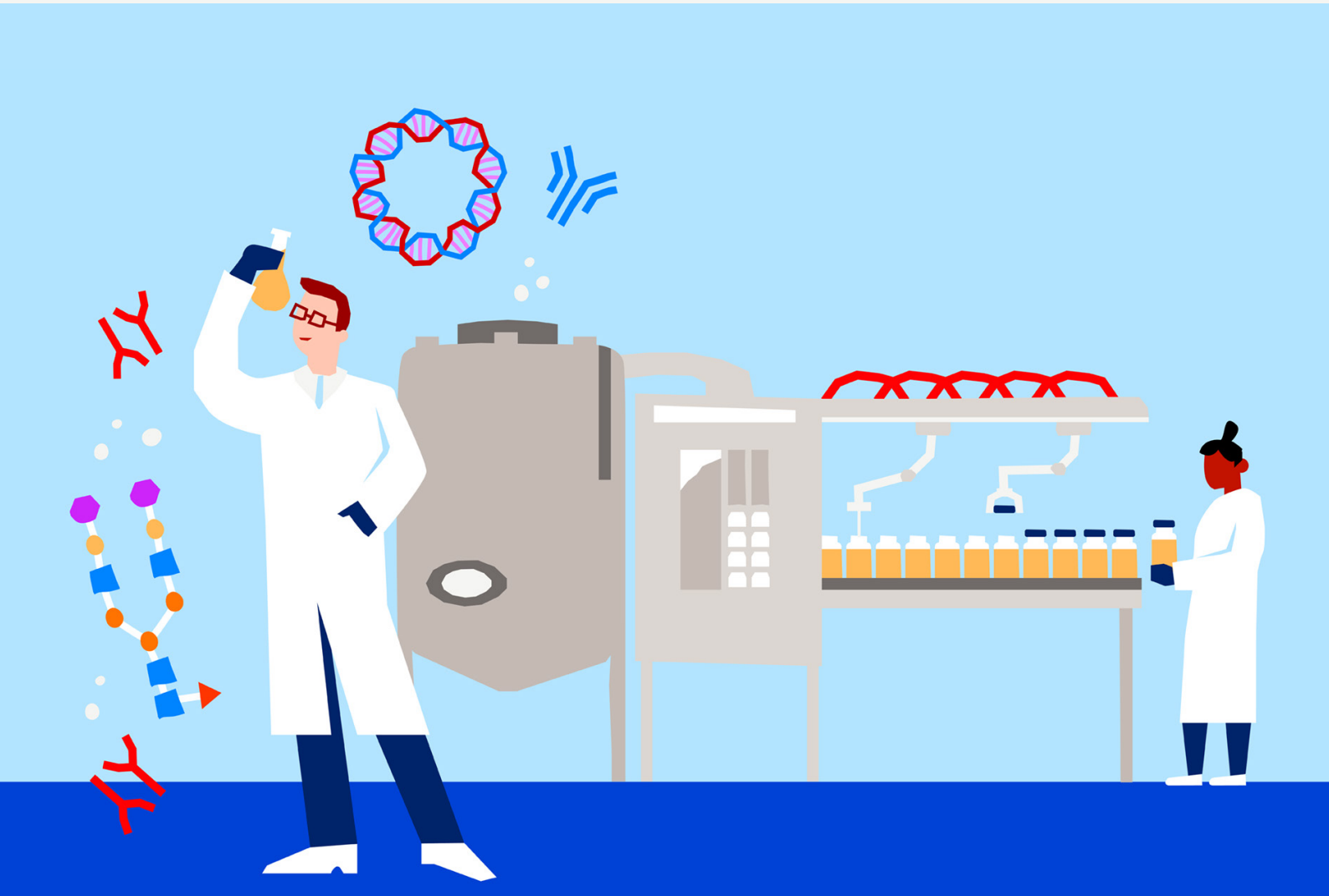
CUSTOMBIOTECH

Roche

Powering excellence in your development & manufacturing process



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Biologics are an important drug class used in oncology, autoimmunity, and chronic inflammatory diseases. A distinguishing feature of these drug therapy products is active substance which is extracted or produced from a biological source. Biologics include monoclonal antibodies (mAbs) and other therapeutic recombinant proteins produced mainly by mammalian cells or bacteria. With decades of experience in developing, improving and providing high-quality raw materials and instruments for biotherapeutics manufacturers, we offer proven and fit-for-purpose solutions for your unique manufacturing process.

Discover products for your Biologics workflow

Cell Culture and Microbial Manufacturing Workflow and Available Products

Drug Development

Lead Identification & Optimization

Pharmacokinetics control
- FcRn Affinity Column

Glycosylation Optimization
- In vitro glycoengineering (IVGE)

Upstream

Raw Material Quality Control

Mycoplasma Control
- MycoTOOL
- QC Sample Preparation

Cell Culture & Cell Expansion

Cedex Bio Analyzer
- Cedex Bio
- Cedex Bio HT
- Cedex HiRes

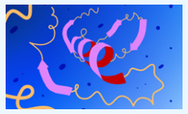
Cell Harvest

Mycoplasma Final Release Test
- MycoTOOL
- QC Sample Preparation

Downstream

Protein Cleavage

Proteases
- Rec. Trypsin
- Rec. Carboxypep-tidase B
- Endoproteinase



Protein Modification & Further Protein Processing

In Vitro Glycoengineering
- IVGE

Filtration & Chromatography Steps

Affinity Chromatography
- FcRn Affinity Column Gen 2

Drug Substance

Quality & Release Control

Mycoplasma Release Test
- MycoTOOL Real-Time PCR Kit
- QC Sample Preparation Kit (DNA extraction)

Lot-to-Lot Consistency
- FcRn Affinity Column

Drug development

Functional characterization: Our FcRn Affinity Column for mAb testing

An accelerated and standardized antibody half-life prediction streamlines your path to a meaningful lead candidate. With the FcRn Affinity Column Gen2 you can analytically differentiate even marginal variations in the structures of monoclonal IgG antibodies, granting you control of the chemical and structural integrity of the antibody during manufacturing, filling and storage.

Subsequently, accelerating and standardizing the antibody half-life analysis to develop a meaningful lead candidate more quickly. As a complete solution, the FcRn IgG Control serves for a reliable and convenient quality check of the FcRn Affinity Column to verify the column functionality and unchanged separation performance.

The easy-to-use column works on your HPLC and allows you to:

- Monitor antibody behavior at multiple pH values, visualizing even minor differences in its structure and half-life.
- Automate antibody processing.
- Eliminate potentially inconsistent coating densities for truly standardized analyses.

Modification: Glycosylation

Glycosylation is a critical quality attribute (CQA) of glycoproteins, a process that can often lead to variable results. Consequently, separating glycosylation management from protein yield grants greater control. In vitro glycoengineering enables creating high levels of galactosylation or sialylation to unambiguously. select and implement the glycoprotein structure with the best therapeutic and pharmacokinetic profile. This accelerates the optimization of the glycoprotein and improves control of the manufacturing process.

Improved outcomes from In-vitro Glycoengineering:

- Time- and cost-saving generation of glycan variants to develop improved drugs
- Optimized glycosylation without compromising other CQAs or product yield
- Improved lot-to-lot consistency to reduce risk of product quality variation and resulting delays
- Generation of glycoprofiles which may not otherwise be generated
- Streamlined analytics in comparability studies

Our in-vitro glycosylation toolbox is a portfolio of well-characterized enzymes and activated sugars designed to:

- Change glycosylation fast and efficiently
- Serve each drug development phase with optimized glycosyltransferases
- Scale from milligram to kilogram and thus integrate into manufacturing workflows

Upstream

Process Control: Cedex Analyzers for metabolite and cell analysis testing

Bioprocess control is essential to identify expected and unwanted changes in cell cultivation and fermentation. The Cedex Analyzer family was designed to streamline and harmonize analyses for bioprocess control by combining the functionalities of multiple instruments into one system and delivering powerful testing capabilities with reduced workflow complexity. Rely on one instrument family and a menu of dedicated assays to capture useful and timely insights into your bioprocess that enable the right decisions at the right time for optimal manufacturing outcomes.

Culture control for mammalian cells, bacteria, yeast & insect cells

Substrates
Ala-Gln (GlutaMAX)
Arabinose
Asparagine
Aspartate
Calcium
Cholesterol
Ethanol
Galactose
Glucose
Glutamate
Glutamine
Glycerol
Iron
Magnesium
Nitrate
Phosphate
Potassium
Pyruvate
Sodium
Sucrose

Metabolites
Acetate
Ammonia
Formate
Lactate
LDH
Osmolality calc.

Products
Ig Fab (human)
IgG (human)
Mouse IgG
Optical Density (bio mass)
Total Protein

Additional assays are in development.
Visit custombiotech.roche.com/cedex for updates or contact your local CustomBiotech team representative.

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 for mammalian, insect cells only. With a long manufacturing history and accurate system suitability tests, the Cedex HiRes Analyzer is a robust, high-performance instrument that minimizes downtime and eases audit compliance.

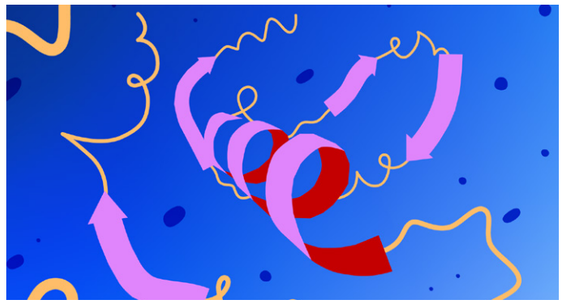
Results include:

- Cell concentration
- Cell viability
- Cell morphology
- Growth curves
- Specific growth rates
- Doubling times
- Debris patterns

Cedex HiRes Analyzers have a wide and flexible range of measurements.

Biologics are defined and ready for future processing

Downstream



Protein Processing: Proteases to modify proteins and anti-body fragments

Highly pure and efficient proteases are essential tools of optimal, sensitive and highly regulated manufacturing workflows in bio-pharmaceutical applications. Our proteases are specifically designed as critical raw materials for the production of Active Pharmaceutical Ingredients (API). They are implemented in a range of applications, from insulin and vaccine production, to tissue dissociation and total protein degradation (e.g., in mRNA manufacturing). Select from a broad portfolio of animalcom-ponent-free and GMP grade enzymes. All our enzymes have a high lot-to-lot consistency, improving the reproducibility and safety of your production processes.

Modification: Glycosylation

The same in-vitro glycoengineering that enables you to develop a glycoprotein that is consistent in structure and function, transfers to downstream steps in your manufacturing process. All enzymes in the portfolio show exceptional performance in steering glycosylation, so you can decouple your strategy to optimize glycosylation from maximizing product yield.

Implementing in vitro glycoengineering in downstream processes allows you to:

- Enrich wanted glycoforms using discrete and predictable enzymatic reactions
- Save reagents and time by eliminating uncertain tweaking during the fermentation process
- Maintain control over the manufacturing process and thus, speed up development cycles

Drug Substances

Quality and release control: Consistency and contamination testing

Test for host cell DNA contamination and mycoplasma with our quality control kits

Quality control and release testing is an integral part of a successful biopharmaceutical business that should enable rather than hinder progress. Your testing strategy must be comprehensive, fast and reliable. That is the foundation of our testing solutions, from the FcRn Affinity Column as a way of quickly and meticulously detecting inconsistencies in antibody products, to our MycoTOOL and Residual host DNA kits to ensure contamination-free production lots.

Robust, specific and sensitive, our quality testing solutions are easily integrated at every step of your process to increase efficiency and enforce stringent quality parameters for medium and high-throughput workflows. These solutions are key components for an optimal quality control strategy to safeguard the manufacture of your products.

Capture lot-to-lot consistency with the FcRn Affinity Column

Highly sensitive and easy to use on your HPLC, the FcRn Affinity Column Gen 2 visualizes even minor differences in the structure, behavior, and predicted in- vivo half-life of an antibody. Easily establish consistency across production batches for a range of characterization parameters, like:

- Intact and oxidized IgG
- IgG protein sequence variants
- Monomeric IgG and aggregates

Residual host cell DNA quantification with the Residual DNA *E. coli* and CHO kits

Host cell DNA levels must be low in final biologics products to meet regulatory guidelines appropriate for the products intended use. A key aspect of testing for host cell DNA is to use a highly sensitive method. Our residual host cell DNA assays are based on quantitative PCR that:

- Provide robust and easy workflow integration
- Deliver accurate results within hours
- Accommodate a broad range of sample types
- Meet WHO sensitivity requirements

Mycoplasma detection with the MycoTOOL Mycoplasma Real-Time PCR kit

Demonstrating the absence of mycoplasma in therapeutic products is a regulatory requirement. Broad testing coverage by conventional methods is a lengthy and resource-intensive process. Our MycoTOOL testing system is an approved testing method that cuts weeks of work to just hours.

- PCR-based assay for high sensitivity
- Detects around 150 mycoplasma species
- High specificity to avoid crossreactivity
- Easy sample prep and suitable throughput

Build excellence into your biologics development and manufacturing. Start with high-quality raw materials and instruments designed for the demands of a robust, efficient and highly productive manufacturing strategy. **Discover Roche CustomBiotech products for your Biologics workflow.**

Cell Culture and Microbial Manufacturing Workflow and Available Products

Products for Biologics Manufacturing – mAbs & Rec. Protein

■ Biopharma products ■ Diagnostics products

Drug Development

Target Identification & Screening

Genotyping
- AptaTaq Genotyping Master
- KAPA3G HotStart Master
- HawkZ05 Fast Master Mix

Gene Expression
- HawkZ05 Fast Master Mix
- NxtScript 2G RT + KAPA3G HotStart Master

Lead Identification & Optimization

Glycosylation Optimization
- α-2,3-Sialyltransferase, rec.
- α-2,6-Sialyltransferase, rec.
- β-1,4-Galactosyltransferase, rec.
- CMP-N-Acetylneuraminic acid
- UDP-Galactose
- UDP-N-Acetylglucosamine
- α-Glucosidase, rec.
- β-Galactosidase, rec.
- β-Glucuronidase, rec.
- Alkaline Phosphatase, rec.

Pharmacokinetics control
- FcRn Affinity Column

Upstream

Raw Material Quality Control

Mycoplasma Control
- MycoTOOL Real-Time PCR Kit
- QC Sample Preparation Kit (DNA extraction)

Culture Media Preparation

Amino Acids
- L-Alanin
- L-Aspartate

(Activated) Sugars
- D-Glucose-6-phosphate
- (D+) Galactose
- UDP-N-Acetylgalactosamine
- UDP-Galactose
- UDP-N-Acetylglucosamine
- CMP-N-Acetylneuraminic acid

Cell Antioxidants
- GSH / GSSG
- N-Acetyl-L-Cysteine
- Catalase

Co-Enzymes
- NAD, NADH, NADP, NADPH, FAD
- ATP, ADP
- UTP, CTP, GTP

Other Supplements
- Bovine Serum Albumin (BSA)
- Rec. Trypsin

Cell Culture & Cell Expansion

Cedex Bio Analyzer
- Cedex Bio
- Cedex Bio HT
- Cedex HiRes

Cell Harvest

Mycoplasma Final Release Test
- MycoTOOL Real-Time PCR Kit
- QC Sample Preparation Kit (DNA extraction)

Downstream

Protein Cleavage

Proteases
- Rec. Trypsin
- Rec. Carboxypeptidase B
- Rec. Endoproteinase Lys-C
- Endoproteinase Glu-C
- Endoproteinase Asp-N
- Pronase
- Papain
- Amino Acid Arylamidase
- Chromozym TRY

Protease Inhibitors
- Aprotinin
- Leupeptin

Protein Modification & Further Protein Processing

Protein Refolding
- GSH
- GSSG
- L-Alanin
- L-Asparagine

Biologic PEGylation
- UDP-N-Acetylgalactosam

***In Vitro* Glycoengineering**
- α-2,3-Sialyltransferase, rec.
- α-2,6-Sialyltransferase, rec.
- β-1,4-Galactosyltransferase, rec.
- UDP-Galactose
- CMP-N-Acetylneuraminic acid
- UDP-N-Acetylglucosamine
- Alkaline Phosphatase, rec.
- β-Galactosidase
- β-Glucuronidase, rec.
- Alkaline Phosphatase, rec.

Antibody Cleavage
- Papain
- Endoproteinase Lys-C, rec.

Filtration & Chromatography Steps

Affinity Chromatography
- cOmplete™ His-Tag Purification Resin

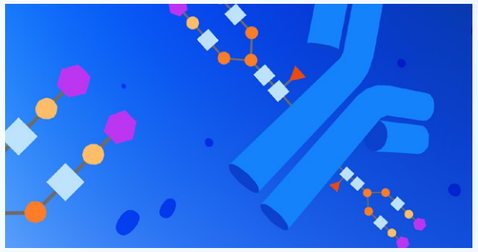
Drug Substance

Quality & Release Control

Residual Protein Testing & Host-Cell DNA Testing
- Residual Protein Trypsin Kit
- Residual Protein (2,6-) Sialyltransferase
- Residual Protein Galactosyltransferase
- Residual DNA CHO Kit

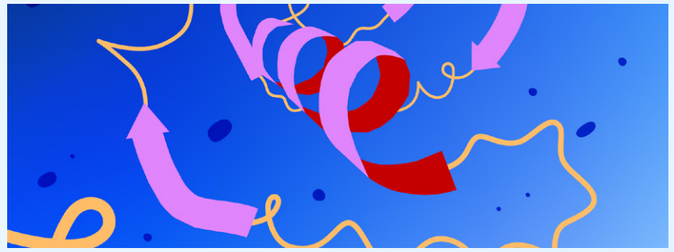
Mycoplasma Release Test
- MycoTOOL Real-Time PCR Kit
- QC Sample Preparation Kit (DNA extraction)

Lot-to-Lot Consistency
- FcRn Affinity Column



01
IVGE

02
Cedex Analyzer Family



03
Proteases

04
FcRn

Regulatory Disclaimers
- ■ **Biopharma products:** For use in quality control/manufacturing processes only.
- ■ **Diagnostics products:** For further processing only. (Biopharma production suitability check is required)

Biologics Catalog

Drug Development | Upstream | Downstream | Drug Substance

Drug development

FcRn Affinity Column + IgG Control

Product	Pack size	Catalog number
FcRn Affinity Column Gen2	1 pre-packed column	09430857001
FcRn IgG Control	1 mL	09494804001

In-vitro glycoengineering

Glycosyltransferases for research	Pack size	Animal-free*	Catalog Number
α-2,3-Sialyltransferase, rec.	Custom fill		07 429 916 103
Glycotransferases for drug development	**Pack size**	**Animal-free***	**Catalog Number**
α-2,6-Sialyltransferase, rec. EQ	Custom fill		08 098 174 103
β-1,4-Galactosyltransferase, rec. EQ	Custom fill		08 098 182 103
Activated sugars	**Pack size**	**Animal-free***	**Catalog Number**
UDP-Galactose animal-free	Custom fill		07 703 562 103
CMP-N-Acetylneuraminic acid	Custom fill		05 974 003 103
UDP-N-Acetylglucosamine	Custom fill		11 787 900 103
UDP-N-Acetylgalactosamine	Custom fill		06 369 855 103
Related products	**Pack size**	**Animal-free***	**Catalog Number**
Alkaline Phosphatase	Custom fill		03 137 031 103
Residual Protein α-2,6-Sialyltransferase Kit	96 tests		08 011 478 001
Residual Protein β-1,4-Galactosyltransferase Kit	96 tests		08 182 990 001

* No animal-derived materials were used in fermentation, purification, and final formulation.

Regulatory Disclaimer
α-2,3-Sialyltransferase is: For life science research only and not for use in diagnostic procedures. α-2,6-Sialyltransferase, rec. EQ, β-1,4-Galactosyltransferase, rec. EQ, activated sugars, Alkaline Phosphatase, N-Glycosidase F and Neuraminidase are: For further processing only. Residual Protein α-2,6-Sialyltransferase Kit and Residual Protein β-1,4 Galactosyltransferase Kit are: For use in quality control/manufacturing process only.

License limitations
The sale of the product does not exhaust or grant any rights in third party patents including patents of companies of the F. Hoffmann – La Roche AG group of companies, in particular, for the use of modified antibodies obtained by using the product.

Upstream

Cedex Bio Analyzer*	06395554001	1 instrument with software and accessories
Cedex Bio HT Analyzer*	06608116001	1 instrument with software and accessories
Cedex HiRes Analyzer*	05650216001	1 instrument with PC, monitor and accessories

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

Downstream

Proteases

Product	Pack size	Catalog number
Trypsin, recombinant, expressed in *Pichia pastoris*	3.5 MU	03358658103
	1 g = 0.23 MU	06369880103
Carboxypeptidase B, recombinant, expressed in *Pichia pastoris,* solution	30 KU	03358682103
Proteinase K, recombinant, PCR Grade, expressed in *Pichia pastoris,* solution	850 ml	03654672103
DNase I, recombinant, Grade I, expressed in *Pichia pastoris,* solution	10 KU	03724778103

Regulatory Disclaimer
For further processing only.

Complementary Kits

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

Drug Substances

MycoTOOL

Analytical QC Testing Kits	Pack size	Catalog number
QC Sample Preparation Kit	1 kit	08146829001
MycoTOOL Mycoplasma Real-Time PCR Kit	1 kit (160 PCR reactions)	06495605001
MycoTOOL Control Plasmid	10 ng	05196132103
Residual Protein Trypsin Kit	96 reactions	07568975001
Collagenase Activity Kit	96 reactions	08074461001
Residual DNA *E. coli* Kit	96 reactions	07728735001

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