



## **European Union Microdose AMS Partnership Programme (EUMAPP) – Background Paper – January 2006**

### ***Developing new drugs***

The development of new drugs is becoming an ever-increasingly complex and expensive process for pharmaceutical companies. Estimates suggest that it takes, on average, 10-12 years to take a molecule from discovery through to regulatory approval; this time period has changed very little over the past 20 years. The costs of drug development are also escalating to in excess of US \$800 million per registered drug. Much of this cost is actually associated with those drugs that do not make it to market.

### ***ADME/PK limiting factors***

One essential and limiting factor for successfully bringing a drug to market is the way the human body absorbs and metabolises the drug. Drug absorption, distribution, metabolism and excretion (ADME) characteristics are defined by its pharmacokinetics (PK) and pharmacodynamics (PD) parameters. A significant proportion of drug candidates (up to 40%) fail to make it past the first human studies (Phase I) due to inappropriate ADME/PK parameters.

### ***Microdosing to overcome limiting factors***

In this very specific context, Human Phase 0 microdosing appears as the most relevant, efficient and innovative approach to use to overcome the identified limiting factors. Indeed, human microdosing is a new concept where one or more drug candidates are directly (without extensive toxicological studies) taken into humans at trace doses (1/100<sup>th</sup> of the pharmacological dose, up to 100 µg) in order to obtain early PK information. Microdosing studies are dependent on ultra-sensitive analytical techniques (Accelerator Mass Spectrometry technique (AMS)) because only it has the necessary sensitivity to follow the fate of a trace drug dose in the human body.

### ***Microdosing to reduce testing time***

The microdosing approach offers the opportunity of early human screening of many more drug candidates offering greater predictability versus animal and/or *in vitro* models. Hence, human microdosing studies offer the promise of (1) improved candidate selection (2) reduced attrition rates (3) safer clinical studies and (4) a potential reduction in the use of animals in early clinical development. The microdosing approach could by this means potentially reduce the time of pre-clinical testing from 18 months to 4 to 6 months and cut down the associated expenses by 10 times.

### ***Data needed to justify microdosing approach***

The potential value of the microdosing approach has been recognised by many pharmaceutical companies but taken on board only by few due to the lack of data justifying the approach. It is therefore imperative that a body of knowledge is built to convince the pharmaceutical industry of the merits of human microdosing as a science driven approach to drug development.

### ***Partnership programme towards certifying ultra-sensitive AMS***

The European Union Microdose AMS Partnership Programme (EUMAPP) project, coordinated by XCELERON Ltd and funded by the European Commission, gathers together 10 organisations from 5 different countries (United Kingdom, Sweden, The Netherlands, France and Poland) towards the certification of high and low voltage ultra-sensitive AMS technologies as the most accurate, reproducible and appropriate analytical methodologies for all measurements required by microdosing studies. The EUMAPP project will contribute, in a 30-month period, to putting Europe at the forefront of microdosing by (i) demonstrating the *reliability* of the microdosing approach for predicting drugs PK when used at pharmacological doses (from 7 different pharmaceuticals), (ii) certifying AMS as the most *accurate*, appropriate and powerful technology for reproducible measurements required by microdosing studies, and finally (iii) developing *in silico* modelling application to predict PK parameters from data derived from microdosing studies.

### ***Boosting drug development and reducing costs important***

Overall, EUMAPP provides a *tremendous* opportunity for Europe to gain leadership in the field of microdosing and avoid being left behind worldwide competitors. It will contribute to the implementation of a new tool kit for boosting the development of drugs and reducing the overall cost thus indirectly contributing to *increasing* the number of *new* marketed *drugs* at more affordable prices which could in turn positively impact the quality of life of unhealthy people.

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