

THE USE OF *IN VITRO* DRUG METABOLISM STUDIES TO COMPLEMENT, REDUCE AND REFINE *IN VIVO* ADMINISTRATIONS IN MEDICATION AND DOPING CONTROL

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Administration studies have long been a vital component for medication and doping control programmes. Understanding the conversion of administered substance into urinary excreted metabolites is crucial in designing appropriate screening tests. Samples from documented administration studies have also been used as reference materials to compare with results from regulatory test samples in confirmatory analysis. This is enshrined in codes of industry practice such as the ILAC G7 document, Accreditation Requirements and Operating Criteria for Horseracing Laboratories and the WADA International Standard for Laboratories. Administration studies also provide information about excretion profiles that inform decisions about required detection times for individual drugs.

In vitro metabolism studies have always provided a theoretical alternative to *in vivo* administrations, but in practice this has in the past been difficult to achieve in a consistent manner. Recent advances in the commercial tissue availability and mechanisms to maintain and control their activity now put

this tool at the disposal of any laboratory with appropriate biological expertise, allied to the analytical capability to characterise the output. Results from our laboratories demonstrate that in addition to providing simple qualitative information regarding the phase 1 and 2 metabolism of drugs, *in vitro* techniques offer the following advantages :

- To generate metabolite reference standards for use in confirmatory analyses.
- The ability to refine and reduce the use of *in vivo* studies.
- To compliment *in vivo* metabolism studies through producing a more concentrated, cleaner extract under conditions that can be modified to favour particular metabolic pathways.
- For studying the fate of designer drugs with undefined toxicological profiles.
- For fast reaction to potential new threats.
- For studying the mechanisms of metabolism in more detail.

This presentation will outline the techniques and their current and potential applications using a range of drugs studied in equine, canine and human as illustrations.

