The utilisation of Quantitative Whole Body Autoradiography (QWBA) methods to investigate whole body tissue distribution in the minipig

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The choice of the correct species for toxicity testing of drug candidates being developed for human use is a critical one. Rodents are the commonly used 1st species and monkeys, pigs and dogs are the candidates available for the 2nd species. These all have sufficient background data to be used in toxicology studies but the choice has to be made which is most appropriate and representative of the clinical target (humans). It has been known for many years that species metabolise drugs differently. The use of minipigs as models for the toxicity testing of new medicines and chemicals is widely established and accepted and there are important differences in anatomy and metabolism that favour the use of minipigs instead of the traditionally-used species as a non-rodent model in safety evaluation. Quantitative whole body autoradiography (QWBA) is a powerful tool in determining the relative tissue distribution of radiolabelled drugs. QWBA provides data on the whole body distribution and can also be used to determine distribution of drugs to specific tissues and localisation within target tissues. However, QWBA is usually restricted to the investigation of distribution in smaller species. In this study, the tissue distribution of radioactivity was investigated in the minipig using QWBA techniques. This appears to be the first application of QWBA for such type of investigation. A minipig was dosed with carbon-14 labelled drug and processed to produce high quality tissue sections and autoradiograms for analysis. The study data showed that it is possible to analyse large specimens such as the minipig by QWBA.