

**DESCRIPTION**

<b>Source</b>	Chinese Hamster Ovary cell line, CHO-derived Ala279-Ser390 Accession # P01137 Manufactured and tested under cGMP guidelines.
<b>N-terminal Sequence Analysis</b>	Ala-Leu-Asp-Thr-Asn-Tyr-(Cys)-Phe-Ser-Ser
<b>Structure / Form</b>	Disulfide-linked homodimer
<b>Predicted Molecular Mass</b>	12.8 kDa (monomer)

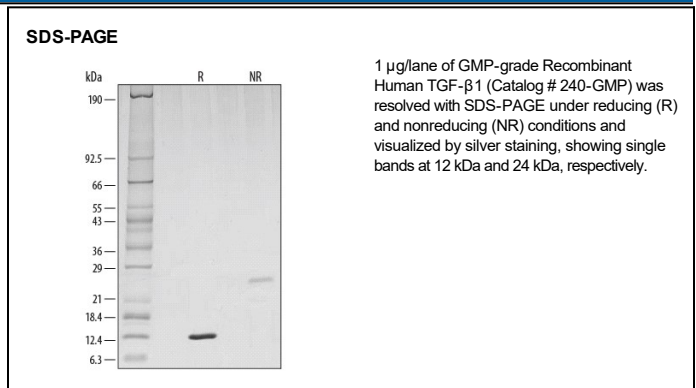
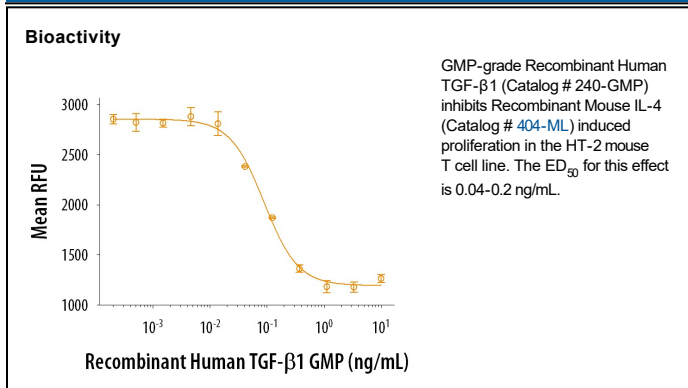
**SPECIFICATIONS**

<b>SDS-PAGE</b>	12 kDa, reducing conditions 24 kDa, non-reducing conditions
<b>Activity</b>	Measured by its ability to inhibit the IL-4-dependent proliferation of HT-2 mouse T cells. Tsang, M. <i>et al.</i> (1995) Cytokine 7:389. The ED <sub>50</sub> for this effect is 0.04-0.2 ng/mL. The specific activity of recombinant human TGF-β1 GMP is approximately 2.5 x 10 <sup>4</sup> U/μg, which is calibrated against human TGF-β1 Standard (NIBSC code: 89/514).
<b>Endotoxin Level</b>	<0.10 EU per 1 μg of the protein by the LAL method.
<b>Purity</b>	>97%, by SDS-PAGE with silver staining.
<b>Host Cell Protein</b>	<0.5 ng per μg of protein when tested by ELISA.
<b>Mycoplasma</b>	Negative when tested in a ribosomal RNA hybridization assay.
<b>Formulation</b>	Lyophilized from a 0.2 μm filtered solution in Acetonitrile and TFA. See Certificate of Analysis for details.

**PREPARATION AND STORAGE**

<b>Reconstitution</b>	Reconstitute at 100 μg/mL in 4 mM HCl.
<b>Shipping</b>	The product is shipped at ambient temperature. Upon receipt, store it immediately at the temperature recommended below.
<b>Stability &amp; Storage</b>	Use a manual defrost freezer and avoid repeated freeze-thaw cycles. <ul style="list-style-type: none"> <li>• A minimum of 6 months when stored at ≤ -20 °C as supplied. Refer to lot specific COA for the Use by Date.</li> <li>• 1 month, 2 to 8 °C under sterile conditions after reconstitution.</li> <li>• 3 months, ≤ -20 °C under sterile conditions after reconstitution.</li> </ul>

**DATA**



## BACKGROUND

TGF-β1 (transforming growth factor beta 1) is one of three closely related mammalian members of the large TGF-β superfamily that share a characteristic cystine knot structure (1-7). TGF-β1, -2 and -3 are highly pleiotropic cytokines that are proposed to act as cellular switches that regulate processes such as immune function, proliferation and epithelial-mesenchymal transition (1-4). Each TGF-β isoform has some non-redundant functions; for TGF-β1, mice with targeted deletion show defects in hematopoiesis and endothelial differentiation, and die of overwhelming inflammation (2). Human TGF-β1 cDNA encodes a 390 amino acid (aa) precursor that contains a 29 aa signal peptide and a 361 aa proprotein (8). A furin-like convertase processes the proprotein to generate an N-terminal 249 aa latency-associated peptide (LAP) and a C-terminal 112 aa mature TGF-β1 (8, 9). Disulfide-linked homodimers of LAP and TGF-β1 remain non-covalently associated after secretion, forming the small latent TGF-β1 complex (8-10). Covalent linkage of LAP to one of three latent TGF-β binding proteins (LTBPs) creates a large latent complex that may interact with the extracellular matrix (9, 10). TGF-β is activated from latency by pathways that include actions of the protease plasmin, matrix metalloproteinases, thrombospondin 1 and a subset of integrins (10). Mature human TGF-β1 shares 100% aa identity with pig, dog and cow TGF-β1, and 99% aa identity with mouse, rat and horse TGF-β1. It demonstrates cross-species activity (1). TGF-β1 signaling begins with high-affinity binding to a type II ser/thr kinase receptor termed TGF-β RII. This receptor then phosphorylates and activates a second ser/thr kinase receptor, TGF-β RI (also called activin receptor-like kinase (ALK) -5), or alternatively, ALK-1. This complex phosphorylates and activates Smad proteins that regulate transcription (3, 11, 12). Contributions of the accessory receptors betaglycan (also known as TGF-β RIII) and endoglin, or use of Smad-independent signaling pathways, allow for disparate actions observed in response to TGF-β in different contexts (11).

## References:

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11. de Caestecker, M. *et al.* (2004) Cytokine Growth Factor Rev. **15**:1.
12. Zuniga, J.E. *et al.* (2005) J. Mol. Biol. **354**:1052.

## MANUFACTURING SPECIFICATIONS

### GMP Proteins

R&D Systems, a Bio-Techne Brand's GMP proteins are produced according to relevant sections of the following documents: WHO TRS, No. 822, 1992 Annex 1, Good Manufacturing Practices for Biological Products; USP Chapter 1043, Ancillary Materials for Cell, Gene and Tissue-Engineered Products and USP Chapter 92, Growth Factors and Cytokines Used in Cell Therapy Manufacturing.

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- Equipment calibration schedules using a computerized calibration program
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- Material review process for variances
- Monitoring of stability over product shelf-life

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- N-terminal amino acid analysis, SDS-PAGE analysis, and endotoxin level (as determined by LAL assay) performed on each bulk QC lot, not on individual bottlings of each QC lot
- Post-bottling lot-specific bioassay results (compliance with an established range) and results of microbial bioburden testing (using broth culture, Sabourand's dextrose and blood agar plates with results reported at 3 days and at 7 days)
- Host Cell Protein testing performed by ELISA
- Mycoplasma testing by ribosomal RNA hybridization assay

Additional testing and documentation requested by the customer can be arranged at an additional cost. Testing may include, but is not limited to, USP <61> bioburden testing, positive identity testing, testing for adventitious agents and testing for residual host cell content.

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