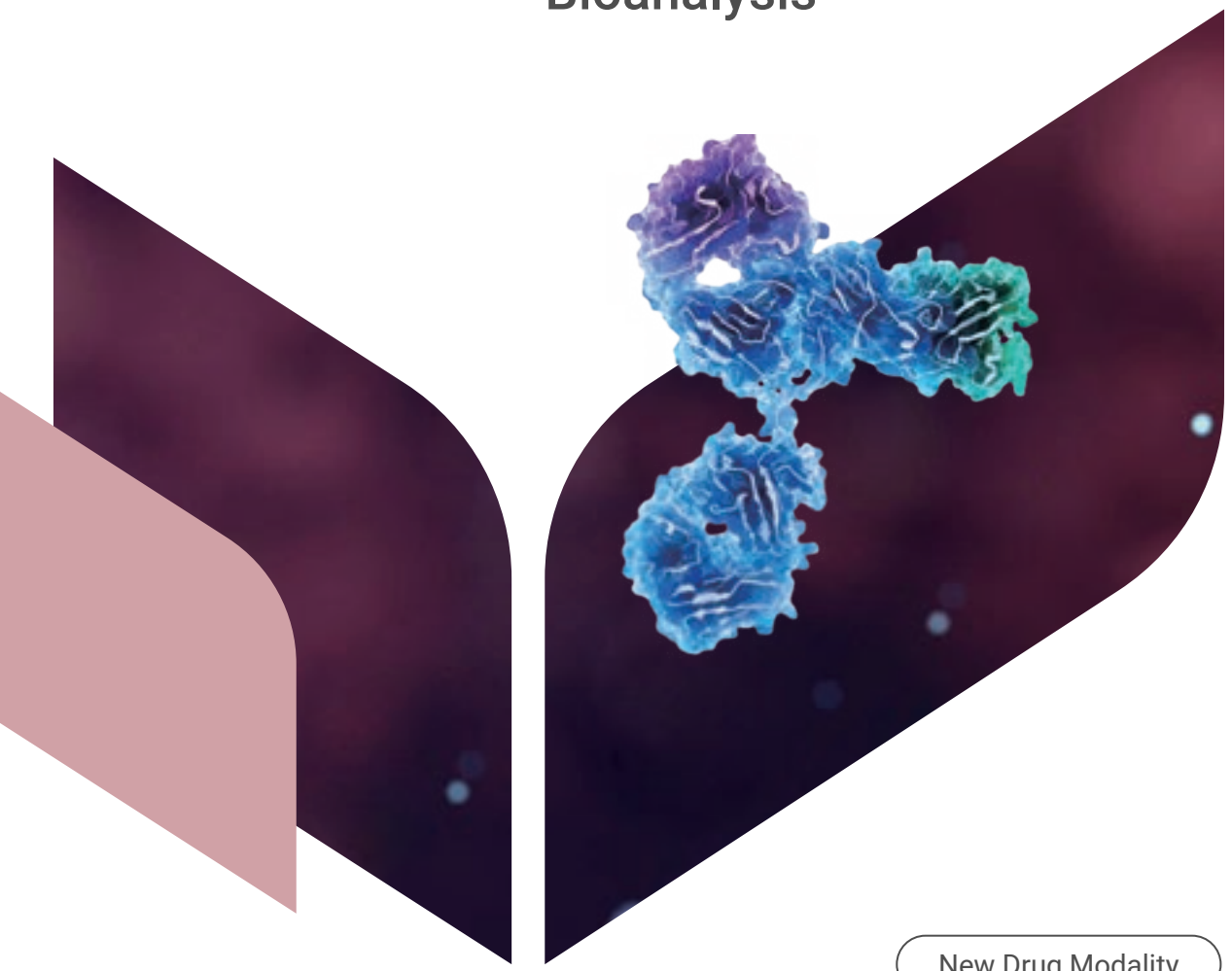
Laboratory Testing Division
Bioanalytical Services

WuXi AppTec

Bispecific/ Multispecific Antibodies

Bioanalysis



New Drug Modality

Bioanalytical Services

Global Integrated Bioanalytical Platform

WuXi AppTec Bioanalytical Services operates globally and has leading integrated laboratories in China and the U.S. We adhere to GLP and GCP principles and strictly follow high industry regulatory standards. Our comprehensive platform, equipped with advanced instruments and staffed by experienced experts, provides professional one-stop services in preclinical/clinical mass spectrometry, immunochemistry, molecular/cellular, and central laboratory services to global clients.

Shanghai, China
Headquarters
Bioanalytical Services (Clinical)
Central Lab

Suzhou, China
Bioanalytical Services (Preclinical)
Antibody Service

New Jersey, USA
Bioanalytical Services (Preclinical/Clinical)
Central Lab

Chengdu, China
Bioanalytical Services (Preclinical)

Nantong, China
Bioanalytical Services (Preclinical)

18+ Years lab operations in China and the U.S.
24,300 m² lab space

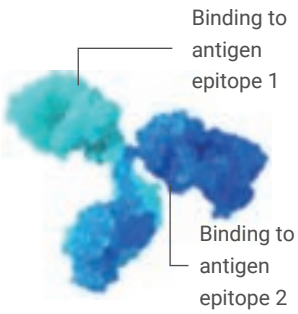
5,000+ small molecule validated methods
2,800+ large molecule validated methods
2M+ samples analyzed per year

Global Regulatory Standards

Successfully passed global regulatory inspections, comply with GLP, GCP, CAP quality standards
200+ China NMPA
30+ International regulatory agencies (U.S. FDA, OECD, EMA, PMDA, CAP)

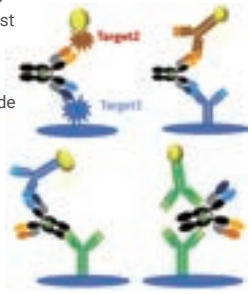
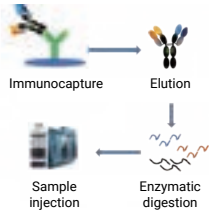
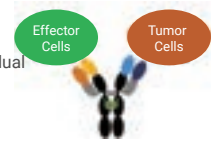
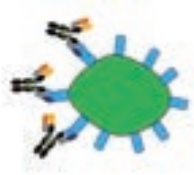
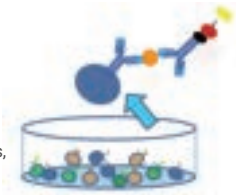
Bispecific Antibodies (BsAbs) are engineered using advanced technologies such as cell fusion, recombinant DNA, and protein engineering. These antibodies can specifically bind to two different antigens or two distinct epitopes of the same antigen simultaneously or sequentially. Multispecific Antibodies (MsAbs) can bind to two or more different epitopes or antigens at the same time.

WuXi AppTec's Bioanalytical Services (BAS) has supported more than 60 preclinical and 50 clinical projects involving more than 50 targets, amassing significant experience in methodological development. This expertise has led to the creation of a specialized bioanalytical research methodology for bispecific and multispecific antibodies, enabling the rapid resolution of various bioanalytical challenges and aiding sponsors in the swift advancement of their bispecific/multispecific antibody drug development projects. Additionally, BAS offers comprehensive quantitative detection and analytical services for bispecific/multispecific antibodies at any stage of preclinical and clinical research, helping sponsors successfully expedite global IND, NDA, and BLA submissions.



Bispecific Antibody

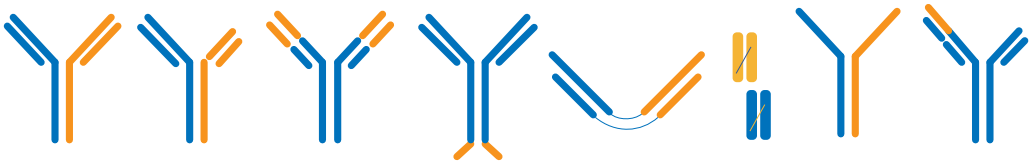
Bioanalytical Solutions for Bispecific/Multispecific Antibody

Content		Analyte	Platform	Methodology
Pharmacokinetics/Toxicokinetics	PK/TK	Intact Drug/ Domain-Specific Drug/ Total Drug	ELISA/MSD	For PK method development, the drug's structure and mechanism of action must be considered to establish a suitable assay format. In the LBA platform, key reagents include (taking a bispecific antibody as an example): ▪ Target proteins for the two functional domains ▪ Specific antibodies against the two functional domains ▪ Horseradish peroxidase, etc. 
			LC-MS (TQ/q-TOF)	Quantitative analysis of antibodies can be achieved by detecting the antibody's light chains, heavy chains, or characteristic peptide segments. It is also possible to quantify or monitor the characteristic peptide segments of different functional domains. Key reagents: ▪ Biotinylated anti-analyte antibodies ▪ Streptavidin-labeled magnetic beads ▪ Trypsin ▪ Isotope-labeled peptides (internally synthesized) 
Immunogenicity	ADA	Anti-Drug Antibodies	ELISA/MSD	The experimental design is similar to that for monoclonal antibodies and includes screening, confirmation, and titer experiments. However, the confirmation experiments need to include the confirmation of the full-length drug as well as the examination of the confirmation experiments for the functional domain portion. 
	NAb	Neutralizing Antibodies	Cell-based assay or Non-cell-based assay	Based on the drug's mechanism of action, immunogenicity risk assessment, and practical factors, a choice is made between cell-based or non-cell-based platforms. Cell-based platforms primarily include dual-cell bridging assays and dual single-cell assays, where the drug targets receptors or antigens on the cell. For non-cell-based platforms, generally two LBA methods are required. 
Pharmacodynamics/Biomarkers	RO	Receptor Occupancy	FACS	The ability of a bispecific antibody to bind to target receptors with its two functional domains is a crucial step in its mechanism of action. Based on the drug, selecting the appropriate cell populations and detection strategies to assess the receptor occupancy of the drug's target provides data support for studies on the drug's efficacy and dosage. 
	Biomarker	Free Target/ Total Target/ Cytokine Storm/ Pharmacodynamic Biomarker	ELISA/ MSD/ Luminex/ ELLA/ Simoa/ Gyros/ SMCxPRO, etc.	Biomarkers are indicators that can objectively measure and evaluate normal biological processes, pathological processes, or responses to drug intervention. They are widely used in clinical settings as tools for diagnosis, prognosis, prediction, pharmacodynamics, safety, and monitoring. 

Bispecific/Multispecific Antibody Clinical and Preclinical Bioanalysis Challenges and Analytical Experience

Challenges		
TK/PK	▪ Sensitivity ▪ Matrix stability ▪ Multiple assay formats	▪ Specificity/endogenous interference ▪ ADA interference
Anti-Drug Antibodies	▪ Drug tolerance ▪ Matrix effect	▪ Positive control and domain binding capability
Neutralizing Antibodies	▪ Drug tolerance ▪ Method robustness	▪ Sensitivity
Receptor Occupancy	▪ Detection strategy ▪ Selection of target cell populations	▪ Drug toxicity
Biomarkers	▪ Sensitivity ▪ Method robustness	▪ Multiplex testing ▪ Specificity

Structural Experience of Bispecific Antibody



Bispecific/Multispecific Antibody Bioanalytical Experience		
Target		
▪ CD3	▪ PD-1	▪ CD33
▪ HER2	▪ PD-L1	▪ 4-1BB
▪ CD19	▪ LAG-3	▪ HER2
▪ EpCAM	▪ IL-2R	▪ c-Met
▪ EGFR	▪ TGF-B1	▪ C-5
▪ MUC17	▪ CTLA-4	▪ FH
▪ Claudin 18.2	▪ OX40	▪ CD-28
▪ CDH17	▪ GARP	▪ IL-10
▪ CD38	▪ IL-2	▪ BCMA
▪ CD54	▪ IL-15	▪ B7H4
▪ TIGIT	▪ TGFNRII	▪ CD20
▪ CD96	▪ CD47	▪ VEGF

Bispecific Antibody Case Study

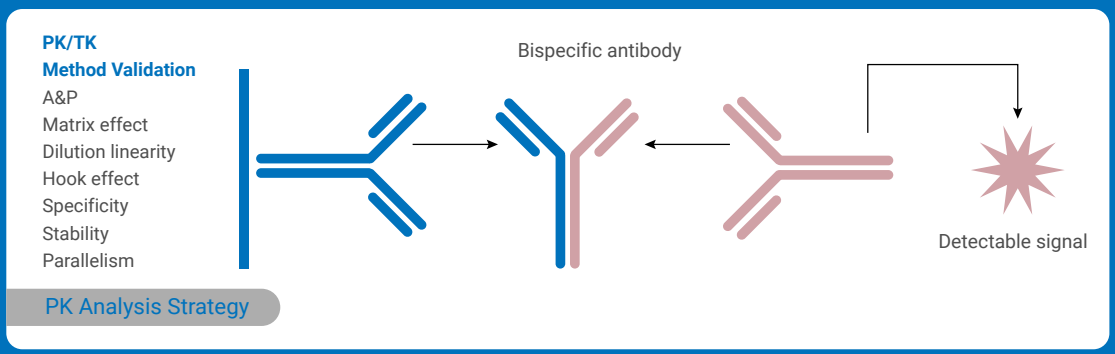
Background:

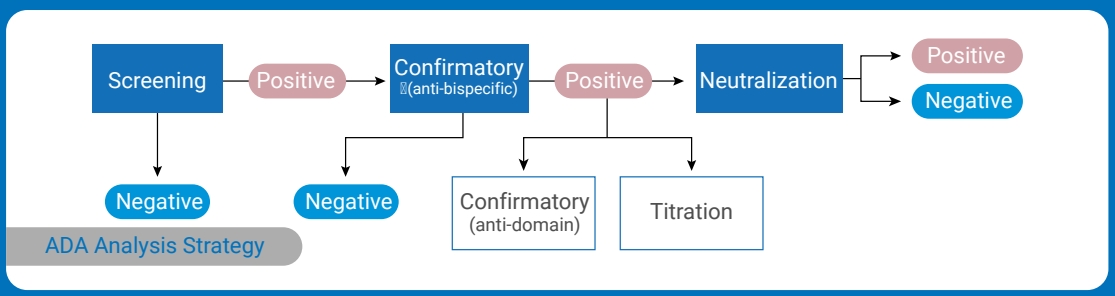
Using a bispecific antibody drug targeting PD-1 and CTLA-4 as an example, this medication, already available on the market, effectively blocks the interaction between PD-1 and its ligands PD-L1/PD-L2 and the interaction between CTLA-4 and B7.1/B7.2. By inhibiting both the PD-1 and CTLA-4 signaling pathways, the drug reduces the immunosuppressive response and enhances tumor-specific T-cell immunity activation. This dual mechanism produces a more potent antitumor effect, demonstrating a clinical efficacy exceeding the impact of individually targeting these pathways.

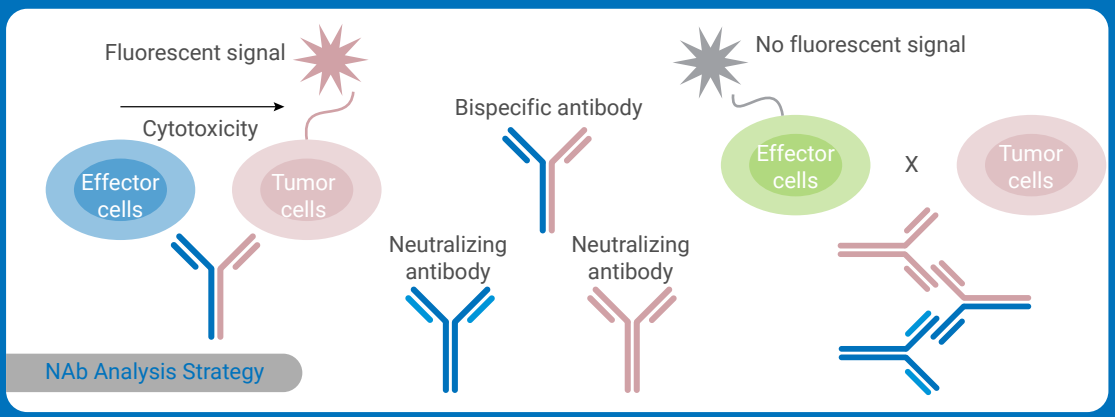
Study Design:

We provide customized services according to global regulatory guidance, supporting IND submission.

- **Bispecific antibody PK/TK:** The ELISA method is used to determine the concentration of bispecific antibody drugs in human/animal serum.
- **Bispecific antibody ADA:** The ECL method is employed to detect antibodies against bispecific antibody drugs in human/animal serum.
- **Bispecific antibody NAb:** The cell-based method is used to detect neutralizing antibodies against bispecific antibody drugs in human/animal serum.







Our Advantages

Global Integrated Platform: We provide one-stop services to global sponsors, from preclinical to clinical stages, supported by multiple BAS sites worldwide.

Customized Services: Our sponsor-centric professional project management team delivers tailored services to meet your specific needs.

Experienced Team: Our core technical team members boast over 10 years of experience, with our management team having more than 20 years.

Statistical Services: Our immunogenicity cut-point determination offers expedited data delivery, ensuring you quickly get accurate, reliable results. Our services are grounded in scientific rigor, providing enhanced accuracy and dependable outcomes.

We have experience with more than 100 bispecific/trispecific and tetravalent antibody projects in preclinical and clinical stages, targeting CD3, CD19, CD20, CD38, CD47, CD54, EpCAM, EGFR, MU17, Claudin18.2, CDH17, PD-1, PD-L1, LAG-3, GARDP, 4-1bb, B7H4, TIGIT, etc.

Common Industry References

1. Guidelines for the Validation of Quantitative Analysis Methods for Biological Samples, Pharmacopoeia of the People's Republic of China, 2020 edition
2. Guidelines for Clinical R&D of Bispecific Antibody Anticancer Drugs, Center for Drug Evaluation of the National Medical Products Administration
3. Bioanalytical Method Validation and Study Sample Analysis M10, International Council for Harmonisation
4. Bioanalytical Method Validation, U.S. Food and Drug Administration
5. Bispecific Antibody Development Programs Guidance for Industry, U.S. Food and Drug Administration
6. Immunogenicity Testing of Therapeutic Protein Products—Developing and Validating Assays for Anti-Drug Antibody Detection, U.S. Food and Drug Administration

LEARN MORE
LABTESTING.WUXIAPPTEC.COM/BIOANALYTICAL-SERVICES

TALK TO AN EXPERT
LABTESTING.WUXIAPPTEC.COM/TALK-TO-AN-EXPERT

WuXi AppTec
Laboratory Testing Division
Bioanalytical Services

Info@wuxiapptec.com