TECHNOTE

CellGenix® rh TGF-β1 – Preclinical vs GMP

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

The difference between both quality levels is that we offer a more comprehensive QC testing including tighter specifications and documentation for our GMP product. Our preclinical grade product therefore offers a cost efficient alternative for the early development phase when safety and quality of raw materials have a lower priority.

Preclinical grade: Intended for preclinical *ex vivo* use

GMP grade: Intended for further manufacturing use

Starting Material	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
Manufacturing Process	**Preclinical grade**	**GMP grade**
Formulation	1% mannitol in WFI	1% mannitol in WFI
Filling and lyophilization under class A in B environment	yes	yes
ADCF Level 1: The final product contains neither animal- nor human-derived Materials. No animal- or human-derived materials are used in manufacturing, except the starting material transformed CAP® MCB	yes	yes
Product Specifications	**Preclinical grade**	**GMP grade**
Identity of product	(#P01137, Ala279-Ser390)	(#P01137, Ala279-Ser390)
Activity value on CoA	≥ 9 x 10^6 IU/mg	9 – 36 x 10^6 IU/mg
Determination of host cell DNA content	n.a.	≤ 20.0 ng/mg
Mycoplasma testing of USP harvest: Ph. Eur. 2.6.7	n.a.	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	n.a.	< 5 %
Host Cell Protein*	n.a.	n.a.

*The production process has been validated to demonstrate suitable clearance of host cell proteins (≤ 1 µg/mg).

Quality Assurance	Preclinical grade	GMP grade
All processes according to released SOPs	yes	yes
Batch documentation	yes	yes
Production and QC equipment qualified	n.a. ***	yes
Monitoring of clean room production environment	n.a. ***	yes
Supplier and raw material control	n.a. ***	yes
Process validation by 3 consistency batches	n.a.	yes
Validation of all analytical methods	n.a.	yes
Validation of shelf life by accelerated and real time testing	n.a. **	yes
Change control, OOS and deviation procedures	n.a. ***	yes
Regulatory support: on-site audits, change notifications, etc.	no	yes
Regulatory compliance: USP <1043>, Ph Eur. 5.2.12, ISO TS 20399	n.a.	yes

n.a.: not applicable, not specified, or not available

** Shelf life is determined according to data generated through stress tests in which the impurity profile is analyzed under forced degradation conditions.

*** All measures are applied for our preclinical grade production batches. We however don't send change notifications for our preclinical grade cytokines and these quality attributes cannot be verified in an audit.

Regulatory Excellence

CellGenix GMP products are based on three major quality standards:

- **Safety** - Safe and qualified raw materials in compliance with our animal-derived component-free and serum-free policy.
- **GMP Compliance** - Manufacturing and quality control following all 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 Technical Standard 20399 Part 1-3.

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.

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Subject to change without notice

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