Eurofins | ADME BIOANALYSES

Your partner in drug development

eurofins | ADME BIOANALYSES

Since 1987, you have placed your confidence in us.
Our responsibility, to which my staff and I commit, is to consistently provide you with relevant solutions to insure reliability, security, and timeliness.
This will be achieved with a particular emphasis on continual investments in innovative and state-of-the-art technologies which combine quality and timeline optimization to benefit you.
Exceeding our clients' expectations is our priority.

Patrick Duchêne
Chief Executive Officer

Eurofins I ADME BIOANALYSES
75, chemin de Sommières
F - 30310 Vergèze

Tel I +33 (0)4 66 73 17 73
Fax I + 33 (0)4 66 73 17 74

www.eurofinsadmebioanalyses.com

GPS
Latitude 43.7446416
Longitude 4.2078112

Welcome

Your partner in DMPK and in Agrosciences

Growing complexity, longer timelines, quality and confidentiality issues, high personnel turnover, continuous searching for expertise along with low costs: these are some of the most daunting pre-clinical and clinical research challenges you face today when outsourcing your priority studies.
Eurofins I ADME BIOANALYSES is a GLP compliant CRO founded in 1987. In recognition of the challenges you face, we offer you our expertise in the fields of pharmacokinetics, metabolism, bioanalysis and residue analysis.

We are part of the **EUROFINS SCIENTIFIC group.**
We have been successfully inspected by GLP Authorities:

- **AFSSAPS, every two years since 1989,**
- **FDA, in July 2009**

We are accredited « Crédit Impôt Recherche » (CIR) by the French Ministry of Education and Research.

Your contacts
at Eurofins I ADME BIOANALYSES

Céline Bonati
CelineBonati@eurofins.com

Specialized on Generic Markets:
Stéphanie Burger Prin
StephanieBurgerPrin@eurofins.com

Candidate

SELECTING your drug candidate

Multiple phases of preclinical drug development are critical to assess the safety and viability of new chemical entities (NCE) as potential drug candidates.

We offer a comprehensive panel of related services that when combined with our expertise and flexibility allow us to support your drug development program and maximize your chance of success. We do so by providing you the data needed to expedite your decision process.

Do you want to bring value to your NCEs and optimize your investment?

We have developed two in-vivo bioavailability tests:

- **an in-vivo screening test to quickly evaluate your NCEs' bioavailability allowing you to select the best leads and cut your drug development time and cost.**
- **an in-vivo blood brain barrier permeability test to evaluate the ability of CNS candidates to reach the brain.**

We optimize your investment bringing value to your molecules with optimal timelines and prices.

Do you want first to get exploratory pharmacokinetic data prior to start regulatory development?

Drug Metabolism Pharmacokinetic (DMPK) is fundamental in drug development and will directly affect your drug's cost of development.

We conduct in vivo Pk screening tests to quickly compare the Pk of your drug candidate between species.

This allows for more precise planning of your drug development budget.

Do you want to know the maximum oral bioavailability?

First Pass Effect
We can examine **the first pass effect** which allows you to determine the maximum oral absorption achievable in each species for your drug candidate.

IN VIVO
BIOAVAILABILITY SCREENING

The process of discovering new drugs and getting regulatory approval is becoming ever more costly. All aspects of the drug discovery and development process should be examined for potential cost savings. Low bioavailability of drugs will lead to increase significantly the budget of development and will reduce the chance of success. **Metabolism** and **first pass effect** will have to be studied early to understand the origin of this low bioavailability. In drug development research, more than 50% of molecules fail because of lack of bioavailability.

DMPK Bioanalyses

Do you want to have more information?

- Metabolic pathway
- Metabolic profiling
- Pre-clinical studies
- Clinical studies

Do you want to know microsomal stability of your molecule?

We perform the following in-vitro screening assays:

- Interspecies comparisons
- Cytochrome P450 enzyme inhibition
- Cytochrome P450 reaction phenotyping
- Stability in plasma and buffer
- Metabolite profiling
- Metabolite assessment and identification

Do you want to evaluate the Absorption, Distribution, Metabolism, and Excretion of your molecule in vivo?

Before the first administration in human, we highly recommend the in-vivo disposition of your drug candidate be determined.

We can conduct the following ADME studies:

- Bioavailability
- Biliary excretion
- Mass balance
- Tissue distribution
- Metabolite profiling

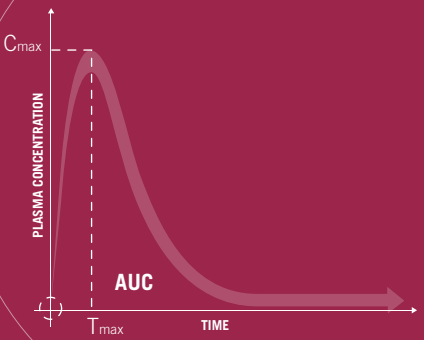
Once you have selected your drug candidate, DMPK services in both the preclinical and clinical areas will be required.

Do you need support in DMPK and Bioanalysis for pre clinical and clinical development?

Do not hesitate to ask for our expertise in:

- Development and validation of bioanalytical methods according to International Regulatory Guidelines
- Bioanalytical assays using various equipment platforms and methodology, including **DBS (Dry blood Spot)**
- Study design: number of subjects, sampling times
- PK modeling: non-compartmental and compartmental analysis
- PK simulation
- Statistical analysis of PK parameters
- Interpretation of studies and report generation

DMPK Bioanalyses



Why is DMPK fundamental?

After entering the body, a drug is absorbed, distributed in the tissues, **metabolised** and then excreted.

Appropriate **pre-clinical studies** and **clinical studies** are required to assess the efficacy and safety of your molecule.

Bioequivalence, **drug interaction** and **pediatric** studies may also be required.

PK parameters are calculated from concentration time profile. Concentrations are measured using a **validated analytical method** according to International Guidelines.

1. **Observed pharmacokinetic behaviour is a function of:**
   - The physicochemical properties of drug
   - The dosage form
   - The route of administration
   - Physiology/anatomy of the body
2. **Poor pharmacokinetic property of a drug may limit its clinical application**
3. **Factors influencing the pharmacokinetics of a drug include genetics, size, age, disease, other drugs, environmental factors**
4. **Components of pharmacokinetics data (primary e.g. concentration, or derived e.g. cumulative amount excreted) and models.**

The **pre-clinical** data help to identify promising drugs and to suggest useful doses for testing in humans. **Phase I**, **Phase II** and **Phase III** of human assessment generally correspond to the first administration to humans, early evaluation in selected patients and the larger trials, respectively. PK data gathered during all phases of drug development help to efficiently define safe and effective dosage regimens for optimal individual use.

PK parameters calculation
We use KINETICA (Version 4.3 - Thermo Electron Corporation - Philadelphia - USA).

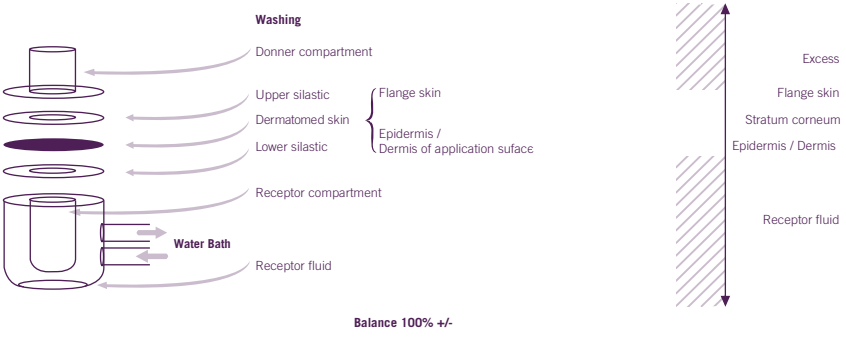
Main plasma PK parameters:

Cmax: Highest drug concentration observed in plasma following administration of an extravascular dose, mg/L or µM.
Tmax: Time at which the highest drug concentration occurs following administration of an extravascular dose, min or hr.
AUC: Area under the plasma drug concentration-time curve, mg-hr/L or µM-hr.
CL: Total clearance of drug from plasma, L/hr.
Vd: Volume of distribution (apparent) based on drug concentration in plasma, L.
Kel: Elimination rate constant, hr-1.
T1/2: Half-life, hr.
MRT: Mean time a molecule resides in body, hr.
F: Bioavailability of drug, no units.

DERMAL studies

DERMAL
studies

Skin penetration is a route by which drugs can enter the body through the skin. The stratum corneum is the first barrier to protect the organism from the environment. After this first layer the drug could reach the plasma after having passed the derma and epidermis. Absorption of substances through the skin depends on a number of factors, the most important of which are concentration, duration of contact and physical condition of the skin. Penetration through the skin can be evaluating by using in vitro models based on Franz-type cells.



Do you want to evaluate your topical formulations or compounds?

We conduct a panel of studies to measure the percutaneous absorption and can advise you on the design of protocols appropriate to the objectives of your drug development.

A dedicated highly-trained team is available to conduct dermal studies using Franz cells.

Studies can be conducted utilizing:

- fresh (only for metabolism studies in order to conserve enzymatic properties) or frozen skin.
- all species available.
- either radiolabelled or nonradiolabelled compound.

Do you need to compare different formulations?

We can develop a screening test to compare different compounds or different formulations of the same compound that helps you select the one which meets your objectives.

Do you need to conduct regulatory studies?

We have significant experienced with in vivo models used to measure the penetration of drug formulations through the skin in accordance to regulatory requirements (OECD 428 guidance).

We will meet Regulatory Authorities' expectations when conducting your studies.

OUR Commitments

Are traceability and report-delivery your priorities?

We have already taken it into consideration and have made significant investments to insure your needs are met:

Watson® Bioanalytical LIMS (Laboratory Information Management Systems), a fully validated software package dedicated to:

- tracking of samples
- operational efficiency -expediting laboratory results
- full traceability of the data
- regulatory compliance with GLPs
- automated report generation eliminating possible transcription errors -delivery of the QA'ed draft report 2 weeks after the final laboratory analysis

How can we build trust?

Because your trust is our goal, we set up Key Performance Indicators (KPI) to monitor our commitments to you

Monthly, the following KPI are compiled and reviewed:

- Quotations within 48 h
- Meeting the timelines indicated in the study plan
- Quality assurance audits within 5 days of data transmission Reports delivered within 15 days of the end all laboratory analyses

Should you observe any variance on the KPIs we will evaluate the reasons and discuss with you improvements to our processes.

You are welcome to follow our monthly KPI results

We can also set up new KPIs dedicated to you or periodically provide you the results you request.
Please, it's as simple as asking our Customer Relationship

How can we adapt our behaviour?

We have defined four different stages in the relationship we hope to establish with you. By dealing honestly and fairly with you and your needs we can adapt to insure you receive the level of service you expect.

Because your expectations and needs are unique…we will adapt our services to your needs:

ADME BIOANALYSES

75, chemin de Sommières
F - 30310 Vergèze

Tel I +33 (0)4 66 73 17 73
Fax I + 33 (0)4 66 73 17 74

www.eurofinsadmebioanalyses.com