Assessing the changing landscape of microsampling use through a global cross-company initiative

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Background

- Advances in bioanalytical techniques have opened up the potential to use microsampling (sample volumes ≤50µl) to assess drug and chemical exposure in blood, plasma and/or serum.
- Microsampling has scientific benefits as it allows the possibility of using main study animals for toxicokinetic (TK) sampling and toxic effects can then be related to exposure in the same animals (Sparrow *et al*. 2011).
- There are a number of additional benefits associated with microsampling. These are summarised in Figure 1.
- To assess current use of microsampling and the barriers to wider uptake, the NC3Rs carried out surveys in 2013 and 2015.
- The NC3Rs also organised workshops in 2013 and 2016 which focussed on overcoming the barriers to uptake of microsampling approaches.

Results

- There is widespread use of microsampling among the companies questioned. Most companies employ microsampling in non-GLP (discovery, dose range finding and pharmacokinetics), but there has been a large increase in the use of microsampling in GLP (regulatory toxicology and safety pharmacology) studies since 2013 (Figure 2a).
- The use of microsampling from non-rodent species is becoming more widespread (Figure 2b).
- Microsampling is being used to sample from a variety of routes (Figure 2c).
- Reductions in rodent usage of between 21% and 40% are most common and there is a realistic potential to reduce mouse numbers on an individual GLP safety assessment study by more than 60% (Figure 2d).
- The major barrier identified was concern regarding the real or perceived impact of microsampling on functional and clinical pathological endpoints. Several publications have now demonstrated that microsampling does not have a significant impact (Powles-Glover *et al*. 2014a, Powles-Glover *et al*. 2014b, Prior *et al*. 2015).

Conclusions and further work

- There are numerous benefits to implement microsampling in toxicology and pharmacology studies (Figure 1).
- An NC3Rs microsampling user group, including representatives from 30 pharmaceutical and chemicals companies as well as regulators, is sharing data on microsampling experience and practice.
- This is feeding into a web-based resource to disseminate good practice, assist with training technicians in microsampling and increase uptake of the approaches (www.nc3rs.org.uk/microsampling).
- Data from this survey and from the NC3Rs microsampling user group is being used to develop the ICHS3a Q&A document on toxicokinetics, which will support the use of microsampling for TK studies.
- The NC3Rs is formulating an action plan to increase uptake of microsampling approaches, directed by the microsampling user group and researchers who are using or wish to use the techniques. Future steps, and the perceived urgency with which they should be implemented, are represented in Figure 3.

Figure 1. The animal welfare, scientific and resource-related benefits of microsampling.

a

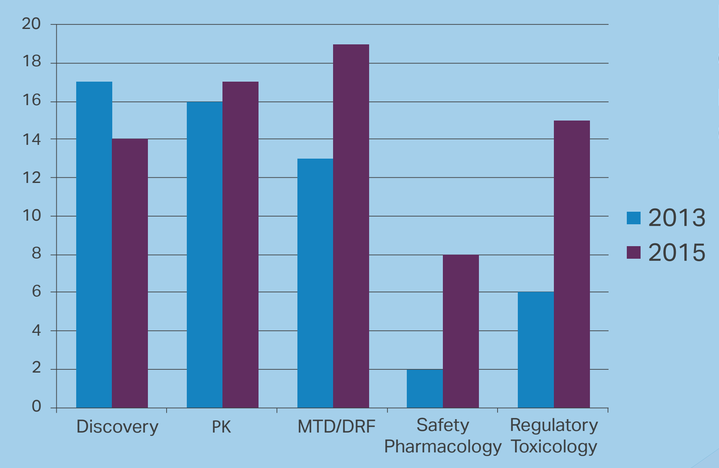

Figure 2a. Number of companies employing microsampling in non-GLP and GLP studies in 2013 and 2015.

b

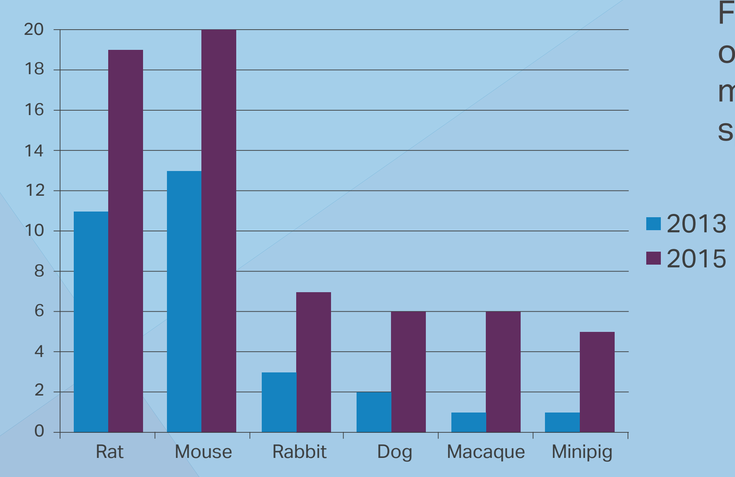

Figure 2b. Number of companies using microsampling from various species in 2013 and 2015.

c

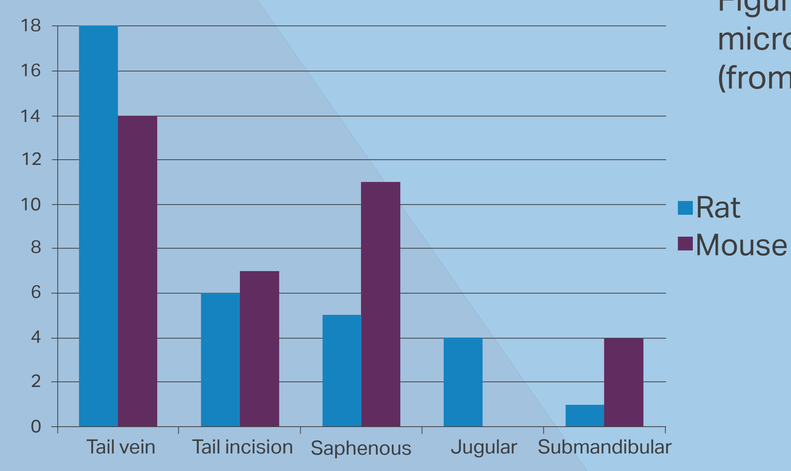

Figure 2c. Routes utilised for microsampling from rodents (from 2015 survey)

d

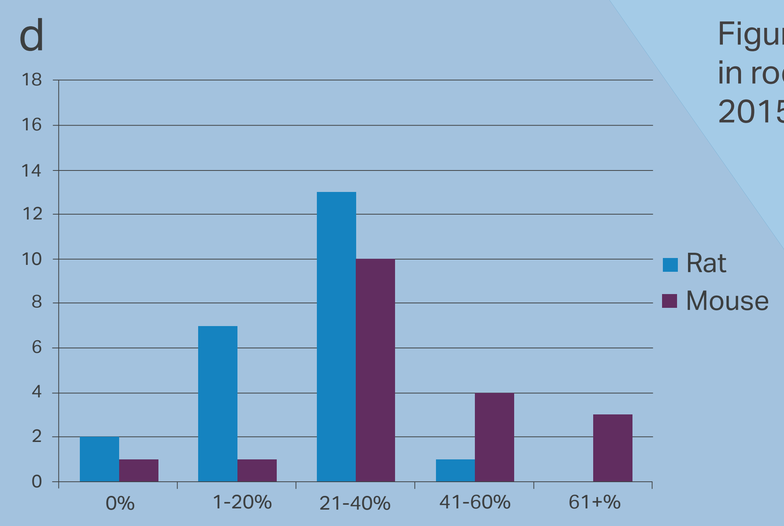

Figure 2d. Reported reduction in rodent numbers used (from 2015 survey).

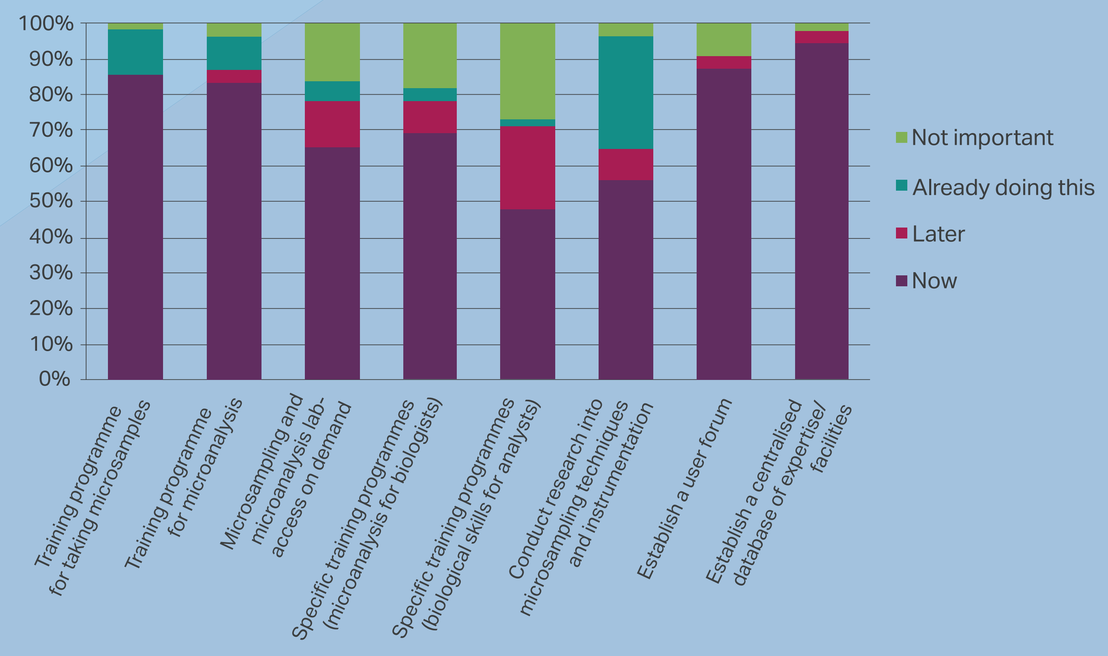

Figure 3. Researcher views on steps to take to increase implementation of microsampling in academia and industry. From the 2016 NC3Rs workshop.

References:
- Powles-Glover N et al. (2014a) *Regul Toxicol Pharmacol*. 69(3):425-33.
- Powles-Glover N et al. (2014b) *Regul Toxicol Pharmacol*. 68(3):325-331.
- Prior H et al. (2015). *Regul Toxicol Pharmacol*. 73:19-26.
- Sparrow et al. (2011) *Regul Toxicol Pharmacol*. 61(2) 222- 229.