

EUMAPP – European Union Microdose Accelerator Mass Spectrometry Partnership Programme

Thematic area: Life Sciences, Genomics and Biotechnology for Health

Instrument: STREP

Co-ordinated by: Professor Colin Garner, Xceleron Ltd.

EC contribution: 2.1m€

Duration of project: 30 months from 2005

Number of partners: 10

Subject of case study:

Professor Colin Garner, Xceleron Ltd.

Mail to: Colin.garner@xceleron.co.uk

Project website: <http://www.eumapp.com/>

The Challenge

The development of new drugs is becoming an ever increasingly complex and expensive process for pharmaceutical companies. Human microdosing is a relatively new concept in pharmaceutical development, where drug candidates are administered to man at trace doses (no more than 1% of the expected pharmacological dose, and not to exceed 100 micrograms) in order to obtain early, useful, pharmacokinetic data. Such approaches are dependent on well-validated, ultra-sensitive analytical techniques to measure the levels of parent drug and metabolites in the circulation.

Microdosing provides a potential opportunity for early human screening of many more drug candidates, with greater predictability, than is often achieved in animal or *in vitro* experimental models. If successful, the use of microdosing studies can be expected to reduce failure rates, support safer and quicker clinical development and, possibly, decrease the use of animals in development work.

The Project

EUMAPP is exploring the strategic and technical issues to bridge the gap between laboratory and clinic. The specific objectives are to:

- Demonstrate the reliability of the microdosing approach for predicting the pharmacokinetics of a drug used at efficacious doses;
- Certify Accelerator Mass Spectrometry as the most accurate, sensitive, appropriate and powerful analytical technology for reproducible measurements required by microdosing studies;
- Develop *in silico* modelling applications to predict pharmacokinetic parameters from data derived from microdosing studies.

The Consortium

The EUMAPP consortium contains 10 partners, coordinated by the UK SME, Xceleron Ltd. The clinical phase of the research is now about to commence.

Certain members of the consortium provide key linkages for disseminating information back to stakeholder communities, for example Servier with the pharmaceutical company sector,

Stichting Beoordeling Ethiek Biomedisch Onderzoek with patient interest groups and the European Federation of Pharmaceutical Sciences with its broad expert membership.

View from Xceleron as Project Coordinator

Validating potential contribution of microdosing to pharmaceutical R&D

As the pharmaceutical sector has yet to adopt microdosing technology as part of its routine procedures, it is necessary to build a coherent body of knowledge using standardised methodology in order to justify wider investment in microdosing as a novel, science-driven, easy-to-use, approach to drug evaluation.

The choice of the different molecules with which to seek to validate the potential for microdosing technology was made so as to cover those drugs whose metabolism is known not to be extrapolatable from animal studies to man, based on demonstrable problems in drug development. In developing the experimental strategy for EUMAPP, Xceleron capitalised on its previous experience with another European industry consortium (Consortium for Resourcing and Evaluating AMS Microdosing). This pioneering work¹ established proof of concept for good concordance between microdose and therapeutic dose pharmacokinetics for some drugs – thereby demonstrating the potential of microdosing to aid in early drug candidate selection.

EU added value of the project

There has been early interest expressed by both EU and US drug regulatory authorities about the microdosing approach in translational medicine. The regulatory authorities have produced guidance documents but, hitherto, there were few data in the public domain to support the concept. Hence, the EUMAPP consortium will be particularly valuable in generating a systematic, well-defined, body of evidence under standardised conditions. This effort will also help to maintain the present European leadership in the science and, if successful, will support innovation by European pharmaceutical companies and develop better, safer, drugs faster for patients.

Tips for success in building the consortium

- Need for disciplined partnership – as a relatively short project, it was important to ensure that all partners understood the need for setting and maintaining a rigorous timetable for reporting and delivery of results. The strategic involvement of all partners was greatly helped by organising a pre-project meeting of potential members to facilitate interaction and agree the intended work programme. One key issue for the project coordinator as an SME has been the obligation to respond to the frequent reporting requirements set by the European Commission. Previous experience in academia with European research (Xceleron is a spin-out company from York University) prepared the coordinator for Commission procedures but the frequency of formal communication mandated would be unusual for many scientific SMEs, who would need to set appropriate project management tracking and reporting procedures in place.
 - Professional project management – the proactive involvement of the French SME ACIES with core expertise in managing international research projects has been very
-

helpful in capitalising on connections with the research and business communities and with the Commission. It would be highly desirable to build a critical mass of similar practical expertise in UK research project management, particularly in specific support of SMEs in coordinating projects.

Looking ahead to Framework Programme 7

The forthcoming work programme – covering the major topics relating to identification and use of biomarkers for drug efficacy and safety – is of considerable interest to Xceleron. If Framework Programme 7 research is to achieve the greatest possible impact, it is important to encourage smaller companies – often with the more radical ideas – to become involved in the new partnerships, for example, the Innovative Medicines Initiative (that in the early days of strategy formulation for the Technology Platform was perceived as dominated by larger companies). It is also critical that the envisaged merging of STREPs and Integrated Projects as instruments for support does not disadvantage SMEs who have found the relatively small size of STREPs to be particularly supportive of their involvement in Framework Programme 6.

¹ G. Lappin, W. Kuhnz, R. Jochemson, J. Kneer, A. Chaudhary, B. Oosterhuis, W. J. Drijfhout, M. Rowland and R. C. Garner (2006) *Use of microdosing to predict pharmacokinetics at the therapeutic dose: Experience with 5 drugs*. Clin. Pharmacol. Ther. 80, 203-215