

Taking the lead in lead optimisation

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Industry is increasingly focused on the rapid and cost-effective development of high-quality candidates from leads. The importance of this prioritisation has been emphasised by major pharmaceutical and biotech companies, and reflects the growing cost of late-phase drug development.

As a pre-clinical contract research organisation, BioDynamics has collaborated successfully with a number of companies to assist them in the lead optimisation process. Its approach is based on three principles:

- A mixture of *in vivo* and *in vitro* data, when used appropriately, provides a good basis for predicting behaviour in man.
- All projects are different, and it is critical to ensure that there is flexibility to fit with the overall project.
- If the data cannot be produced fairly quickly, it will be of limited value.

BioDynamics' *in vitro* capabilities are underpinned by a strong bioanalytical group with significant metabolite identification expertise. The company places emphasis on producing high-quality data, which is checked by experienced analytical scientists. As one client said recently: 'All drug development decisions can be critical'. The ability to look at metabolite identification during lead optimisation can provide invaluable information to the medicinal chemists in terms of achieving the desired half-life, and so this is an area of growing interest.

BioDynamics' expertise in *in vivo* metabolism has allowed its scientists to develop an innovative serial bleeding technique: its potential 3R benefits were recognised by an award for best poster at the recent IAT Congress. In addition, the company's metabolism group has many years' experience in undertaking classical absorption, distribution, metabolism and excretion studies.

BioDynamics is now increasingly designing initial pharmacokinetic studies to integrate with pre-clinical 'proof of concept' studies as these are frequently a development milestone. This trend has resulted in the company setting up a number of Xenograft models; combined with quantitative whole body autoradiography and rapid tritium labelling, these can provide key data on the tumour:blood and tumour:organ ratios, all of which can be critical in the

BioDynamics' *in vitro* capabilities

- Metabolic stability
- Absorption screening
- Solubility testing
- Cytotoxicity testing
- Cytochrome P450 inhibition

BioDynamics' *in vivo* capabilities

- Cassette-dose and single-dose pharmacokinetic studies
- Excretion balance
- QWBA
- Pharmacological models

development of anti-cancer agents. The company is also looking at developing relationships with other groups to undertake a wider range of pharmacology studies.

Meanwhile, its sophisticated systems enable lead optimisation studies to be turned around in one to two weeks. They also allow rapid and easy initiation, and rapid electronic reporting.

When BioDynamics first became involved in this area a few years ago, it was not clear how it would develop. The company has therefore been encouraged to see the high degree of collaboration with some clients, and the first of the lead compounds it screened going into development. ■



BioDynamics' sophisticated systems allow rapid electronic reporting

COMPANY PROFILE

BioDynamics Research Ltd is an independent contract research organisation providing R&D services to the pharmaceutical, chemical and agrochemical industries worldwide. It was established in 1992, and is based in Northamptonshire, UK.