

PX' Therapeutics

The Protein'expert group



*Your partner for the development of biotherapeutics
from early stage R&D up to cGMP manufacturing
(recombinant proteins – vaccines - monoclonal antibodies)*



Protein'eXpert Platform

Development and Production of Recombinant Proteins (research grade)



A thorough scientific evaluation is performed for every incoming project before issuing a custom programme displaying clear milestones and deliverables.

The programmes proposed are designed to meet our clients' specifications and can include some or all of the expertises described hereafter :

- Gene synthesis and molecular biology (including mutagenesis)
- Protein engineering
 - Optimization of the protein sequence in order to solve specific solubility or refolding issues for instance
 - Definition of relevant combinations of vectors, signal peptides, strains/host cells to achieve improved expression or secretion yield.
- Production protocol transfer from the client and protein batch production
- Development and optimization of expression and purification protocols
- Development of refolding protocols for insoluble proteins
- Cell culture in transient conditions
- Development of stable monoclonal mammalian cell lines
- Development of fermentation process (batch, fed-batch) and scale-up of purification scheme in view of large scale industrial or cGMP manufacturing.
- Production of protein batches (from mg to gram scale, research to crystallography grade)
- Quality controls
 - SDS-PAGE, Western-Blot, IEF, N-terminal sequencing, mass spectrometry, endotoxin dosage, HPLC, ELISA, etc.

Research Contracts

Protein'eXpert also proposes integrated research contracts including all protein development steps from molecular biology up to the delivery of protein batches. This type of contract and our project management competences allow the development and production of up to 40 proteins in parallel for various applications : cristallography, animal studies, in vitro assays, etc.

Expression Systems

Our team displays expertise with the following systems :

- bacterial (*E. coli*). Specific know-how for insoluble protein.
- yeast (*S. cerevisiae*, *Pichia pastoris*)
- baculovirus / insect cells
- mammalian cell lines (CHO, HEK, COS, etc.)

Quality Assurance

All project steps are performed according to ISO 9001 standards and are compliant with pharmaceutical and diagnostic industries requirements.

PX' Monoclonals Platform Development and Production of Monoclonal Antibodies



We differentiate from other service companies by our vocation to propose:

1. original and relevant approaches to address antibody development related issues such as immunization of animals with difficult-to-express antigens or generation of antibodies directed against rare and weakly antigenic epitopes.
2. strategies for the development of humanized antibodies based on a « fee for service » model. Those strategies are essentially based on know-how and not on proprietary technologies in order to lower the level of intellectual property associated to the product and increase its value for the client.

1. Development of Murine Monoclonal Antibodies

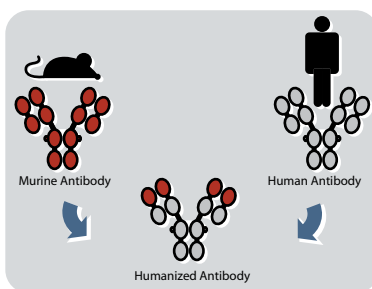
As regards the generation of high affinity murine antibodies, PX' Monoclonals offers the following competences which can be selected according to the client's requirements and project specifications.

- Mice immunization protocols adapted to the material available
 - from DNA if the protein material is not accessible
 - from peptide and protein
 - from transfected cells
- Substractive immunization strategy for the development of antibodies directed against rare or weakly antigenic epitopes
 - Example : discrimination of antibodies directed against multimers versus monomers, against a protein variant versus the wild type form, against a human protein versus a murine protein displaying sequence homologies, etc
- Fusion with myeloma cells, generation and screening of hybridomas
 - Development of primary screening methods : Western-Blot, ELISA, etc. Secondary screening to be performed by the client or transferred to PX' Monoclonals.
- Cloning and characterization of producing hybridomas
- Production and purification of antibody batch (optional)
- Other services upon request

2. Development of humanized monoclonal antibodies

PX' Monoclonals offers 3 different strategies targeting the development of chimeric, humanized or fully human antibodies dedicated to therapeutic applications :

- A. Molecular engineering strategy : RT-PCR cloning of variable part of the antibody, gene optimization and sub-cloning into expression vectors adapted to the production in CHO cell lines (TR base, CMV promoters), chimerization of constant human Ig parts, humanization based upon structural biology data in order to prevent immunogenicity.
- B. Development of humanized mice which allow the production of antibodies partially humanized (R&D programme Hus'Map carried out in collaboration with Genoway).
- C. Development of human antibodies from human B lymphocytes isolated from seroconverted patients after an infection (R&D programme Hus'Map carried out in collaboration with the INSERM).



PX'Pharma Platform

cGMP Development & Manufacturing of Biotherapeutic Products

The pharmaceutical platform PX'Pharma allows to perform all the manufacturing operations associated with the production, characterization and clinical release of therapeutic candidates batches according to Good Manufacturing Practices (GMP). The clinical batches and associated documentation are compliant with the European (EMA) and American (FDA) standards.

The PX'Pharma cGMP facility is dedicated to bacterial and yeast expression systems. The platform is equipped with a 30L bioreactor which allows the manufacturing (USP/DSP) of up to 100L of biomass via several fermentation runs. This production capacity actually meets the manufacturing objectives of therapeutic proteins or recombinant vaccines for Phase I/II clinical trials.

PX'Pharma offers the following services :

- Cell banking (Master Cell Bank / Working Cell Bank)
- Development and validation of analytical methods
- Scale up of production process and technical batch manufacturing
- Preclinical batch manufacturing
- Clinical batch manufacturing (Phase I/II) and batch release
- Clinical manufacturing (large scale, PIII, market) through our partner Althea Technologies (www.altheatech.com)
- Fill & Finish (through qualified partners)
- Regulatory support all along the project



In prospect : Additional cGMP facility

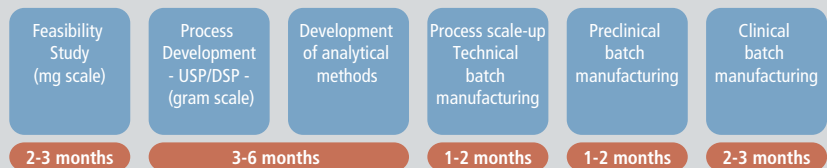
From Q4 2009, PX'Pharma will also assure the preclinical and clinical manufacturing of recombinant proteins and antibodies in mammalian cell lines (CHO). Please contact us for further information.

Our Added Value

Our specific organization and the mix of R&D and manufacturing competences of our team ensure added value to customers. Our strengths rely on :

- a scientific expertise associated with the regulatory understanding of biotherapeutic products development
- the capability to accompany our clients from early stage research and engineering up to clinical batches manufacturing
- the optimization of timelines for the development of therapeutic candidates due to the synergy between the research (Protein'eXpert, PX'Monoclonals) and cGMP manufacturing (PX'Pharma) platforms

Added Value



From gene to preclinical batch within 12 months

PX Therapeutics Company Profile



Funded in 2000 in Grenoble, France, PX Therapeutics (formerly known as Protein'eXpert) is offering contract research services focusing on the engineering, development and cGMP clinical manufacturing of valuable recombinant proteins and monoclonal antibodies.

PX Therapeutics particularly differentiates from other CMOs by its integrated way of working from early stage research and protein engineering to phases I & II clinical production. Since the creation of the company, we have been extensively involved into the discovery, development and manufacturing of drug targets and therapeutic proteins with over 500 projects performed through customers and R&D collaborative programmes. We have thus gained substantial experience in the production of challenging proteins and developed trusted relationships with now more than 130 pharmaceutical, biotech and academic partners (European & American). For example, we are closely working with the R&D teams of Meril, Sanofi Pasteur, Biomerieux, Tibotec, Galderma, Necker Hospital or Stallergenes.

To sustain our development, we also plan to integrate complementary technologies and multiply our production capacities. The recent collaboration with Althea Technologies now allows us to propose large scale manufacturing capabilities for phase I to III clinical trials and market production in bacterial and yeast systems. In addition, we plan to set up a new cGMP manufacturing unit dedicated to preclinical and clinical manufacturing in mammalian cells. We also work at strengthening our global presence and are currently opening an office in Boston (United States).

Today, our company's strategy is to accompany biotech and pharma clients all along the development of their biotherapeutic candidates with a mission to optimize timelines and bring value to their pipeline. The combination of protein expertise and manufacturing capabilities of the PX Therapeutics group indeed allows to ensure a seamless transfer from the discovery stage up to clinical manufacturing steps for complex biotherapeutic project (therapeutic proteins, recombinant vaccines and monoclonal antibodies).

To meet these requirements for scientific expertise and for optimization of biotherapeutics development schemes, PX Therapeutics is structured around three synergistic technological platforms which are perfectly coordinated to ensure optimal project management.

- Protein'eXpert : engineering, development and production of recombinant proteins
- PX'Monoclonals : development of murine and humanized monoclonal antibodies
- PX'Pharma : analytical development and cGMP clinical manufacturing of biotherapeutics

Company History

- **2000** Creation of Protein'eXpert, Contract Research Organization devoted to the engineering, development and production of valuable recombinant proteins.
- **2004** Set up of the PX'Pharma platform offering preclinical and cGMP clinical manufacturing services.
- **2007** Set up of the PX'Monoclonals platform dedicated to the development of murine and humanized monoclonal antibodies for research and therapeutic purposes. This subsidiary is located in Lyon.
- **2008** Protein'eXpert changes name to PX Therapeutics. This new corporate identity better reflects the company's mission - to provide its clients with an access to a high technical expertise as well as an efficient and comprehensive approach for their therapeutic projects development.

PX' Therapeutics

 *The Protein'eXpert group* 



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