HEK293	
HZ-1100	FGF-7 (KGF)	≤7.5	>95%	HEK293	
HZ-1103	FGF-8b	≤10	>95%	HEK293	
HZ-1151	FLT3 Ligand	≤0.8	>95%	HEK293	10
HZ-1207	G-CSF	≤0.1	>95%	HEK293	6
HZ-1311	GDNF	≤ 10	>95%	HEK293	
HZ-1002	GM-CSF	≤0.5	>95%	HEK293	11
HZ-1084	HGF	≤20	>95%	HEK293	
HZ-1007	HGH	≤0.5	>95%	HEK293	2
HZ-3001	HSA	N/A	>95%	HEK293	
HZ-1066	IFN alpha 2A	≤0.4	>95%	HEK293	4
HZ-1072	IFN alpha 2B	≤0.12	>95%	HEK293	2
HZ-1298	IFN beta	≤0.1	>95%	HEK293	
HZ-1301	IFN gamma	≤0.05	>95%	HEK293	3
HZ-1164	IL-1 beta	≤0.05	>95%	HEK293	16
HZ-1015	IL-2	≤5	>95%	HEK293	5
HZ-1074	IL-3	≤2	>95%	HEK293	10
HZ-1004	IL-4	≤0.6	>95%	HEK293	18
HZ-1019	IL-6	≤0.5	>95%	HEK293	19
HZ-1281	IL-7	≤1	>95%	HEK293	
HZ-1240	IL-9	≤1	>95%	HEK293	2

Cat. No	Product name	Activity (ng/ml EC50)	Purity	Expression source	
HZ-1145	IL-10	≤1.5	>95%	HEK293	
HZ-1256	IL-12	≤2	>95%	HEK293	
HZ-1113	IL-17A	≤2	>95%	HEK293	3
HZ-1116	17F	≤10	>95%	HEK293	
HZ-1254	IL-23	≤4	>95%	HEK293	11
HZ-1275	IL-27	≤12	>95%	HEK293	1
HZ-1235	IL-28A	≤5	>95%	HEK293	2
HZ-1245	IL-28B	≤1	>95%	HEK293	3
HZ-1156	IL-29	≤5	>95%	HEK293	2
HZ-1109	Lefty-1	≤40	>95%	HEK293	
HZ-1292	LIF	≤0.2	>95%	HEK293	
HZ-1192	M-CSF	≤4	>95%	HEK293	5
HZ-1118	Noggin	≤15	>95%	HEK293	6
HZ-1030	OSM	≤1	>95%	HEK293	3
HZ-1215	PDGF-aa	≤10	>95%	HEK293	
HZ-1278	Pleiotrophin-PTN	N/A	>95%	HEK293	
HZ-1308	proIGF-II	≤3	>95%	HEK293	1
HZ-1161	pro-IGF-II	≤50	>95%	HEK293	1
HZ-1024	SCF	≤25	>95%	HEK293	9
HZ-1306	Sonic Hedgehog	≤350	>90%	HEK293	
HZ-1011	TGF beta 1	≤0.5	>95%	HEK293	84
HZ-1092	TGF beta 2	≤0.5	>95%	HEK293	4
HZ-1090	TGF beta 3	≤0.5	>95%	HEK293	8
HZ-3010	Thrombin	N/A	>95%	HEK293	1
HZ-1014	TNF alpha	≤0.5	>95%	HEK293	9
HZ-1248	TPO	≤5	>95%	HEK293	2
HZ-1204	VEGF 121	≤15	>95%	HEK293	14
HZ-1038	VEGF 165	≤5	>95%	HEK293	12
HZ-1296	Wnt3A	≤20	>90%	HEK293	1

 This number shows the amount of times our protein has been cited in a publication.

Nous contacter

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