Custom Monoclonal Antibody Production

Product Description

A fully project managed service providing detailed consultation throughout the stages of immunisation, cell line development through to optimisation, expansion and purification. Projects are broken down into defined stages enabling maximum flexibility in project design and deliverables. Production services can be further combined with additional contract services depending on your project requirements and available in-house resources.

Key Features:

- **Fully customisable:** Full consultation is the key to a successful project. Each project is developed to exact requirements - no off-the shelf, one-size fits all packages
- **Antibody production:** Antibodies can be produced to Research Grade, Clinical Diagnostic Grade or cGMP production standards
- **UK Licensed:** All antibody production services are carried out in secure UK facilities under veterinary supervision meeting current ethical requirements, ensuring the highest quality of care for host animals, and the production of premium quality antibodies
- **Complete confidentiality:** We understand the absolute requirement for complete confidentiality in all the custom projects. No project information will be disclosed except to clients – can be qualified with NDA's when required
- **First class customer services:** All clients can expect excellent customer care. We recognise the importance of regular communication with our clients throughout each project
- **Technical Expertise:** Over 30 years' experience in antibody production

Standard Custom mAb Production Workflow:

A typical project includes the immunisation of 4 mice, fusion of screened cell lines (providing 20-30 candidate clones), cloning to produce up to 5-10 clones, and finally expansion and cryopreservation of the chosen clones. Additional services, such as antibody production can be included as required. Please contact us at sales@antibodyproduction.co.uk to discuss your project requirements in detail.

Prior to any project commencing, a Justification Application must be completed and returned in order to acquire the necessary veterinary approval to proceed. All schedules are also sent for pre-approval and sign-off prior to any work commencing on the project. No project will be terminated without written consent.

Antibody Production Services, a Division of Life Science Group Ltd.
Tel: +44 (0) 1234 889180; Email: sales@lifesciencegroup.co.uk
Web: www.lifesciencegroup.co.uk

Project Requirements

All custom monoclonal antibody projects are produced in the UK under Home Office licence. The Custom Monoclonal Antibody Production Unit holds a licence under the Animals (Scientific Procedures) Act. Our facilities are regulated and controlled under strict UK Home Office guidelines, ensuring a high standard of care by experienced and dedicated staff.

- **Staff**: The Custom Monoclonal Antibody Production Unit has qualified licensees to carry out procedures and to cover husbandry and animal care.
- **Plan of work**: Before any work is started, a Scientific Justification must be completed and COSHH forms for the antigen supplied. APS supplies Justification forms for completion prior to commencement of any project. Once approved, the project is logged onto a database and animals are allocated to the project. A protocol is generated and sent for customer approval. The project is then carried out according to the schedule. Any changes to the protocol need to be confirmed in writing. Should and changes be adopted during the course of a project, a new protocol is generated and sent to the customer to sign. Termination of the project is not performed until written confirmation is received from the customer.
- **Health Checks**: Animals are checked at least once daily, and more frequently if required.

Scientific Justification

A scientific justification is required before production can be carried out. The justification is then assessed as part of the Ethical Review Process. All requests are forwarded to the Home Office for approval. The following is a summary of requirements:

- A brief summary about the target antigen.
- An explanation as to why this specific antibody is required.
- Background of the scientific study.
- Potential benefits: It is important to explain how your work will benefit mankind. Antibodies can be made for the following purposes:
    - The prevention (whether by the testing of any product or otherwise) or the diagnosis or treatment of disease, ill health or abnormality, or their effects, in man, animals or plants.
    - The assessment, detection, regulation or modification of physiological conditions in man, animals or plants.
    - The protection of the natural environment in the interest of the health or welfare of man or animals.
    - The advancement of knowledge in biological or behavioural science.
    - Education or training other than in primary or secondary schools.
    - Forensic enquiries.
    - The breeding of animals for experimental or other scientific use.

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Antigen Selection

An immunogen is an antigen or any substance that may be specifically bound by components of the immune system. The immunogenicity of the chosen antigen is of paramount importance to the success of any custom polyclonal antibody project. The characteristics of the antigen must be determined as this will impact the choice of host and protocol used to create the antibody and the eventual success of the project.

Whatever antigen is used, there will probably be multiple epitopes against which antibodies could be generated. When choosing epitopes for your antibody production, it is best to look for those with exposed hydrophilic regions as these will be easily accessible for antibody binding. Hydrophobic regions are usually hidden within the protein.

Antigens can be derived from a variety of sources:

Peptides	Peptides are biologically occurring short chains of amino acid monomers linked by peptide (amide) bonds. APS offer both engineered and custom peptides. Our **Custom Peptide Synthesis Service** includes design, synthesis and modification. Peptides are synthesised using solid-phase chemistry and fully automated multiple peptide synthesisers. APS offers peptides at a variety of purities, from >70% to 98%, dependent upon the proposed application. Peptides may also be customised to different lengths (# residues). Modifications to peptides include the addition of a functional group, such as phosphorylation, coupling to a carrier protein and labelling. Peptides are supplied lyophilised.
Proteins	Protein antigens can be either naturally occurring or recombinant when choosing your protein antigen you should consider the following:- The size of the protein, the amount of aggregation and the relative nativity of the protein can all affect the quality and quantity of antibody produced. Generally, the larger the immunogenic protein the better. Soluble, non-aggregated proteins may induce tolerance in the host rather than a satisfactory antibody response. Antibodies to native proteins react best with native proteins and antibodies to denatured proteins react best with denatured proteins. For example if antibodies are to be used on membrane blots, or other assays where the proteins are subjected to denaturing conditions, then antibodies should be made against denatured proteins. Alternatively, if antibodies are to be used to react with a native protein or to block a protein's active site, then antibodies should be made against the native protein.
Bacteria / Viruses	Live bacteria or viruses, should not be used except as a last resort. There are many fixatives and inactivation techniques and one can generally be found that does not damage the antigenic determinants.

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Plants / Yeast	Sometimes high backgrounds can be found in host animal sera for plant or yeast antigens. We can supply pre-immune serum for screening for selecting candidate animals for immunisation.
Other Antigens	Small polypeptides, polysaccharides and other non-protein antigens generally need to be conjugated or cross-linked to larger, immunogenic carrier protein such as Bovine Serum Albumin (BSA) to increase immunogenicity.

Antigen Preparation

With the selection of a suitable antigen being critical to the successful initiation of an immune response in the host animal, we can provide immunogen preparation services, including peptide synthesis and carrier protein conjugation.

- Antigens should always be prepared using techniques that ensure that they are free of microbial contamination. Most protein antigen preparations can be sterilized using a 0.22 micron filter.
- Where possible, antigens should be free of preparative by-products and chemicals such as polyacrylamide gel, urea, endotoxin, particulate matter and extremes of pH.
- The buffer used to re-suspend your protein is important as some buffers may have an adverse effects on the animal's welfare. The least toxic option available should be used.
- The final immunogen used is an oil/water emulsion so therefore detergents should be avoided if possible as these may affect the stability. SDS can be used provided the concentration is less than 0.1%.
- APS can accept antigens as either lyophilised or liquid material. Antigens may be also be provided prepared as a conjugate to a carrier protein. This is also a service option available as part of a custom project.
- **Carrier Protein Conjugation:** A standard peptide of 15-20 amino acids in length is too small to elicit an immune response on its own. As a result, it is necessary to conjugate the peptide to a larger carrier protein. We can accept antigens as lyophilised or liquid material, which can be conjugated to a carrier protein or we can provide this service for you.
- **Adjuvant:** the adjuvant, Complete Freunds, is typically used for Primary immunisation, with subsequent immunisations using Incomplete Freunds. In order to eliminate or reduce discomfort, APS pre-screens batches of adjuvant and reserves suitable batches. A number of other adjuvants are available on request.

Species Selection

We routinely use Mouse BALB/C as the host species for the production of mAbs.

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Immunisation Schedule

A project can take from 6 to 12 months depending on the immunisation schedule and overall project complexity. Charges are based per round of serial dilution cloning as opposed to the best screened. This offers a greater level of flexibility and potential cost savings.

	Process	Deliverable	Estimated timescale in weeks
Phase I	Antigen preparation and immunisation: Serum samples are screened by ELISA *Requires 1 mg of antigen (1 mg/mL)*	Serum samples are supplied for client verification. Spleen tissue or terminal bleed serum can also be provided from additional targets if required.	12 - 20
Phase II	Hybridoma development: Cell fusion and screening of candidate colonies by ELISA	Typically 20-30 candidate clones are identified. A small volume of culture supernatant can be generated from these clones, if required.	4 - 6
Phase III	Screening: Limiting dilution cloning and cryogenic preservation	For each cell line, ELISA-screened clones are cryopreserved. 2-5 mg of purified monoclonal antibody is delivered for client testing. Client selected cell line is then delivered.	6 - 8
Phase IV	Large scale production of purified monoclonal antibody	mg to g quantities of mAb can be produced as required. Our standard 1 L batch culture typically yields 25-40 mg purified mAb.	3 - 6

APS can also produce large volumes of purified antibody from customer cell lines. Our standard 1 litre batch culture and purification typically yields 25 - 40 mg from an average cell line.

Project Termination

Following the successful completion of the Custom Polyclonal Project protocol the terminal bleeds, processed into serum, are supplied to the customer in entirety. The resulting serum will contain the whole antibody as well as other protein types. Whole antisera may be suitable for use in many applications but it may be necessary to improve specificity by applying purification steps to the whole serum.

Antibody Specifications

The following parameters will be reports on a Certificate of Analysis for each antibody (when supplied as purified material). Molecular weight (MALDI MS), Purity (HPLC), Solubility, Concentration, label, buffer, preservative.

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Shelf life

Antibodies have a shelf life of 1 year from date of opening.

Storage & Handling

Recommended storage is -20° C.

Antibodies are relatively fragile so repeated freeze/thaw cycles should be avoided. If an antimicrobial agent such as sodium azide is added, product may be stored at +4°C for up to 2 weeks. For long term storage, it is recommended to aliquot the antibody and store at -20°C.

Shipping

Antibodies are supplied as frozen material and will be shipped at -20°C.

For additional materials supplied as part of a custom antibody product service, shipping conditions are as follows:

- Test bleeds will be supplied as serum and shipped frozen at -20°C.
- Anti-sera will be supplied as serum and shipped frozen at -20°C.
- Custom cell lines will be shipped frozen at -20°C.
- Custom peptides are supplied as lyophilised material and shipped at ambient temperature.

Additional Contract Services

Monoclonal antibody production can be combined with additional services including:

- Peptide design and synthesis. We specialise in the production of peptides for the raising and purifying of antibodies.
- Antibody labelling including conjugation, phosphorylation, tagging and other modifications.
- Downstream processing, purification and protein analytics.
- Bulk antibody production from clients' own hybridoma.
- Cell line services including recovery, characterisation, optimisation, storage and transformation to serum-free conditions.

Regulation of the use of animals in research

All antibody production services are carried out in secure UK facilities by qualified licensees, under UK Home Office licensing to ensure the highest quality of care for the host animals, and the production of premium quality antibodies. All procedures are performed under veterinary supervision, meeting current ethical standards according to the Animal (Scientific Procedures) Act 1986 (ASPA), which has been revised to transpose European Directive 2010/63/EU. Central to the ASPA is a cost-benefit assessment which must be applied before any research project involving animals can go ahead.

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Ownership

Antibodies remain the property of the client.

Support

Antibody Production Services is a division of Life Science Group Ltd.

To learn more, contact us:

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