GLP Tissue Cross Reactivity Testing

Your needs, our expertise

Tailored Methodology for Biotherapeutic Safety Studies

Asterand Bio's unique combination of research discovery services and tissue procurement capabilities form the pillars of our GLP Tissue Cross Reactivity (TCR) Services.

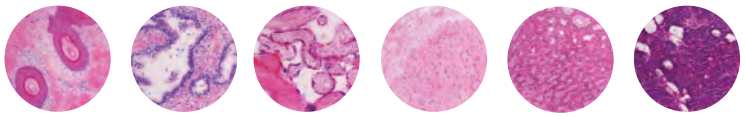
For more than 20 years, our PhaseZERO® Research Discovery Services platform has provided human tissue-based solutions to leading pharmaceutical and biotechnology companies, generating the data they need to support decisions for advancing the best targets.

Asterand Bio also has a heritage of tissue procurement. As a leading global supplier of well characterized human tissue, we are specialists in the procurement, assessment, characterization, and the use of human biospecimens for research. All human tissues recommended for testing by the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have been sourced with full consent for commercial research, and pre-assembled from at least 3 male and 3 female donors.

Clients may elect to have their TCR studies conducted in compliance with Good Laboratory Practice (GLP) or under non-GLP conditions. For preliminary TCR studies, our service provides clients with an accurate assessment of the on and off-target binding of their therapeutic antibody candidates, or related products, in human tissues. Our scientists are experts in their fields; this expertise, combined with a tailored scientific approach, enables us to deliver high quality data to our clients in a defined time to accelerate the development of their therapeutic antibody candidate programs.

Key Benefits:

- Prior collection and characterization of 36 human tissue types; providing a quick turnaround for your study without delays awaiting scarce tissues
- Robust qualification of tissues from procurement to assay use; resulting in superior data quality and reduced time lost due to experimental failure
- Full scale assay optimization; increasing your confidence in the scientific integrity of the results
- Flexible study design; either non-GLP tissue microarray (TMA) screening to provide an initial assessment or GLP study using full-face sections
- Fully automated immunohistochemical (IHC) assays offers consistent and reproducible results
- State of the art MHRA-certified; GLP compliant facility, complying with FDA and EMA data generation recommendations
- Experienced scientific and pathology staff; resulting in accurate completion of even the most technically challenging assays



Meticulously Qualified Specimens for your TCR Studies

Each of our TCR studies begins with well characterized human specimens that have been rigorously qualified to meet the exacting requirements of this research.

Our specimens undergo a four point inspection to qualify for GLP TCR studies:

1. Donor clinical history evaluation to ensure experimental suitability
2. Specimen review by board certified pathologists to validate normal morphology
3. Examination of site audit to ensure compliance with ethical, legal and regulatory requirements
4. Tissue antigenicity testing (as recommended by the FDA) available to confirm binding, upon request

Confirmation of Tissue Antigenicity

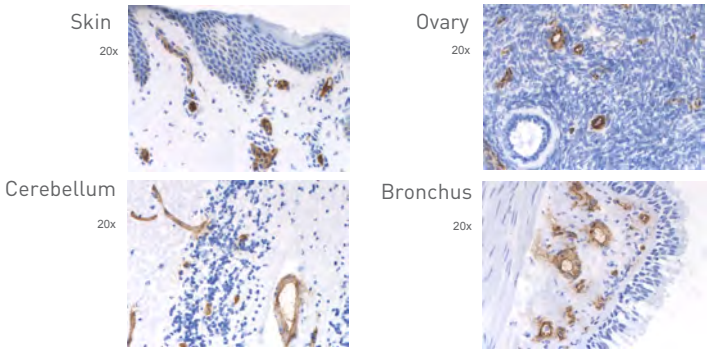


Figure 1. Confirmatory assays are preformed to validate the antigenicity of tissues used in TCR studies.

One such test involves the immunostaining of tissues with von Willebrand Factor (vWF) antibodies. Images show the binding of vWF antibodies to the microvascular endothelium proteins in frozen sections of skin, ovary, cerebellum and bronchus .

Complete, Comprehensive GLP Compliant TCR Services

Guidelines issued by the FDA and EMA for the development of therapeutic antibodies and related products recommend their testing for TCR on a range of human tissues (1,2). Given that such testing is performed in the pre-clinical phase of drug development prior to submission of Investigation New Drug (IND) applications to the FDA in the United States or Regulatory Authorities elsewhere, it is recommended that the data are generated to GLP.

Asterand Bio's Molecular Pathology team provides a customized service to meet your particular requirements for your biotherapeutic agent. We utilize a two or three phase approach that provides a cost effective solution for making confident decisions regarding the best parameters for your study and minimize the risk of GLP study failure. We deliver a final report, in compliance with GLP, that is suitable for submission as part of an IND application to the FDA or other Regulatory Authorities.

Tissue Types are Available from Multiple Male and Female Donors

Adrenal gland
Bladder
Blood cells
Blood vessel endothelium
Bone marrow
Breast
Cerebellum
Cerebral cortex
Eye
Fallopian tube
Heart
Ileum
Kidney - glomerulus and tubule
Liver
Lung - bronchus and parenchyma
Lymph Node
Ovary
Pancreas
Parathyroid gland
Parotid salivary gland
Peripheral nerve
Pituitary gland
Placenta
Prostate
Skeletal muscle
Skin
Spinal cord
Spleen
Stomach
Testis
Thymus
Thyroid gland
Tonsil
Ureter
Uterus - cervix and endometrium

Please contact us regarding availability of other tissues

Our 3-Phase Approach Provides Quality Data for Your Study

Phase 1
Assay Optimization

- Selection of control tissues/cell lines
- Testing of 2 fixation protocols
- Testing of up to 5 primary antibody (Test Item) concentrations
- Negative control (Control Item) run in parallel
- Assay control antibody run in parallel
- Expert analysis, recommendation of optimal IHC conditions

Phase 1b (Optional)
TMA Screening (non-GLP)

- Proprietary formatted, frozen TMA
- Control tissues/cell lines (from Phase 1)
- Fully optimized, automated assay
- Single fixation protocol
- Single Test Item concentration (as obtained from Phase I)
- Matching Control Item concentration
- Board certified pathologist review
- Tabular data, digital photomicrograph, report options available

Phase II
GLP Tissue Cross Reactivity

- Full face, frozen tissue sections, validated for use in GLP TCR
- Control tissues run in parallel
- Optimized fixation protocol (from Phase I)
- Optimized Test Item concentration (from Phase I)
- Matching Control Item concentration
- Assay automation
- Assay control
- Board certified pathologist review
- Final report suitable for Regulatory Authorities submissions

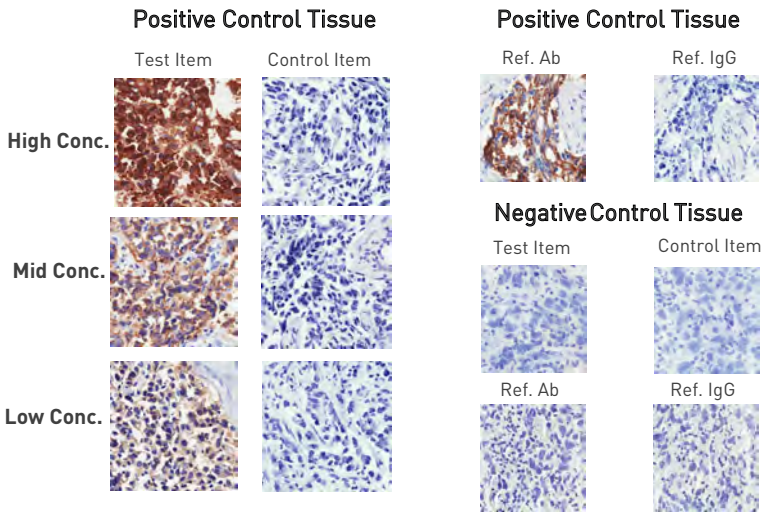


Figure 2. Phase 1 assay optimization data.

Left hand panels show frozen sections of positive control tissue incubated with three concentrations of Test Item and Control Item. The panels demonstrate specific, concentration-depending Test Item binding. Binding of a reference antibody (same target - Ref . Ab.) and an equivalent concentration of non-immune IgG (Ref. IgG) are shown for comparison. The pattern of binding appears quantitatively similar. No binding of either the Test Item nor the reference antibody was observed in the negative control tissue.

(1) Points to Consider in the Manufacture and Testing of Monoclonal Antibody Products for Human Use, Docket No. 94d-0259, February 28, 1997
(2) Guideline on Development, Production, Characterisation and Specifications for Monoclonal Antibodies and Related Products, EMEA/CHMP/BWP/157653/2007, Adopted on 18 December 2008

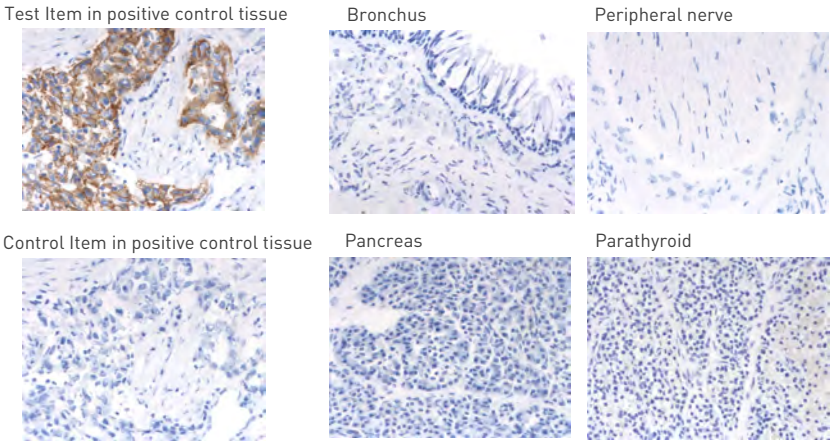


Figure 3. Phase II GLP TCR data.

The left hand panels show the binding of Test Item and Control Item to the positive control tissue. The right hand panels show absence of Test Item binding to cryosections of bronchus, peripheral nerve, pancreas and parathyroid.

Frozen Tissue Microarray Screening (Phase 1b)

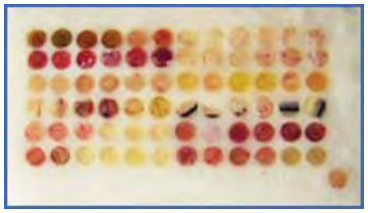
Swift, Accurate Detection

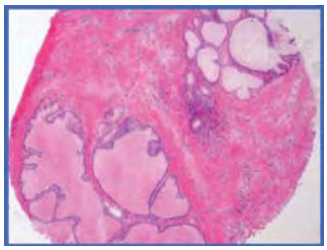
TCR screening using frozen TMAs in place of full face tissue sections offers an economical alternative for rapid feedback on Test Items. Our scientists have developed a panel of TMAs containing the 36 tissues required by the FDA and EMA for assessment of therapeutic antibody candidates. Utilization of this approach is designed to accelerate the de-selection of antibody candidates which exhibit significant 'off target' immunoreactive profiles.

Advantages of this service include:

- Assessment of all 36 FDA and EMA tissues; provides actionable feedback on 'off target' effects that can be incorporated into early antibody evaluations
- Single assay format; provides economical alternative to full face sections
- Experiments performed with the same experts, tissues and IHC methods employed for our GLP studies provide confidence in the results

Frozen TMA for TCR screening





Quality Construction

- Three array set - each block containing 12 tissues from 3 donors each, in duplicate
- Tissue selection using the same parameters as our GLP level studies
- Pathology review to ensure all cores are representative of the full tissue section
- Tissue remains frozen throughout the coring and mounting process

Excellent Results

- Tabulated data with secure online access to Aperio scanned images -suitible to identify 'off target' effects
- Reporting options available

Meet Our Experts

A thorough personal service is of utmost importance to our Asterand Bio GLP experts, and essential to the success of every project. Each of our experts is highly committed to their project role, and their duties honor the need and demand as required by our GLP Study Sponsors. With over 20 years of experience, our project specialists include Study Directors and authorities on Quality Assurance.

Study Directors

Regular communication to understand exact requirements of every study, and to build a mutually trusting relationship is the most important part of the Study Director's role. The assigned Study Director is the core contact for the Study Sponsor and is responsible for conveying all information during the project. They inform the sponsor of any changes or issues that arise, and are responsible for approving any decision that may affect the integrity of every study.

At the final sign-off on each study report, the Study Director is responsible for the statement that the work has been done in full compliance with GLP. All data is thoroughly reviewed by the Study Director, as the project progresses, and sign-off is never completed if there is not 100% certainty of the credibility of the collected data.

Quality Assurance

Our Quality Assurance experts work closely with our Study Directors, from draft of the Study Plan, through experimental work, and right to the Final Report, ensuring that all GLP studies conform to GLP regulations. Through scheduled Quality Assurance audits of the critical aspects of each study, its processes and our facility, our QA experts ensure our GLP accredited laboratory is operated in compliance with regulations and our internal Quality Management System.

Every study audit is achieved through the following steps:

- Review the Study Plan before research begins
- Ensure each study is executed in compliance with the plan and relevant Standard Operating Procedures, protocols and work instructions
- Examine all reported Deviations and Corrective and Preventative Actions to ensure resolution in a timely manner
- Audit the detailed Final Report as compliant with GLP

Asterand Bio has made a significant investment to create a state of the art facility and quality management system from providing GLP compliant immunohistochemical studies. Asterand Bio has been a full member of the Medicines and Healthcare Products Regulatory Agency (MHRA) UK GLP Compliance Monitoring Programme since February 2010, and had a recent successful inspection by the MHRA in February 2015. These resources allow us to provide our clients with efficient delivery of high quality data to support their IND submission.

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ABOUT ASTERAND BIOSCIENCE®

Asterand Bio is the leading global provider of high quality, well characterized human tissue and human tissue-based research solutions to drug discovery scientists. Our mission is to provide human-based solutions to accelerate the identification and validation of drug targets and enhance the selection of drug candidates with an increased likelihood of clinical success.

ETHICAL AND REGULATORY CONTROL

All human tissue samples are obtained with informed donor consent and are de-identified prior to banking and distribution. Asterand Bio acts in strict compliance with the US Health Insurance Portability and Accountability Act (HIPAA) and the United Kingdom Human Tissue Authority (HTA) and is accredited by the College of American Pathologists (CAP) and ISO 9001. Asterand Bio has GLP accreditation according to the requirements of Good Laboratory Practice (GLP) - Directive of the European Commission 2004/9/EEC.

RESEARCH SERVICES:

- Immunohistochemistry
- ISH & FISH
- TMA, FDA & Custom
- Digital Pathology
- Histopathology
- qRT-PCR
- LCM
- siRNA Knockdown
- Western Blotting
- Autoradiography
- Primary Cell Isolation
- 2D and 3D Culture
- Cell Based Assays
- Assay Development
- OrganDOT™
- Mutation Analysis

BIOMATERIALS AVAILABLE:

- Fresh, Frozen & FFPE
- Normal & Diseased Tissue
- OCT Embedded
- Serum, Plasma & Blood
- Synovial Fluid
- RNA, DNA & Protein
- TMA, FFPE & Frozen
- Primary Cells
- Proprietary Cell Lines

THERAPEUTIC AREAS:

- Oncology
- Cardiovascular
- Metabolic
- CNS
- Respiratory
- Inflammation
- Genitourinary

XpressBANK™ BIOREPOSITORY

The Asterand Bio XpressBANK™ Biorepository is an invaluable source of high-quality, thoroughly characterized and validated tissue, biofluids, cell lines and molecular derivatives, all intended for research use in the drug and diagnostic development process. Our extensive repository contains over 200,000 human tissues and biofluids. This bank includes material that is prospectively obtained in a variety of formats including fresh frozen and FFPE, supported by comprehensive clinical data.

BioSPOKE™ CUSTOM BIOSPECIMEN PROCUREMENT

Through our BioSPOKE™ service, human tissues and clinical data are custom collected to meet unique research requirements within a wide range of disease categories or as normal controls. Samples are provided fresh or in multiple preserved formats. Specialized processing may be tailored to each research request. This service allows Asterand Bio to deliver human tissues, biofluids and accompanying clinical information to our clients that are collected in a manner which is most compatible with their experimental design.

PhaseZERO® RESEARCH SERVICES

For over 20 years, Asterand Bio's trusted scientists have worked collaboratively with clients to facilitate the efficient selection of drug targets and candidate therapeutics with the highest likelihood for clinical success by providing a variety of pre-clinical drug discovery services. From target and biomarker validation to characterizing the effects of drug candidates for both potency and safety using human tissue-based approaches, Asterand Bio provides clients with high-quality experimental design, execution, data interpretation and reporting. Each project is managed by a dedicated scientific project manager and customized to meet each client's specific needs.

Please contact our Business Development Directors in the following regions to discuss your requirements:

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ASTERAND BIOSCIENCE
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