Powering Excellence in Cell and Gene Therapy Manufacturing

Conceptualize. Optimize. Standardize. Commercialize.

CUSTOMBIOTECH

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.

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

Implement fit-for-purpose materials to reduce uncertainties

Modification

Anticipating growth in mRNA therapy development, we have designed raw materials to support manufacturing scale-up and regulatory approval of these new drug modalities. Our raw materials enable traceable quality control, as well as change and deviation management that contribute to a standardized and reliable manufacturing process. Choosing fit-for-purpose raw materials early in development minimizes the risk of project delays that can jeopardize a fast time-to-market. Plus, we continually optimize our mRNA portfolio to meet fit-for-purpose standards, bearing in mind that specifications are determined by the intended use of the manufactured therapeutic mRNA.

Use fit-for-purpose materials for a smooth manufacturing transition

- Manufactured under GMP quality standards
- Highly consistent from lot to lot
- Available in the right scale and quality for commercial manufacturing
- Produced free of animal-derived components and beta-lactam antibiotics
- Tested for critical impurities, like endotoxin, bioburden, residual metals, host-cell DNA and protein

Ensure your product is free of host-cell impurities

Make confident product safety decisions based on reliable detection of Escherichia coli DNA. Our ready-to-use and flexible qPCR assay adheres to WHO and FDA sensitivity requirements for biopharmaceutical quality control and delivers results within hours.

- **Residual DNA *E. coli* Kit**
  Quickly verify absence of E. coli according to regulatory requirements

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. In absence of a standard approach, implementing validated commercial technologies to monitor cell viability, cell function and culture conditions potential culture contamination during process development and manufacturing saves resources and minimizes risks.

Cedex Analyzers – gain insights into your process to optimize cell expansion performance

Featuring proven data reliability as well as options for and automated workflow integration, our Cedex Bio Analyzer and Cedex HiRes Analyzer enable flexible quality control of bioprocesses. With a broad assay menu, the Cedex Bio Analyzer accurately measures 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.

Rapid and reliable analytical quality control tools

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

MycoTOOL kits – Mycoplasma-free results 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 third-party 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]	05172969103	No	Custom
Collagenase II, Mammalian Free, Liquid[1]	05172942103	No	Custom
Thermolysin MTF[1]	06981828001	Yes	15 mg
Enzyme Blends			
Collagenase I/II, Mammalian Free, Lyo[1]	05349907103	No	500 mg
Liberase T-Flex[4]	05989132001	No	1 kit 1 × 500 mg Collagenase blend 2 × 15 mg Thermolysin
Liberase MTF C/T[1]	05339880001	Yes	1 kit 2,000 U Collagenase I/II MTF, 2x 15 mg Thermolysin MTF, 3x
Liberase MNP-S[1]	05578566001	No	35 mg
Liberase MNP-S[1]	06297790001	Yes	5 mg
DNase I, Recombinant, RNase-free[1]	03724751103	Yes	4 kU

Complementary Testing Kits

Product	Catalog number	Pack size
Residual Protein Liberase Kit[5]	07758693001	1 kit (96 reactions)
Collagenase Activity Test[2]	08074461001	1 kit (96 reactions)

Modification

Product	Catalog number	Pack size	GMP Grade	Animal-free*	ß-Lactam-antibiotic-free	Tested for RNase / DNase activity	Extended impurity testing****
T7 RNA Polymerase,rec., GMP Grade[1]	08 140 669 103	10 ml (ca 10 mg)	Yes	Yes	Yes	Yes	Yes
Pyrophosphatase,rec., GMP Grade[1]	08 140 677 103	20 ml (ca 40 mg)	Yes	Yes	Yes	Yes	Yes
RNase Inhibitor, rec., GMP Grade[1]	In development	2 MU 100 kU	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)	No**	Yes	Partially	No
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
UTP[1]	04 979 818 103	100 mL	Yes	No**,***	Yes	Yes	No
On-going project							
N1-Methyl-Pseudo-UTP[1]	09 188 991 103 09 522 409 103	100 mL 1.0 mL	In development	Yes	Yes	Yes	Yes
Pseudo-UTP[1]	In development	100 mL 1.0 mL	In development	Yes	Yes	Yes	Yes

* For details see Certificates of Origin.
** 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.

Expansion

Product	Catalog number	GMP grade	Animal free	Pack size
Trypsin[1]	06369880103	Yes	Yes	1 g (0.23 MU)

Complementary Testing Kits

Product	Catalog number	Pack size
Residual Protein Trypsin Kit[5]	07568975001	1 kit (96 reactions)

Analytical Quality Control

Analytical QC Instrumentation	Catalog number	Pack size
Cedex Bio Analyzer*[2]	**6395554001**	**1 instrument with software and accessories**
LDH Bio[2]	06343767001	200 tests
Lactate Bio[2]	06343759001	200 tests
Glucose Bio[2]	06343732001	200 tests
Glutamine V2 Bio[5]	07395655001	200 tests
Glutamate V2 Bio[5]	07395582001	200 tests
NH3 Bio[2]	06343775001	200 tests
Ala-Gln Bio[5]	08056978001	200 tests
Cedex HiRes Analyzer*[2]	**5650216001**	**1 instrument with PC, monitor, and accessories**
Cedex HiRes Reagent Kit[2]	05650798001[2]	1 set for approximately 100 measurements

*Not intended to be a complete list of required materials for use

Analytical QC Testing Kits	Catalog number	Pack size
QC Sample Preparation Kit[2]	08146829001	1 kit
MycoTOOL Mycoplasma Real-Time PCR Kit[2]	06495605001	1 kit (160 PCR reactions)
MycoTOOL Mycoplasma Detection Amplification Kit[2]	05184240001	1 kit
MycoTOOL Carrier DNA[2]	05619424001	1 kit (5 × 320 µL)
MycoTOOL Control Plasmid[2]	05196132103	
Residual Protein Liberase Test[2]	07758693001	96 reactions
Residual Protein Trypsin Test[5]	07568975001	96 reactions
Collagenase Activity Test[2]	08074461001	96 reactions
Residual DNA *E. coli* Kit[2]	07728735001	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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