



A leading Australian contract research organisation (CRO) providing integrated preclinical drug development services to the biotech and pharmaceutical industries



The TetraQ Difference

- ❖ Provide advice and tailored solutions, not just a menu of choices
- ❖ We assist clients with data interpretation to facilitate and guide timely decision-making
- ❖ Quality science behind all services (no short cuts)
- ❖ Highly skilled scientific and commercial team
- ❖ Services backed by a leadership team with wealth experience in all 4 areas of preclinical drug development
- ❖ Aim to be a 'one-stop shop' to simplify early stage drug development

- ❖ Located at The University of Queensland in Brisbane (UQ), Queensland
- ❖ “*State of the art*” facilities & equipment including LC-MS/MS, HPLC and ELISA equipment
- ❖ Modern PC2, SPF central animal breeding facilities
- ❖ Quality Preclinical Solutions
- ❖ GLP Recognised facilities
- ❖ NATA ISO 17025, Research & Development Accreditation
- ❖ Data acceptable for Australian and international regulatory submission

ADME – Bioanalytical Services

(absorption, distribution, metabolism elimination)

GLP Recognised & NATA ISO 17025, Research & Development Accredited

- ❖ World leaders in bioanalytical method development & sample analysis of drugs/metabolites in biological fluids
 - Human and animal samples
- ❖ Validated bioanalytical methods
 - HPLC, LC-MS/MS, ELISA
 - Screening, partially validated, fully validated to satisfy FDA requirements
- ❖ Bioavailability and pharmacokinetic studies
- ❖ Drug metabolism studies including metabolite identification
- ❖ Biodistribution and plasma protein binding studies
- ❖ Toxicokinetics and plasma stability studies



Efficacy – Biological Services

Proof-of-concept studies in animal models of human disease

- Pain: nociceptive, inflammatory, neuropathic
- Arthritis
- CNS Models - Multiple sclerosis, Parkinson's disease, Alzheimer's disease
- Obesity
- Diabetes
- Cancer (through partner)



TetraQ Services

Toxicology

GLP recognised

- ❖ Genotoxicity assays (Ames Test, Micronucleus, Mouse Lymphoma Assay)
- ❖ *In vivo* acute & repeat dose (chronic) toxicity studies
- ❖ *In vivo* safety pharmacology (including hERG, respiratory and CNS)
- ❖ Cytotoxicity assessment
- ❖ *In vivo* – two species, rodent and non rodent (dog, primates)



Pharmaceuticals

- ❖ Physicochemical characterization
 - FTIR, UV, NMR, MS
- ❖ Formulation development
- ❖ Structure elucidation, solubility
- ❖ Stability trials & stability indicating method development
- ❖ Dissolution studies
- ❖ Lead compound optimisation

TetraQ are focused to provide solutions to meet your preclinical needs. Contact us now for more information – www.tetraq.com.au

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TetraQ – Q-Pharm Strategic Alliance Boosts Bio-Pharmaceutical Service Delivery



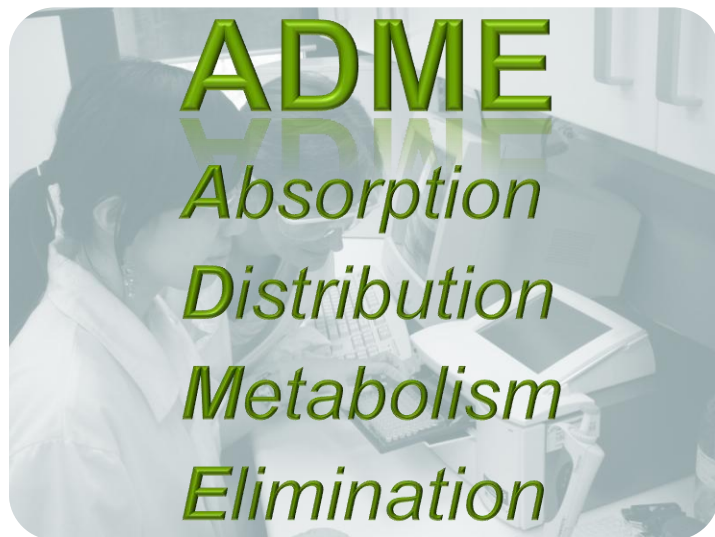
Q-Pharm Pty Limited

In June 2008 TetraQ, the integrated preclinical contract research organisation based at The University of Queensland (UQ), and Q-Pharm, a leading early phase clinical trial facility in Australasia, announced a strategic alliance to enhance the delivery of bioanalytical services to clients in the biotechnology and pharmaceutical industries.

The alignment of the two organizations at the interface of the preclinical and early phase clinical stages of the drug development pathway presents significant opportunities for capturing operational economies, co-marketing of services, cross-referral of potential clients and providing a more complete and streamlined service.

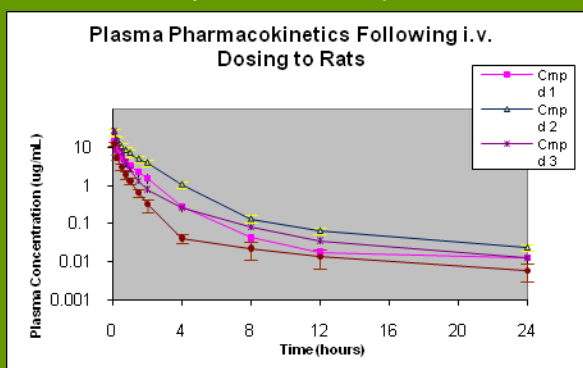
Since its announcement in June, this alliance has been positive and has already resulted in 6 projects of significant size being undertaken at TetraQ with many more in the pipeline.

TetraQ ADME offers a range of *in vitro* and *in vivo* ADME services for the analysis of drugs and metabolites in biological fluids. We also frequently analyse samples generated from externally conducted studies. We are recognised as leaders in the development of validated assays for drugs and metabolites and use the latest equipment. We take pride in having highly interactive relationships with our clients and work seamlessly with the other areas of TetraQ to provide a complete solution.



Analytical Services

- Method development for drugs in biological fluids using LC-MS/MS (4000-QTrap), HPLC, etc.
- Full validation of methods to regulatory requirements, or reduced level of validation as appropriate
- Analysis of samples generated from studies conducted in-house (including from efficacy or toxicology studies) or contract analysis of samples from external sources
- Validated assays for >100 compounds on hand



Consulting

In addition to providing a range of contract services for clients, we are available to consult to your business and advise on early stage drug development activities. This may include participation in meetings of scientific advisory boards, providing an expert opinion, or reviewing documentation.

Key Contacts

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TetraQ – ADME is accredited with NATA in the field of Research and Development, and operates in accordance with ISO/IEC 17025 (2005)

in vivo ADME Services

TetraQ conducts a range of studies in rats and mice (other species are possible), including:

- Pharmacokinetics including dosing *via* i.v., oral, subcutaneous, intraperitoneal or intramuscular routes
- Calculation of basic PK parameters
- Bioavailability following dosing by any of these routes
- Metabolism studies, including metabolite identification (mass spectral and/or after enzymatic incubations)
- Recovery of parent drug and/or metabolites in urine, faeces or bile
- Tissue distribution studies, including dosing with non-radiolabelled or radiolabelled (supplied by the Sponsor) versions of the investigational drug

in vitro ADME Services

TetraQ conducts *in vitro* screening including:

- Metabolic stability screening or profiling due to Phase I (CYP450) or Phase II (glucuronidation / sulfonation) processes
- Studies conducted using cryopreserved hepatocytes (pooled human or male or female animal), microsomes or S9 as appropriate
- Identification of CYP450 isoforms responsible for metabolism using recombinant human CYPs
- Isolated perfused rat liver – TetraQ-ADME has many years experience with this model
- Caco-2 cell *in vitro* absorption studies are offered by TetraQ

TetraQ offers a range of techniques for investigating the effectiveness of potential drugs with a focus on *in vivo* models. We are leaders in *in vivo* pain models and are continually expanding our range to include other models. We also plan to offer a wider range of models sourced from our partners. We take pride in having highly interactive relationships with our clients and work seamlessly with other areas of TetraQ to provide a complete solution.



Pain Testing Models

TetraQ offers a range of *in vivo* rodent models of pain:

- Pain sensitivity and perception
- ✓ Mechanical sensitivity to stimuli
- ✓ Thermal sensitivity to stimuli
- Acute stimulus-evoked pain models:
 - Persistent pain using formalin injection
 - Acute and chronic inflammatory pain models:
- ✓ Capsaicin
- ✓ Postsurgical pain (Brennan model)
- ✓ FCA: Freund's Complete Adjuvant
 - Neuropathic pain models:
 - HIV induced neuropathy
 - Cytotoxic induced neuropathy
 - ✓ Chronic Constrictive Injury (CCI): Tying of four loose ligatures around the sciatic nerve. This peripheral nerve injury results in the development of mechanical (tactile) allodynia in the ipsilateral hindpaw
 - ✓ Painful diabetic neuropathy (PDN): Streptozotocin (STZ)-induced diabetes which is characterized by tactile allodynia after ~ 6-8 wks of STZ administration.

A variety of methods are used to quantify pain, including von Frey filaments, tail flick and paw pressure and paw thermal (Hargreave's) tests. TetraQ also offers an *in vitro* opioid agonist and antagonist screening assay.

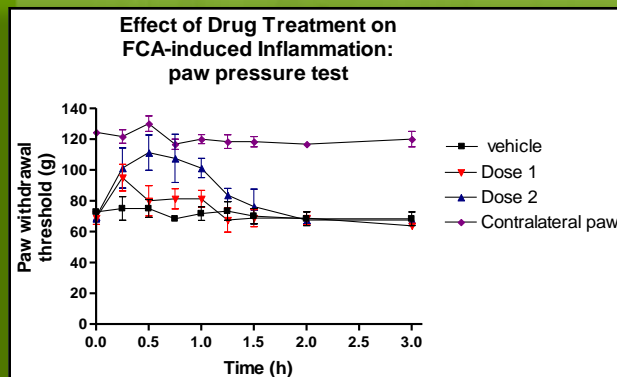
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Obesity Model

Multiple Sclerosis Model

Alzheimer's Disease Model

Diabetes Model

Parkinson's Disease Model

Arthritis models

TetraQ also has , inflammatory bowel disease (IBD) and access to models of other diseases Through alliance partners.

Consulting

In addition to providing a range of contract services for clients, we are available to consult to your business and advise on early stage drug development activities. This may include participation in meetings of scientific advisory boards, providing an expert opinion, or reviewing documentation.

TetraQ Pharmaceuticals aims to assist companies to characterise and optimize lead compounds in development. Assessment of the identity, purity, solubility and oral absorption of a lead compound is essential before a drug can be progressed through the development pipeline. We offer drug characterisation services as well as measurement of properties such as *in vitro* absorption and stability. Furthermore, we offer a range of drug formulation services to assist clients with poorly water soluble drugs and also offer modified peptide synthesis services to improve oral availability of peptide drugs.

Pharmaceuticals

*Drug characterisation,
formulation development
In-vitro absorption
and stability*

Physicochemical Characterisation

Structure determination and purity:

- NMR, UV/Visible spectra, Infra-Red, Raman spectroscopy, LC-MS, GC-MS, HPLC

Physicochemical properties:

- Partition coefficient (logP), Melting point, Solubility determination, pH, Particle sizing/ Zetasizing
- Packages of the above services are available

Custom Peptide Synthesis

TetraQ Pharmaceuticals offers a specialised service for the synthesis of peptides that may have improved membrane permeability and stability properties.

Formulation Development Services

TetraQ Pharmaceuticals offer extensive formulation services. Based on preformulation evaluation, we will tailor the dosage form and delivery route to the customer's request. We can also assist clients with formulating poorly water soluble drugs to improve their efficacy and bioavailability.

Other Services

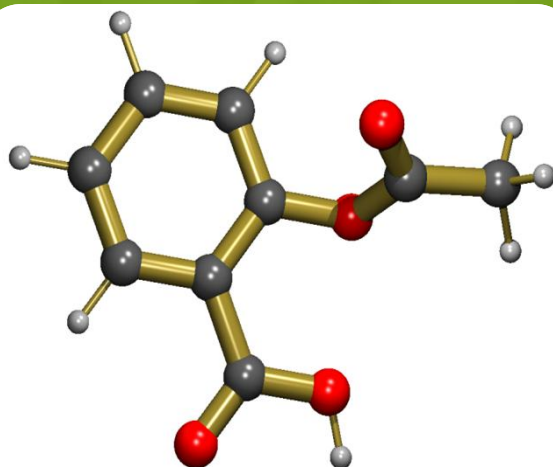
Dissolution testing

Analytical method development and validation

- HPLC, GC-MS, LC-MS

Stability Studies

- Chemical and biological stability to ICH guidelines



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TetraQ offers a range of *in vitro* and *in vivo* toxicology services to the biotechnology / pharmaceutical and related industries to assist in candidate selection and to prepare for first-in-human studies. We are able to assess novel therapeutics, complementary medicines, food additives and other chemicals for toxicity. Along with a battery of standardised toxicological tests, TetraQ also offers advice on cytotoxicity, genotoxicity and acute *in vivo* toxicity data interpretation. We take pride in having highly interactive relationships with our clients and provide a complete solution.

Toxicology

In-vitro and in-vivo toxicity evaluation

In-Vivo Toxicity Studies

- Rapid and efficient method of gaining preliminary *in vivo* toxicological data.
- Dose ranging studies to determine the highest dose of drug with No observable adverse event limit. (NOAEL)
- Escalating doses of test article administered to rats or mice.
- Repeat dose toxicity studies
- Acute and sub-chronic toxicity studies (rodent and large animal models).
- Mammalian cell gene mutation test.
- *In vivo* cytogenetic assay.
- Safety pharmacology (behavioural and cardiovascular).
- GLP toxicology for IND submissions.
- Observations typically include water intake, body weight measurement, behaviour recording, blood biochemistries and gross pathology of major organs and associated histopathology.

Candidate Selection

A suite of *in vitro* tests to assist in final candidate selection:

Cytotoxicity screening in mammalian cells (human and non-human).

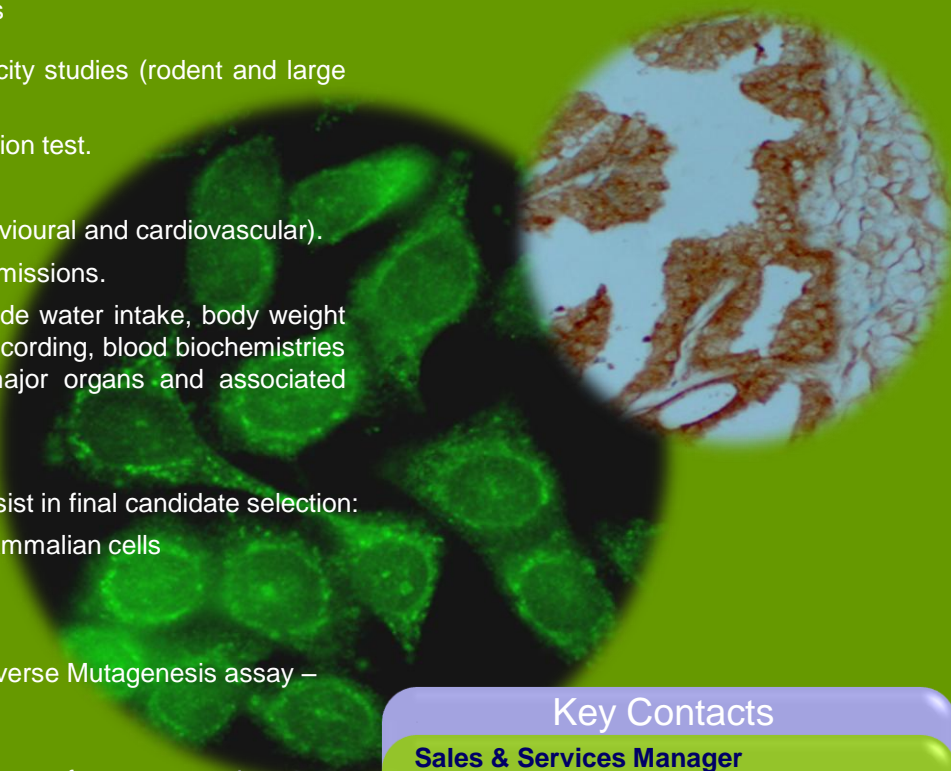
- Apoptosis Assay.
- Genotoxicity (Bacterial Reverse Mutagenesis assay – Ames test).

Consulting

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TetraQ – Toxicology is recognized for compliance with the OECD Principles of Good Laboratory Practice (GLP)



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