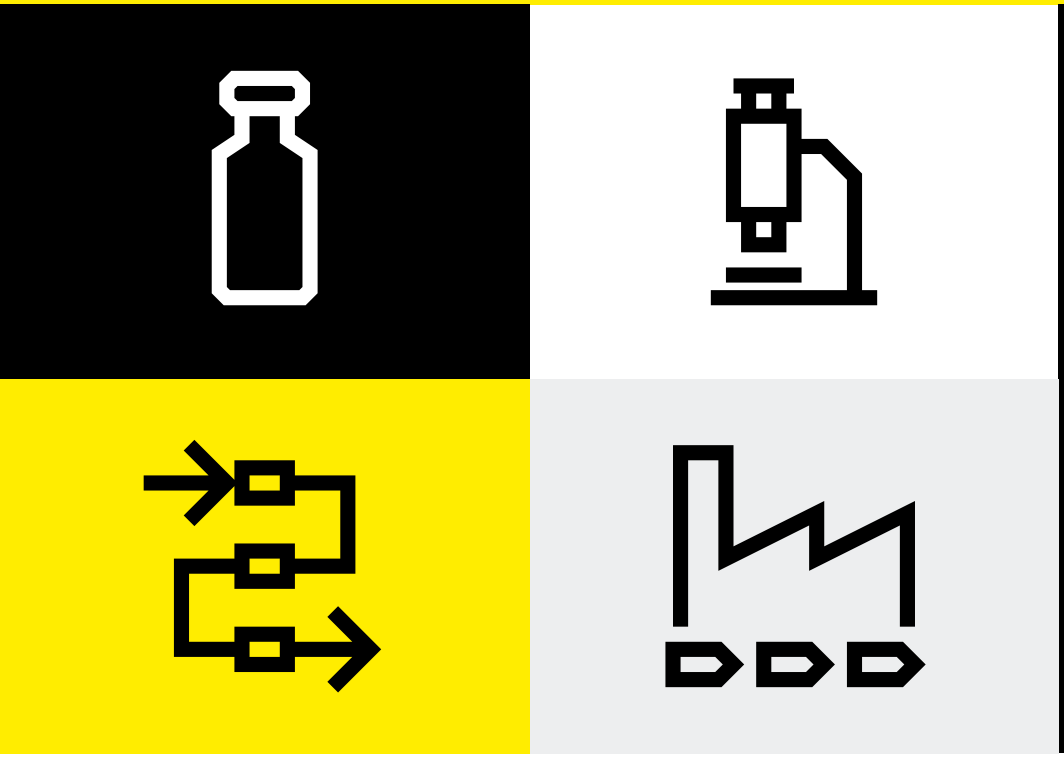
SARTORIUS

CellGenix® rh Cytokines

Preclinical vs GMP



Technical Note

The quality, safety and efficacy of cell therapies are significantly influenced by the raw (ancillary) materials used in manufacturing. We prioritize safety and reliability to provide the highest quality products for clinical *ex vivo* cell processing.

Executive Summary

To allow for a seamless transition from preclinical development to the clinical stage, we offer both preclinical and GMP growth factors and cytokines. Both product grades are produced under the same conditions, using identical production steps and expression systems. This ensures equal product quality and performance.

The difference between both quality levels is that we offer more comprehensive QC testing including tighter specifications and documentation for our GMP products. Our preclinical grade products, therefore, offer a cost-efficient alternative for the early development phase when regulatory support and quality of raw materials have a lower priority and access to GMP-relevant documentation is not required yet.

Preclinical grade: Intended for preclinical *ex vivo* use

GMP grade: Intended for *ex vivo* use in clinical trials and commercial cell therapy manufacturing

CellGenix® Growth Factors and Cytokines other than rh TGF-β1

Quality attributes	Preclinical grade	GMP grade
MCB/WCB fully characterized	no	yes
All processes according to released SOPs	yes[1]	yes
Access to batch documentation	no	yes
Change control, OOS, and deviation procedures	yes[1]	yes
Production and QC equipment qualified	no	yes
Supplier and raw material control	no	yes
Cleaning validation for production equipment	yes[1]	yes
Process validation by 3 consistency batches	no	yes
Validation of all analytical methods	no	yes
Determination of DNA content	no	yes
Sterility testing	yes	Ph. Eur.
Purity	≥ 95%	≥ 97%
Endotoxin testing (all cytokines except IL-2, IL-7, IL-15 and IL-21)	≤ 1000 EU/mg	≤ 50 EU/mg
Endotoxin testing (IL-2, IL-7, IL-15 and IL-21)	≤ 25 EU/mg	≤ 25 EU/mg
Expiry date on CoA	yes	yes
Validation of shelf life by long-term testing[2]	no	yes[2]
Identity of product confirmed	one method	≥ two methods
Activity value on CoA	specific	specific
Determination of host cell protein	no	yes
Regulatory support: DMF, on-site audits, change notifications, etc.	no	yes
Regulatory compliance	USP <1043> Ph. Eur. 5.2.12	USP <1043> Ph. Eur. 5.2.12 ISO 20399:2022

CellGenix® rh TGF-β1

Quality attributes	Preclinical grade	GMP grade
CAP® MCB characterized according to ICH Guidelines Q5A and Q5D	yes	yes
Biologics Master File (BB-MF) for the originating CAP® cell bank available	yes	yes
All processes according to released SOPs	yes[1]	yes
Access to batch documentation	no	yes
Change control, OOS, and deviation procedures	yes[3]	yes
Production and QC equipment qualified	no	yes
Supplier and raw material control	yes[3]	yes
Cleaning validation for production equipment	yes[3]	yes
Process validation by 3 consistency batches	no	yes
Validation of all analytical methods	no	yes
Activity value on CoA	≥ $9 \cdot 10^6$ IU/mg	$9 - 36 \cdot 10^6$ IU/mg
Determination of host cell DNA content	no	≤ 20 ng/mg
Mycoplasma testing of USP harvest: Ph. Eur. 2.6.7	no	negative
Sterility testing	sterile	sterile (Ph. Eur. 2.6.7, USP <71>)
Purity	≥ 95%	≥ 97%
Endotoxin testing: Ph. Eur. 2.6.14, USP<85>	≤ 10 EU/mg	≤ 10 EU/mg
Expiry date specified on CoA	yes	yes
Product Related Proteins	no	≤ 5%
Host Cell Protein[4]	n.a.	n.a.
Validation of shelf life by long-term testing[2]	no	yes[2]
Regulatory support: DMF, on-site audits, change notifications, etc.	no	yes
Regulatory compliance	USP <1043> Ph. Eur. 5.2.12	USP <1043> Ph. Eur. 5.2.12 ISO 20399:2022

Regulatory Excellence

CellGenix® GMP growth factors and cytokines are based on three major quality standards:

- Safety - Safe and qualified raw materials in compliance with our animal-derived component-free policy.
- GMP Compliance - Manufacturing and quality control following applicable GMP guidelines to provide documented evidence of purity, potency, consistency, and stability.
- Regulatory Compliance & Support - GMP products are manufactured, tested, released, and distributed under an ISO 9001:2015 certified Quality Management System and allow for the safe use in accordance with USP Chapter <1043>, Ph. Eur. General Chapter 5.2.12 and ISO 20399:2022. GMP growth factors and cytokines are tested and released according to USP Chapter <92> as applicable.

We offer expert regulatory and technical support as well as FDA Drug Master Files for most of our products. Customized solutions can be provided to meet special compliance needs.

n.a.: not applicable

1As soon as a corresponding GMP product is available, these quality attributes are true for our preclinical grade production batches. These quality attributes cannot be verified in an audit for our preclinical grade products.
2Shelf life for preclinical grade cytokines is determined according to data generated through stress tests/accelerated studies in which the impurity profile is analyzed under forced degradation conditions. Complete long-term data for GMP grade cytokines are available 3 years after product launch.
3All measures are applied for the TGF-β1 preclinical grade production batches. These quality attributes cannot be verified in an audit for our preclinical grade products.
4The production process has been validated to demonstrate suitable clearance of host cell proteins (≤ 1 µg/mg).

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Status: 05 | 2026