

Powering Excellence in Cell and Gene Therapy Manufacturing

Conceptualize. Optimize. Standardize. Commercialize.





Roche CustomBiotech - our commitment to next generation manufacturers

Advancing concepts to commercialization

Cell and gene therapies have the potential to revolutionize healthcare, but their implementation is technically complex because they build on living systems. Now that industry has progressed technologies to the point of commercial approvals, it is essential that producers of advanced therapeutics leverage well-defined, ready-to-use, and scalable raw materials and analytical quality control solutions to ensure state-of-the-art manufacturing efficiency that meets regulatory requirements.

With decades of experience in tackling challenges relevant to the manufacturing of advanced therapeutics, we offer proven solutions and support documentation tailored to your unique process, quality and regulatory needs, to advance process development and manufacturing of cell and gene therapies, from cell isolation to quality control release testing.

Modification **Isolation Expansion Analytical Quality Control**



High-quality, high-purity digestive enzymes for isolation

Maximize yields of viable cells with efficient cell isolation

Isolation

Only high-purity digestive enzymes with well-characterized performance parameters enable safe and efficient cell isolation from many different tissue sources that yields maximum numbers of viable cells needed for further use in manufacturing.

We offer research-grade and GMP Grade single enzymes and enzyme blends to support your process development, from preclinical feasibility through commercial manufacturing. Our digestive enzymes are manufactured at our state-of-the-art manufacturing facility in Penzberg, Germany. Thus, we can ensure reproducible performance and volume scalability without compromising quality, which translates to the streamlined qualification and optimization of our enzymes as critical starting materials in your processes.

Minimize reworks in raw material qualification

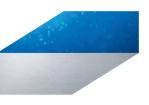
Dissociation enzymes and enzyme blends:

- Maximize cell viability, functionality and yield to meet your performance requirements
- Exhibit high lot-to-lot consistency for reproducible results
- Reduce risk of contamination and animal disease transmission
- Enable processing various cell sources and easily transitioning to clinical manufacturing
- Reduce qualification and risk mitigation activities that are costly and time-consuming
- Include standard or custom-generated documentation to support regulatory submissions

Focus early on process control and product safety

Build safety into your processes by detecting impurities early on. Use our complementary, ready-to-use test kits to assess removal of enzyme impurities after cell isolation and for final product safety testing.

- Residual Protein Liberase Kit Ensure removal of Liberase enzyme blend components
- Collagenase Activity Test Kit Test residuals for collagenase activity with high precision and convenience



Raw materials for mRNA therapeutics

Fit-for-purpose biopharma manufacturing

Modification

At Roche CustomBiotech we continuously optimize our portfolio of mRNA raw materials to provide materials that meet needs of customers with innovative drug development pipelines. In the area of Cell and Gene Therapy our mRNA raw materials are suitable for novel applications in Cell and Gene Therapy like protein replacement therapy, or CRISPR/Cas9 applications in e.g. CAR-T cell therapy, using mRNA encoding for CRISPR-based gene editors to edit genomic DNA in target cells.

We deliver critical raw materials for the key steps of mRNA manufacturing, like the in vitro mRNA transcription. Our mRNA raw materials pipeline and strict quality criteria are designed to support the success of our customers' manufacturing scale-up and regulatory drug approval. Proven by and tailored to the needs of our mRNA manufacturing customers, our mRNA raw materials have fit-for-purpose quality.

CustomBiotech raw materials enable traceable quality control, as well as change and deviation management that contribute to a standardized and reliable manufacturing process.

Use our fit-for-purpose materials for your mRNA manufacturing and rely on our strict quality measurements

- Manufactured under GMP and ISO 13485 quality standards
- Animal-origin-free
- Antiobiotic-free (entirely antibiotics free or β-lactam antibiotics-free)
- Tested for critical impurities, like endotoxin, bioburden, heavy metals, host-cell DNA and protein
- Highly consistent from lot-to-lot
- Available in the scale and quality for biopharma manufacturing purposes

Learn more about our products and quality aspects: www.custombiotech.roche.com/mrna



High-quality, gentle cell detachment enzymes for expansion

Effective cell detachment without compromising product quality

Expansion

Fast, effective, yet gentle detachment of cells is vital for scaling manufacturing of cell and gene therapies. At the same time, the final product must be safeguarded against variability or contamination that raw materials like enzymes can introduce into processes. Manufactured in state-of-the-art Penzberg manufacturing facilities that are certified according to DIN EN ISO 13485, our GMP Grade recombinant trypsin enzymes can be delivered at any scale to catalyze detachment of various adherent cell types on artificial substrates, such as plastic ware.

Use GMP Grade recombinant trypsin from the start

Early incorporation of our GMP Grade recombinant instead of research-use-only trypsin enzymes into clinical manufacturing has many advantages:

- Non-aggressive cell detachment leads to maximum viable cell recovery
- Animal-free origin reduces contamination risk for greater safety assurance
- Stringent GMP specifications guarantees lot-to-lot consistency and reproducible quality
- Reduced qualification and risk mitigation activities save time and resources
- Included standard or custom-generated documentation streamlines regulatory submissions

Guarantee process control and product safety with optimized testing

Be sure the tools you use for cell detachment do not affect the quality and safety of your final product. Establish in-process and final quality controls based on highly sensitive and reliable testing.

 Residual Protein Trypsin Kit Ensure removal of complete and fragmented trypsin



Rapid and reliable analytical quality control tools

Deliver constant product quality with proven ready-to-use control solutions



Establishing predictable product quality and reproducibility of manufactured cell and gene therapies is a challenge by the diversity of starting materials and processes used. Implementing validated commercial technologies to monitor cell viability, cell function and culture conditions during process development and manufacturing saves resources and minimizes risks.

Cedex Analyzers – gain insights into your process to ensure the optimal outcome

Featuring proven data reliability as well as options for an automated workflow integration, our Cedex Analyzers enable flexible quality control of bioprocesses. With a broad test menu, the Cedex Bio and Cedex Bio HT Analyzers accurately determine substrate and metabolite levels in low-volume samples of cell culture supernatant.

The Cedex HiRes Analyzer uses scanner-based high resolution imaging to detect changes in cell concentration, functionally relevant morphology, and aggregation. Furthermore, a long manufacturing history as well as system suitability tests, ensure optimal instrument performance to minimize downtime and ease audit compliance.



Cedex HiRes Analyzer



Cedex Bio Analyzer



Cedex Bio HT Analyzer

Rapid and reliable analytical quality control tools

Deliver constant product quality with proven ready-to-use control solutions

MycoTOOL kits - a "free-of-Mycoplasma" result in just a few hours

Our MycoTOOL Mycoplasma test kits use nucleic acid amplification techniques (NAT) and highly specific probes to detect over 140 cultivable and non-cultivable mollicute species. Validated according to EP 2.6.7 NAT guidelines,* MycoTOOL kits are sensitive, specific, reliable and precise, delivering results that are comparable to compendial mycoplasma detection methods but in a fraction of the time. Qualify our convenient kits for ongoing in-house testing to save costs and time compared to thirdparty testing.**

Revolutionize advanced therapy manufacturing with our proven solutions

The advancement of cell and gene therapies requires building unprecedented manufacturing processes. Success of innovative concepts hinges on anticipating and mitigating risks and overcoming barriers to commercialization. At Roche CustomBiotech, we support your development and manufacturing activities by eliminating uncertainties from critical raw materials and providing quality control analytical tools that fit your specific manufacturing requirements. More than a supplier, we aim to be your partner in bringing the next generation of therapies to market. With past expertise, a commitment to advancement, and a unique portfolio primed for the realization of advanced therapies, we help you stay ahead and reach your target at every step of the way.

Stay at the forefront – create advanced therapies powered by Roche CustomBiotech solutions

^{*} Deutschmann, S.M. et al. (2010). Validation of NAT-based Mycoplasma assay according to European Pharmacopoiea. Biologicals 38: 181-248. Please note, matrix interference and compatibility must be evaluated by the user.

^{**} Chisholm, J. et al. (2017). "Strategy for an abbreviated in-house qualification of a commercially available Rapid Microbiology Method (RMM) for canadian regulatory approval." Cytotherapy Journal 19.12: 1529-1536. celltherapyjournal. Web. 25 Apr. 2018.



Isolation

Raw materials

Product	Catalog number	GMP Grade	Pack size
Single Enzymes			
Collagenase I, Mammalian Free, Liquid ¹	05 172 969 103	No	Custom
Collagenase II, Mammalian Free, Liquid ¹	05 172 942 103	No	Custom
Enzyme Blends			
Collagenase I/II, Mammalian Free, Lyo¹	05 349 907 103	No	500 mg
Liberase T-Flex ⁴	05 989 132 001	No	1 x 500 mg Collagenase blend 2 x 15 mg Thermolysin
Liberase MTF C/T ¹	05 339 880 001	Yes	2x Collagenase I/II blend (500 mg) 3x Thermolysin (15 mg)
Liberase MNP-S ¹	05 578 566 001	No	35 mg
Liberase MNP-S ¹	06 297 790 001	Yes	5 mg
DNase I, recombinant, RNase-free ¹	03 724 751 103	Yes	4 kU

Complementary Testing Kits

Product	Catalog number	Pack size
Residual Protein Liberase Kit ⁵	07 758 693 001	1 kit (96 reactions)
Collagenase Activity Test ²	08 074 461 001	1 kit (96 reactions)



Modification

Product	Catalog number	Pack size	GMP Grade	Animal- origin- free (AOF)*	(β-Lactam-) antibiotics- free	Tested for RNase/ DNase activity	Extended impurity testing****
T7 RNA Polymerase, rec., GMP Grade, AOF ¹	08 140 669 103	10 ml	Yes	Yes	Yes	Yes	Yes
Pyrophosphatase, rec., GMP Grade, AOF ¹	08 140 677 103	20 ml	Yes	Yes	Yes	Yes	Yes
RNase Inhibitor, rec., GMP Grade, AOF ¹	09 537 589 103	2 MU	Yes	Yes	Yes	Yes	Yes
DNase I, rec., RNase-free ¹	03 539 121 103	200 kU	Yes	No********	Yes	Yes	In development
Proteinase K, rec. ¹	03 654 672 103	850 ml	Yes (except for Hb assay)	-	Yes	Yes	No
Xba I, recombinant, AOF ¹	09 520 848 101 09 520 848 103	50 kU 250 kU	-	Yes	Yes	Yes	Partially
Ribonucleotides, 100 mM							
ATP ¹	04 980 824 103	100 ml	Yes	No*****	Yes	Yes	No
CTP ¹	04 980 875 103	100 ml	Yes	No**,***	Yes	Yes	No
GTP ¹	04 980 859 103	100 ml	Yes	No**,***	Yes	Yes	No
UTP1	04 979 818 103	100 ml	Yes	No**,***	Yes	Yes	No
On-going project							
N1-Methyl-Pseudo-UTP, AOF ¹	09 188 991 103 09 522 409 103	100 ml 1.0 ml	In development	Yes	Yes	Yes	Yes
Pseudo-UTP, AOF ¹	In development	100 ml 1.0 ml	In development	Yes	Yes	Yes	Yes

For details see certificates of origin.

Expansion

Product	Catalog number	Pack size	GMP Grade	Animal-free
Trypsin ¹	06 369 880 103	1 g (0.23 MU)	Yes	Yes

Complementary Testing Kits

Product	Catalog number	Pack size
Residual Protein Trypsin Kit ⁵	07 568 975 001	1 kit (96 reactions)

 $^{{\}sf TSE/BSE}\ certificate\ available.$

Orthogonal virus depletion steps included in manufacturing process (e.g. virus retentive filter). Further information on virus depletion study is available.

^{****} Includes e.g. testing for bioburden, endotoxin, heavy metals, host-cell DNA, host-cell protein.

^{*****} Process uses a carrier-bound animal-derived Pharma Grade material.

Analytical Quality Control

Analytical QC Instrumentation	Catalog number	Pack size
Cedex Bio Analyzer*2	06 395 554 001	1 instrument with software and accessories
Cedex Bio HT Analyzer*2	06 608 116 001	1 instrument with software and accessories
Cedex HiRes Analyzer*2	05 650 216 001	1 instrument with PC, monitor and accessories

^{*}Depending on the application, several system reagents and test-specific kits are required.

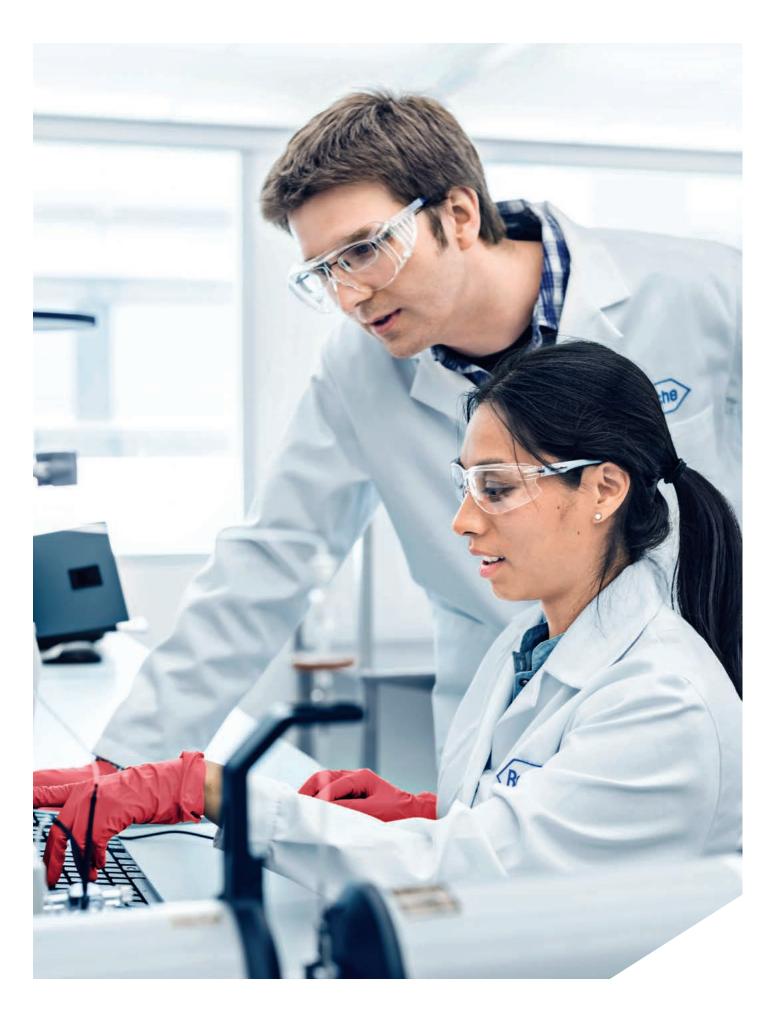
Analytical QC Testing Kits

QC Sample Preparation Kit ²
MycoTOOL Mycoplasma Real-Time PCR Kit ²
MycoTOOL Mycoplasma Detection Amplification Kit ²
MycoTOOL Carrier DNA ²
MycoTOOL Control Plasmid ²
Residual Protein Liberase Kit ²
Residual Protein Trypsin Kit⁵
Collagenase Activity Kit ²
Residual DNA E. coli Kit²

Catalog number

		_	
08	146	829	001
06	495	605	001
05	184	240	001
05	619	424	001
05	196	132	103
07	758	693	001
07	568	975	001
08	074	461	001
07	728	735	001

Pack size	
1 kit	
1 kit (160 PCR reactions)	
1 kit	
1 kit (5 × 320 μL)	
10 ng	
96 reactions	



Regulatory disclaimer

- 1 For further processing only.
- 2 For use in quality control/manufacturing process only.
- 3 Blended proteolytic enzyme for tissue dissociation. For further processing only.
- 4 For life science research only. Not for use in diagnostic procedures.
- 5 For quality control/manufacturing of IVD/medical devices/pharmaceutical products only.
- 6 Raw materials can also be used for other applications.

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