

INVIVO



InVivo BioTech Services GmbH  
a BRUKER company

**InVivo BioTech Services**  
*Excellence in Custom Bioproduction*

**Service Portfolio**





# INVIVO BIOTECH SERVICES

*One of the leading contract manufacturing organizations in Europe*

**InVivo was founded in 1998 and is proud of more than 20 years of experience in mammalian cell culture and the production of high-quality antibodies and recombinant proteins.**

Based in Hennigsdorf just outside of Berlin, the company has consistently grown over time and exhibits today more than 2500 square meters (~ 26 900 square feet) of laboratory and operational space. The 65+ employees possess a strong scientific background and biochemical expertise.

With satisfied clients worldwide, InVivo is a trusted and well-established partner for cost-effective outsourcing solutions. Companies of all sizes, including small university spin-offs, major research institutes, and biopharmaceutical companies, have taken advantage of our expertise as an independent contract manufacturer.

As an ISO 9001 and ISO 13485 certified company, InVivo is dedicated to meet every client's needs and to provide excellent service and highest quality products.

In 2017 Bruker Daltonics acquired InVivo to gain a reliable partner for the production of *in vitro* diagnostic kits, biological standards and chemical matrices.



**YEARS OF EXPERTISE**





# HISTORY AND MILESTONES



**2019**

InVivo obtained ISO 13485 certification.

**2017**

InVivo was acquired by Bruker Daltonics.

**2016**

Launch of InVivo's proprietary system InVEST for transient gene expression in HEK cells.

Acquisition of ICI operating facility in Berlin to expand service portfolio to include immunoassay development and sample analysis.

Collaboration with Bruker as supplier of chemical matrices and biological standards for MALDI-based diagnostics.

**2013**

Development on INVect, a novel polycationic reagent for transient transfection.

Large-scale transient transfection of HEK and CHO suspension cells.

**2011**

Development of a stable CHO cell line.

Increase of production capacity to 14 bioreactors.

**2010**

Implementation of the first 100 L bioreactor.

**2004**

InVivo obtained ISO 9001 certification.

**2001**

Development of proprietary serum-free media for the cultivation of mammalian cells.

Implementation of continuous high-cell density fermentation.

**1998**

InVivo was founded.

**1999**

First production and fermentation facilities at the biotech campus in Hennigsdorf.

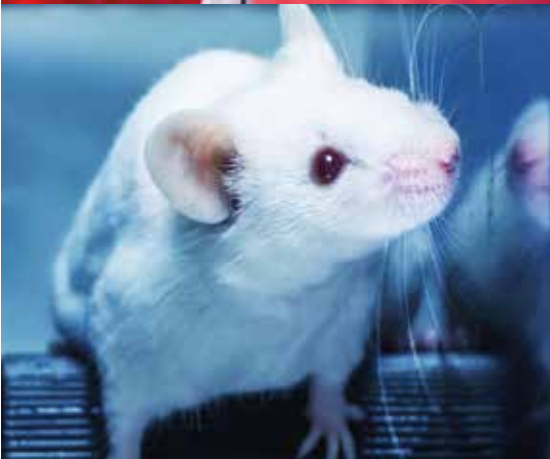




*“Our goal is to provide individualized solutions, exactly tailored to every client’s needs, and to create lasting relationships by providing outstanding services and high quality products”.*



# SERVICE PORTFOLIO



- ✓ ***Monoclonal antibody production from hybridoma***
- ✓ ***Recombinant protein production in mammalian cells***
- ✓ ***Recombinant protein production in E. coli***
- ✓ ***Mouse hybridoma development***
- ✓ ***Stable CHO cell pool and cell line development***

InVivo's comprehensive service portfolio includes antibody development, small-to bulk-scale production of monoclonal antibodies, subclass switches, antibody sequencing and labelling. A special focus lies on the production of recombinant antibodies and proteins via transient gene expression in mammalian HEK293 cells or from stable CHO cell pools.

Moreover, InVivo offers hybridoma and stable CHO cell line development, transfer of cell lines to serum-free media, low endotoxin level production, and cell banking. Further services include lyophilization, immunoassay development, DNA design and large-scale DNA preparation.

**This makes InVivo a one-stop solution for all your research needs.**



# MONOCLONAL ANTIBODY PRODUCTION FROM HYBRIDOMA LINES

## APPLICATIONS:

- Research and development
- Preclinical use
- Human *in vitro* diagnostics
- Veterinary diagnostics
- Food and feed safety

## SCALE:

- Milligram to kilogram quantities

## TURNAROUND TIME:

- 8-10 weeks

## QUALITY GUARANTEED:

- Highest purity
- Aggregate-free
- Endotoxin-free
- Batch-to-batch consistency

## EXTRAS:

- **Welcome Offer:** Test production of mAB from hybridoma lines; 10 mg yield guarantee; **€ 999**
- Cell line adaption to serum-free medium ISF-1
- Lyophilization
- Antibody labelling
- Aliquoting



**InVivo has cultivated more than 3500 different hybridoma lines so far, producing antibodies from all kinds of species (rat, mouse, rabbit, human, etc.) and of various subclasses (IgGs, IgMs, IgAs).**

*In vitro* production in super spinner systems or bioreactors (2 L to 100 L) through high-cell density fermentation, occurs exclusively under serum-free conditions. For this purpose we use our proprietary medium **ISF-1** that allows cost-effective production processes and high product yields.

Antibodies ordered in larger quantities (> 1g) and on a regular basis, qualify for our special **Antibody-on-Demand service**. This reduces costs and saves storage capacities at your facility. Just define your demand for 24 months, choose a batch size (min. 100 mg per call-off order) and delivery dates (fixed dates or flexible interval, e.g. monthly, quarterly, etc.) and we take care of the rest.



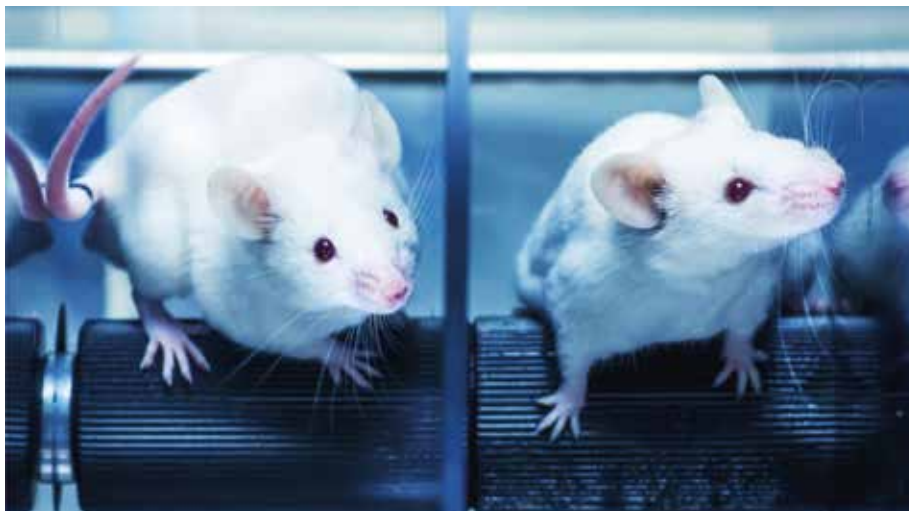


# MOUSE HYBRIDOMA DEVELOPMENT

**InVivo provides custom services for the development of mouse hybridoma cell lines to produce monoclonal antibodies against your antigen of interest.**

With passion and know-how, InVivo has successfully realized more than 500 hybridoma development projects to date. The entire project, including mice immunization, cell fusion, screening, cloning and initial characterization of the developed monoclonal antibodies, usually takes around 22 weeks.

For immunization ~ 5 mg of antigen (protein, peptide or hapten) is needed. In case the antigen (protein) is not available yet, InVivo can produce the protein of interest via expression in *E. coli* or via transient gene expression in HEK cells.



## APPLICATIONS:

- Development of mouse monoclonal antibodies against haptens, peptides and proteins

## EXTRAS:

- Screening of antibody candidates for sandwich ELISA development
- Negative screening to avoid cross-reactions of antibodies with unspecific partners
- Isotyping
- Mycoplasma testing
- Cryoconservation of clones

## TURNAROUND TIME:

- ~ 22 weeks

## OPTIONAL:

- Small-scale pilot production of monoclonal antibodies (Welcome Offer); 10 mg antibody guaranteed

## CELL BANKING

At InVivo, your cell culture clones are always handled with special care. After an initial test for mycoplasma contamination, samples are cryopreserved for storage in liquid nitrogen, so they are available for future productions.

To avoid the loss of cell lines, we highly recommend to store important clones at least at two additional locations. For this purpose, InVivo offers cultivation and preparation of clones for safe or patent deposit at long-term safe storage facilities, such as the DSMZ in Braunschweig.

Moreover, we offer cultivation of cells and preparation of multi-generation working cell banks.



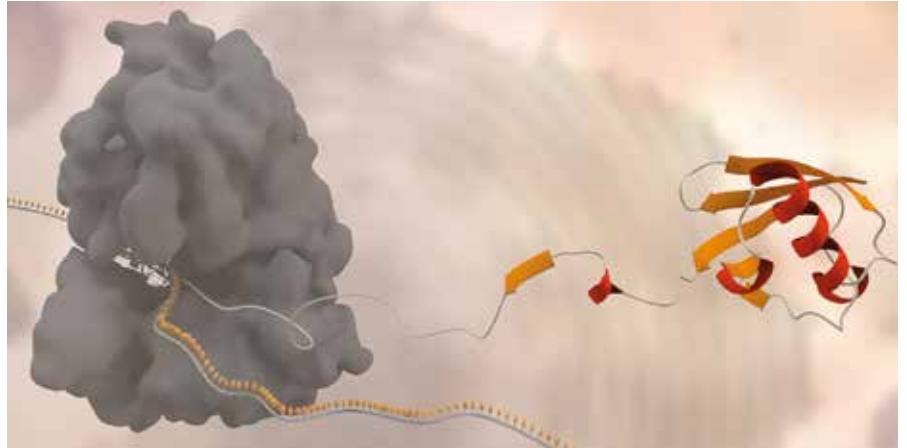




# INVEST: INVIVO'S EXPRESSION SYSTEM FOR TRANSIENT TRANSFECTION

Transient gene expression (TGE) is a commonly used method for the production of recombinant antibodies and proteins in mammalian cells within a short time.

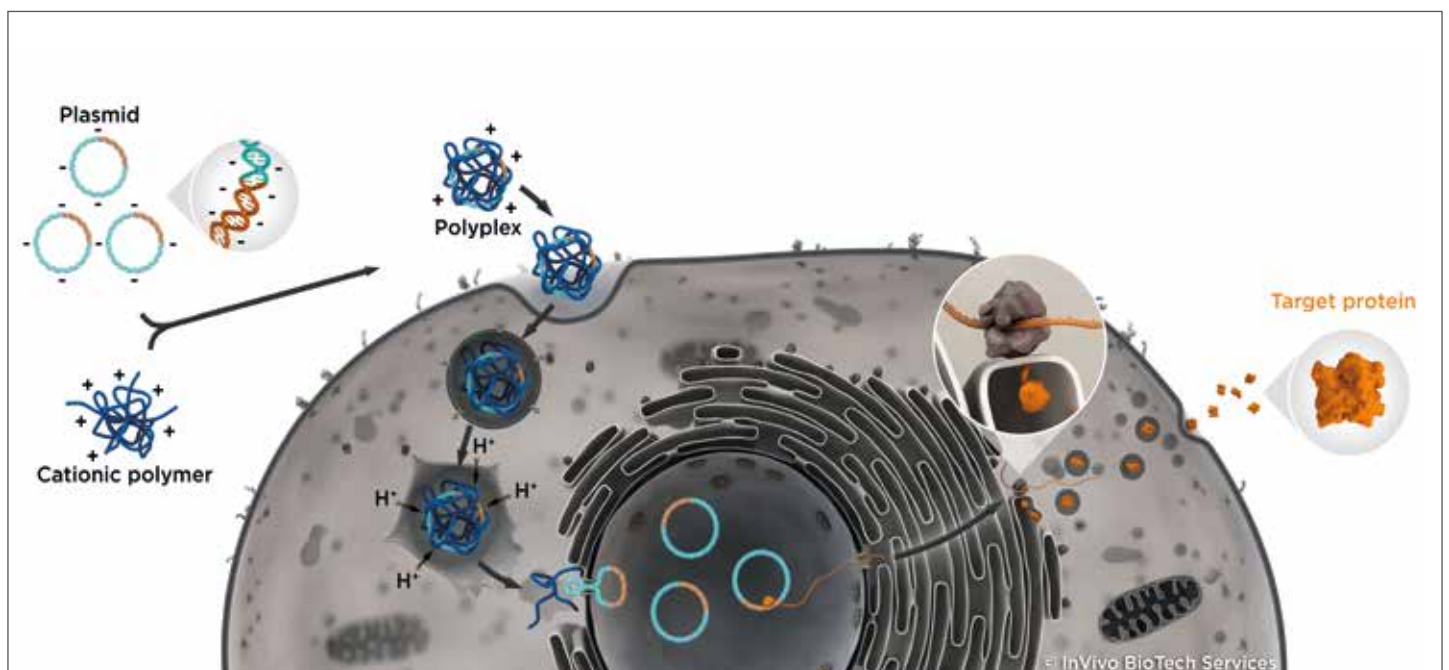
However, effective results can only be achieved, if all components of the TGE system are carefully matched and harmonized.



Following years of research and development, InVivo established an optimized system for the production of mammalian-derived proteins via transient gene expression in HEK cells. This system is called **InVEST** and it combines:

- ✓ Optimized host cell line
- ✓ Customized cell culture media
- ✓ Cost-effective large-scale plasmid preparation
- ✓ Sophisticated vector design
- ✓ Novel polycationic transfection reagent

Via InVEST, a production increase of up to 80 fold is possible and more than 700 successfully completed projects demonstrate the efficiency of the system. Whether you wish to express recombinant antibodies or proteins, InVEST is equally suitable for both. We generate functional mammalian-derived proteins with native folding and relevant post-translational modifications within only 8-12 weeks.







# RECOMBINANT PROTEIN PRODUCTION IN MAMMALIAN CELLS



Every new project starts with cDNA design and synthesis; this is how we ensure efficient expression rates and optimal product yields. After an initial small-scale pilot production to assess the feasibility of the project and to refine production parameters, upscaling in production is possible and we can easily meet your demand for protein quantities of up to 2 g per batch.

We always aim for the best quality to provide exactly what you wish for: highly pure, aggregate-free proteins with reliable lot-to-lot consistency.

For more information please visit our website:  
[www.transient-transfection.com](http://www.transient-transfection.com)

## APPLICATIONS:

- Research and development
- Preclinical use
- Human *in vitro* diagnostics

## SCALE:

- Up to 2 g per batch

## TURNAROUND TIME:

- 8-12 weeks

## QUALITY GUARANTEED:

- Highest purity, aggregate-free
- Endotoxin-free
- Batch-to-batch consistency

## EXTRAS:

- **Welcome Offer:** Test production of rec AB in HEK cells; 40 mg yield guarantee; **€ 5 500**
- Tag-removal via protease cleavage
- Antibody subclass switching
- Introduction of protein mutations
- Lyophilization
- Protein labelling
- Aliquoting

## LARGE-SCALE DNA PREPARATION

Transient gene expression in mammalian cells requires large amounts of high-quality plasmid DNA. As commercially available kits exclusively use single-use columns and have a limited capacity of only 10 mg, InVivo established a proprietary procedure for large-scale DNA preparation.

Here, reusable ion exchange columns are used which easily allow the cost-efficient preparation of up to 100 mg plasmid DNA\* with a standard size ranging from 1500 bp to 9000 bp. This transfection grade DNA is animal component-free with a very low level of endotoxins.

\*For individual projects, we can also offer larger DNA yields, if required.





# RECOMBINANT PROTEIN PRODUCTION IN *E. COLI*

## APPLICATIONS:

- Research and development
- Target discovery
- Drug screening
- Antigen development

## SCALE:

- Up to 5 g per batch

## TURNAROUND TIME:

- > 8 weeks (dependent on the protein sequence length)

## QUALITY GUARANTEED:

- Highest purity, aggregate-free
- Batch-to-batch consistency

## EXTRAS:

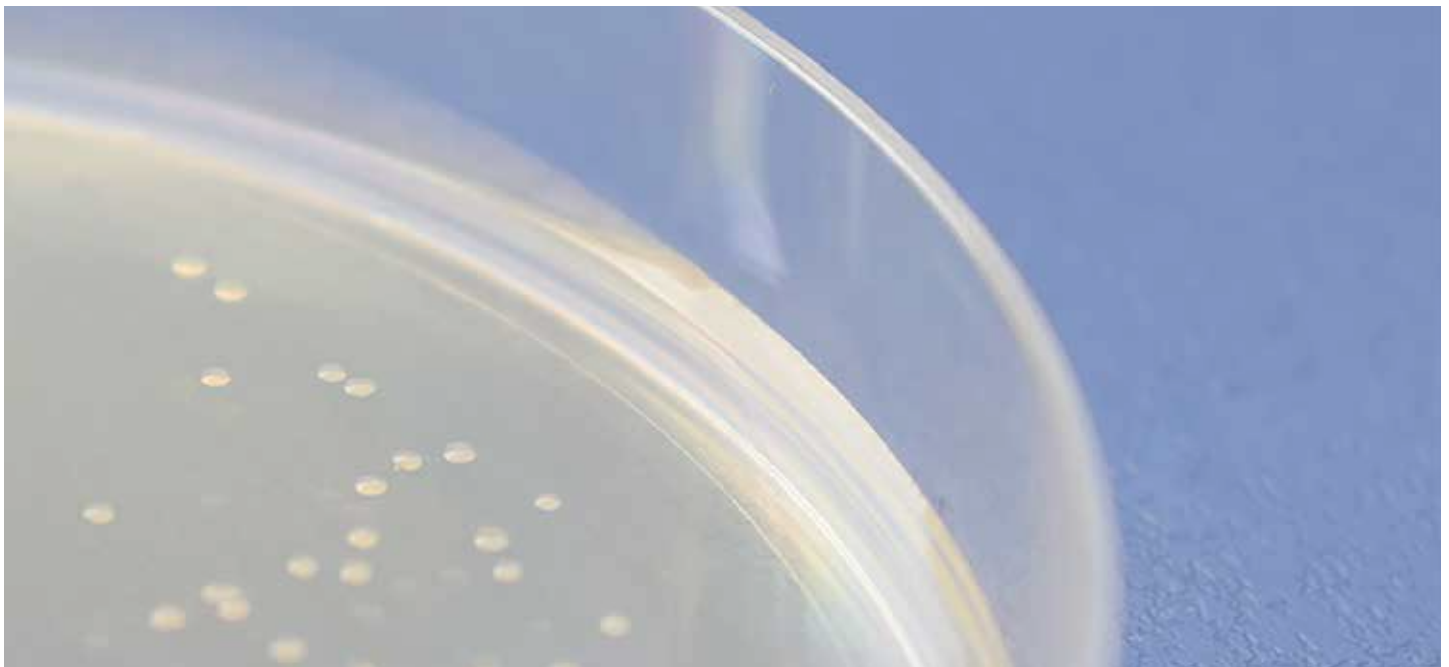
- Tag-removal via protease cleavage
- Scalable protocols for maximum flexibility in production scale
- Tag-free protein purification
- Lyophilization
- Aliquoting
- Endotoxin-free purification



Using *E. coli* as expression system for the production of recombinant proteins, has several advantages: A shorter timeline for the entire process from cloning to protein recovery, inexpensive production processes, high protein yields and highest flexibility in production scale.

Smaller peptides and proteins without posttranslational modifications, such as antigens, hormones, tumor markers or cytokines, can be expressed in bacterial cells.

Every *E. coli* protein production project includes cDNA design and efficient codon optimization for expression in bacterial cells. With a small-scale test production, InVivo evaluates the ideal production parameters to ensure the success of your project. Different host strains, media, growth conditions and purification methods can be used to optimize production and protein yield. Besides standard cultivation (from 2 L shake flask to 50 L bioreactor), InVivo also offers high cell density fermentation (OD 30-80) for protein production. Using this method, up to 500 g of cell pellet can be obtained.



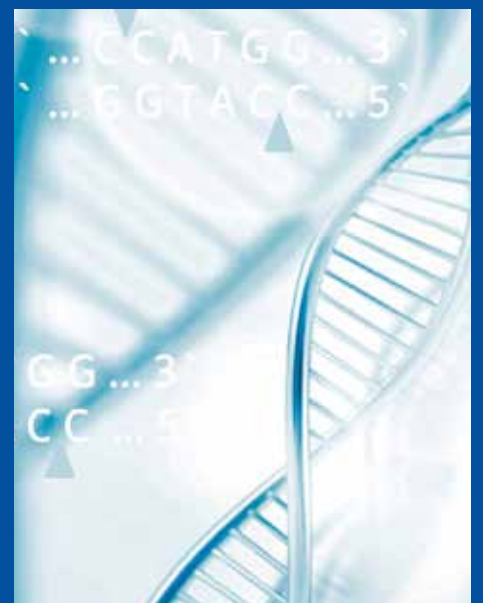


## DNA DESIGN

### *Make the most of your expression project*

To reach ideal production rates in eukaryotic or prokaryotic expression systems, it is highly recommended to optimize DNA sequences depending on the specific project requirements.

In this regard, InVivo offers a range of different DNA design services, such as codon optimization, insertion of restriction sites for subsequent cloning into InVivo's proprietary expression vectors, addition of signal peptides for efficient protein secretion and the addition of tags for subsequent protein purification.





# STABLE CHO CELL POOL AND STABLE CHO CELL LINE DEVELOPMENT

## APPLICATIONS:

- IVD kit manufacturing
- Target discovery
- Drug screening
- Pre-clinical studies

## SCALE:

- Several gram per batch

## TURNAROUND TIME:

- 4-6 weeks (stable cell pools)
- 4-6 months (stable cell lines)

## QUALITY GUARANTEED:

- Highest purity
- Aggregate-free
- Batch-to-batch consistency

## EXTRAS:

- Production from stable CHO cell pools
- GMP-compliant documentation
- Lyophilization
- Aliquoting
- Endotoxin-free purification

Transient gene expression in mammalian cells provides reasonable amounts of recombinant proteins and antibodies which is sufficient for most applications. However, certain projects such as pre-clinical studies for biopharmaceutical development or IVD kit manufacturing, often require bulk-scale quantities of material (up to several grams per batch) which can only be generated from a stable cell line.

Transient gene expression is temporary in mammalian cells as the inserted DNA gets broken down after a while. In contrast, upon production of a stable cell line, the gene of interest gets stably integrated into the genome which allows permanent production of the target protein.

However, DNA insertions take place at different locations of the genome and the number of inserted copies can vary. Therefore, it can be challenging to identify a high producing clone for efficient protein production.

This makes stable cell line development a tedious and often very expensive process with several bottlenecks that have to be overcome. In order to achieve the best possible results you need:

- ✓ An optimized cell line
- ✓ Efficient expression vectors
- ✓ Highly-optimized processes



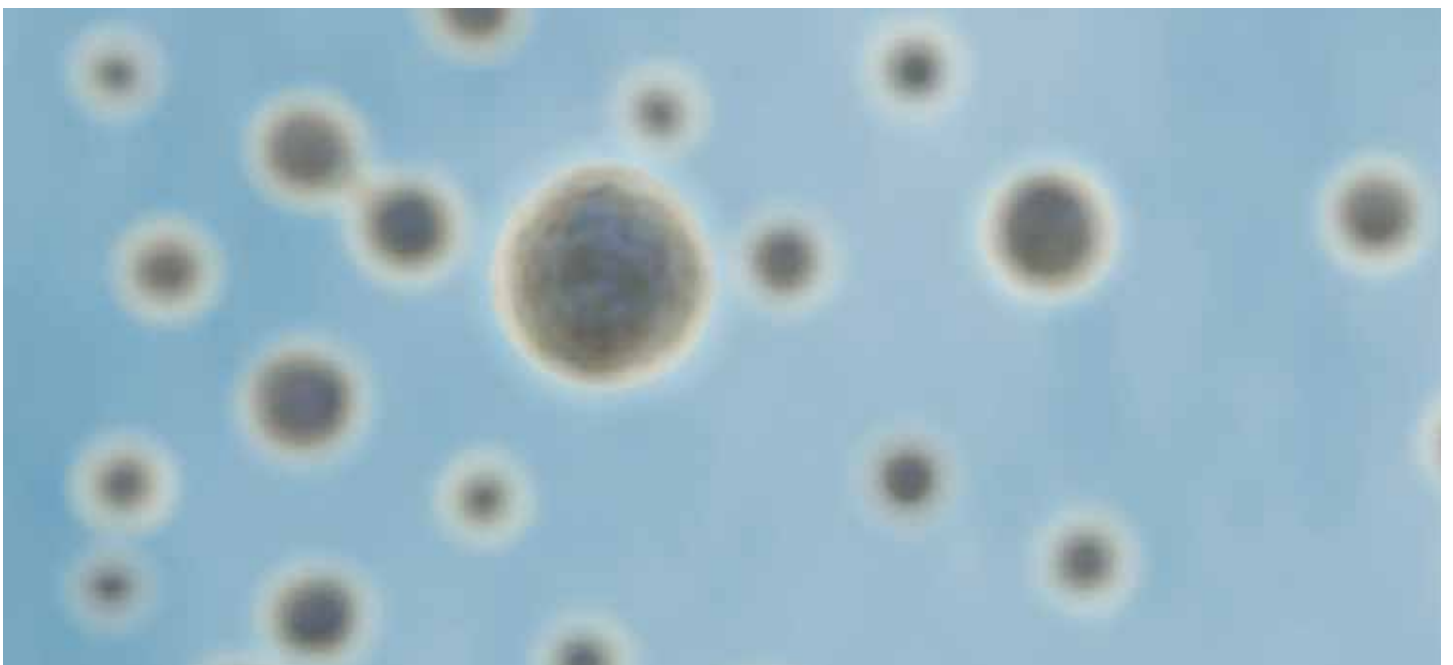
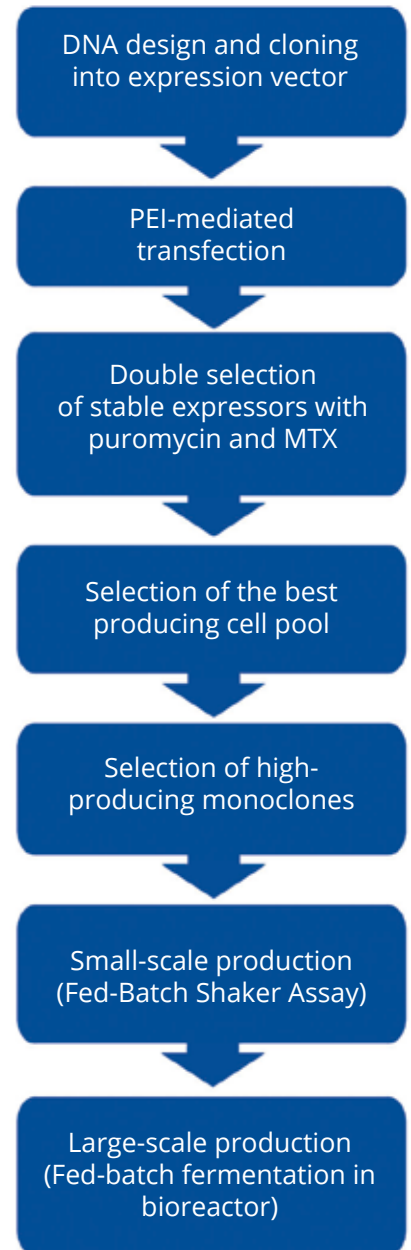




InVivo chose a well-established, cGMP-banked CHO cell line and tailored it to its highly optimized cell culture processes using a high-performance chemically-defined, animal component-free medium.

Through intensive research and process development, novel expression vectors were designed that are compatible to the PiggyBac system, a well-established tool for transposon-mediated active gene transfer. Using these customized vectors, high protein yields and a substantially reduced timeline from transfection to stable CHO cell pools could be achieved.

To further increase product yield, high cell-density fermentation processes were established. All these combined with a highly optimized process for the selection of best producing cell pools and screening for high-producing monoclonals, lead to cost-optimized production of target proteins in large quantities.



# InVivo: Excellence in



## Customized Production

Each project is uniquely designed to address every customer's special needs. Whether you want a specific kind of purification, a higher percentage of purity or need customized certificates designed to suit your audience.



## High Yield

20+ years of experience have made us experts in navigating stubborn proteins and getting them to yield in the range you wish for. A highly optimized system helps our experts flex their way through feasibility studies in the milligram range to upscaling orders at gram level.



## Fast Turnaround

We understand how keen you are to receive your product once an order is placed. Every official order is processed from the get-go through proactive internal and external communication. Our responsibility ends only after you tell us the product arrived safe, well and exactly when you expected it.



# Custom Bioproduction



## Premium Quality

Quality is our highest priority and > 90% returning customers are proof of it. Biological material can be a tough negotiator when it comes to reproducibility. However, thorough internal protocols and extensive documentation make sure nothing misses the eye and you get what you ask for - every single time



## Economical Production

As Europe's largest contract manufacturer, we deal with major orders regularly. Customized resources that sync with processes in production and upscaling help cater to budget needs - both yours and ours!



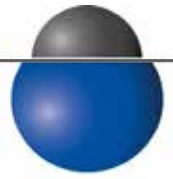
## Transparent Collaboration

The expertise and efforts are ours but we do not hold any intellectual rights over your product. Our collaboration will always be legally secured and your information will never be shared with third parties without consent. The product needless to say, will be yours to claim.





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