

## Antibodies to Scale

### Custom Bulk Production Services - Mammalian Cell Culture

BioServ UK offers a fully customised service for bulk production of high value antibodies and proteins from mammalian cell culture:

- Up to 100 g quantities from customer-supplied cell lines
- State-of-the-art UK facility with over 15 years OEM antibody production experience
- Comprehensive cell line optimisation and recovery
- Full traceability – ISO 9001:2015 accredited

#### Deliverables:

- Purified monoclonal antibody, protein, or concentrated cell culture supernatant to requested scale (up to 250 L)
- WCB of scaled-up cell line
- Project report with SDS-PAGE, Western blot, ELISA & SEC performance data (where applicable)

#### Standard services:

- Bulk scale growth of hybridoma or other cell line (CHO, HEK, NS0 etc) expressing target protein
- Cells can be grown in standard serum-supplemented medium or adapted onto a regulatory compliant protein free medium, with an increased yield of up to 20%
- Cells are expanded from T flasks to roller bottle culture ensuring scaled process development and subsequent lot-to-lot consistency
- Purification: Protein A/G, affinity, and non-affinity chromatography
- Time scale: 1-4 months dependent upon scale

- Mycoplasma screening and testing
- Cell line adaptation to protein-free medium
- Cell line banking and storage
- Recovery of recalcitrant cell lines
- Re-cloning of poorly secreting cell lines
- Antibody fragmentation: Fab and F(ab')<sub>2</sub> generation

#### Standard production schedule:

- Receipt of cell line from client as either a frozen ampoule or growing culture
- Initial growth of cell line in serum-supplemented medium in a quarantined environment
- Mycoplasma screening of cell line supernatant (PCR)
- Adaptation of cell line on to protein-free medium
- Scale-up through T flask culture to 2 x 500ml roller bottles for initial 'pilot scale' growth
- Roller culture grown to extinction (<20% viability)
- Confluent supernatant harvested and concentrated by tangential cross flow filtration
- Supernatant purified using Protein A/G, immuno-affinity, IMAC chromatography
- Sample dialysed and formulated to client's requirements (standard of 1mg/ml, sterile in PBS)
- QC of final material (SDS-PAGE, Western, SEC)
- Dispatch and client validation of test material
- Subsequent scale-up based on initial pilot data

#### Additional services:

- Antibody labelling – Enzymes (HRP, AP), FITC, Biotin etc.
- Antibody isotyping
- Assay development and affinity determination
- Bulk supply of isotype control antibodies (IgG1, IgG2a, IgG2b, IgG3, IgM, IgA)

## Custom De Novo Antibody Production Services

- Monoclonal or polyclonal
- Modular pricing structure
- Range of purification services available
- Full characterisation and validation services available

### **Monoclonals**

#### **Deliverables:**

- Up to 30 mg purified monoclonal antibody
- Hybridoma cell line (licence free)
- Project report with ELISA results
- 50 µl Post-immunisation serum
- 50 µl Pre-immune serum
- 2-5 mg Immunising peptide (for peptide targets)

#### **Standard services:**

- Antigen: Recombinant protein or KLH conjugated peptide
- Peptide: EPITOPE predictive design, synthesis, and conjugation
- Species: 4 x Balb/c Mice
- Immunisation schedule: 45 day
- Hybridoma fusion and screening: ELISA, end-point assay
- Production and purification: Protein A/G affinity chromatography
- Data: ELISA test against the antigen
- Deliverable: Affinity purified monoclonal antibody and hybridoma cell line
- Time scale: 5-6 months

#### **Antigen requirements:**

- Peptide: 2 mg for immunisation and screening
- Protein: 2 mg for immunisation and screening
- Antigen configuration: 1 mg/ml in PBS, filter sterilised

#### **Additional services:**

- Phospho-specific polyclonal/monoclonal antibody service
- Modified, phospho and control peptide synthesis
- Antibody fragmentation: Fab and F(ab')<sub>2</sub> generation
- Customised and extended immunisation schedules
- Western blot (WB) screening

### **Polyclonals**

#### **Deliverables:**

- >2 mg affinity purified polyclonal antibody or 80-100ml terminal sera
- Project report including ELISA data
- 5 ml Post-immunisation serum (up to 3 bleeds)
- 1 ml Pre-immune serum

#### **Standard services:**

- Antigen: Recombinant protein or KLH conjugated peptide
- Peptide: EPITOPE predictive design, synthesis, and conjugation
- Species: mouse, rat, rabbit, guinea pig (other species available on request)
- 28, 69 or 77-day immunisation schedules
- Purification: Protein A/G or antigen affinity chromatography
- Data: ELISA test against the antigen
- Deliverable: Affinity purified antibody or terminal sera
- Time scale: 1-4 months

#### **Antigen requirements:**

- Peptide: 2-5 mg for immunisation and purification
- Protein: 2-5 mg for immunisation and purification
- Antigen configuration: 1 mg/ml in PBS, filter sterilised

## Custom Protein Production Services - Cloning

BioServ UK's dedicated molecular biology team provides a broad range of cloning services and proprietary vectors for successful recombinant protein expression.

### Cloning service:

- Codon optimisation and design service
- Gene synthesis
- Standard and non-standard restriction enzyme cleavage
- Clone into any vector of your choice: including all standard or licence free vectors
- Tags: polyHis, SuMO, GST, FLAG, V5, Myc, MBP, NusA, Strep-tag
- Time scale: 2-3 weeks
- Quality assured and sequence verified

### Licence free proprietary vectors:

- Based upon same core plasmid backbone
- Available for bacterial, insect, and mammalian expression
- Standard or custom designed
- Dual expression versions
- Modular design
- Choice of 156 individual components including: promoters, reporters, antibiotic resistance, origins, tags, signal peptides and more



## Custom Protein Production Services – Expression & Purification

With dedicated teams and extensive experience our UK based facility provides a wide range of high quality services.

### Expression service:

- Platform: Bacterial, insect (baculovirus, Sf9 or Hi5), mammalian (transient and stable), hybridoma
- Screening: strains, clones, media
- Trial expression: < 0.5 litres
- Small scale expression: < 10 litres
- Large scale expression: 50-250 litres
- Analysis: SDS-PAGE, Western blot

### Purification service:

- Untagged
- Tag removal: TEV, enterokinase, thrombin
- Affinity: SuMO, polyHis, GST, Biotin, Fc, MBP etc
- Ion-exchange and size-exclusion chromatography

### Additional services:

- Method development
- Labelling: Selenomethionine, Selenocysteine, N<sup>15</sup>
- Validated ELISA assay development
- Endotoxin removal from protein sample
- Fragmentation: Fab and Fab' generation
- Cell line banking and storage

### Time scale: (1 litre expression and purification)

- Bacteria: 2-3 weeks
- Insect cells (baculovirus): 4-5 weeks
- Insect cells (stable): 6-7 weeks
- Mammalian: 6-7 weeks

# Custom Peptide Synthesis

BioServ UK provides a high quality custom peptide synthesis service with expertise in modified and difficult peptides.

## Peptide service:

- Epitope design & prediction
- Sequence: 2 to 100 amino acids
- Purity: Crude to >98%
- Quantity: Milligrams to 100 grammes
- Quality: Full mass spec and HPLC analysis
- Time scale: 2-3 weeks

## Peptide antigens for antibody production:

- Conjugations: KLH, BSA and OVA

## Modified and difficult peptides:

- Hydrophobic peptides
- Non-standard amino acids: Phosphorylated, D-isomers, methylated, non-natural
- Spacers and linkers: PEG, AVA, GABA, AEA, Gly, ANP
- Labels: Biotin, FITC, 6-FAM etc
- Cyclic peptides: Disulphide or amide terminal/side chains
- N (NH<sub>2</sub>) & C (COOH or CONH<sub>2</sub>) terminal

