The Minipig as an Alternative Nonrodent Model in Non Clinical Research

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Introduction

The ICH Harmonised Tripartite Guideline Guidance on Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals M3(R2) recognizes the use of a rodent and non rodent species in non clinical toxicology studies. The non rodent species is not specified and although traditionally canines and non human primates have been used, the use of the minipig as an alternative has been recently highlighted by the 2010 RETHINK European FP6 project.

Experimental Designs

Charles River Laboratories uses the minipig for a wide range of safety studies including pharmacokinetic, safety pharmacology, and toxicity studies using various dose routes, namely oral (gavage and capsule), intravenous and subcutaneous injections or infusion, target tissue dosing, intranasal, dermal and ocular (instillation, intravitreal and subretinal injections) and wound healing studies. Increasing interest is also being shown in diabetic and juvenile models.

Discussion

Are conventional models, namely canines and non human primates being replaced by the minipig? Analysis of data from our laboratories show there is no evidence to suggest that minipigs are becoming the more commonly selected large animal model in safety assessment studies. The one exception is dermal safety assessment for which the swine is regarded as the species of choice. At both our North American and European facilities minipigs constitute 6 percent of the large animals used in preclinical studies over a 6 year period suggesting geography has little to do with efforts to replace conventional large animal species with minipigs. If dermal studies are excluded from this data for the reason previously stated, the numbers are closer to 2 to 3 %. These internal data are reflected in the statistics compiled by the US Department of Agriculture, which tracks the number of pigs, including minipigs, in research settings, which finds that little has changed in the last five years.

The number of pigs used in biomedical research dropped from 58,763 in 2008 to 55,729 in 2013, it should be noted that USDA does not track minipigs separately from swine. Additionally the overall trends at Charles River in the use of minipigs has not increased significantly over time. If the number of animals used in dermal studies is considered, the percentage numbers are actually lower. The reasons why the minipig has not replaced other animal models is undoubtedly due to multiple factors and subject to interpretation. The overall benefits that minipigs provide have been well documented. Cost and supply factors are a potential advantage over some large animal species. Indeed, the RETHINK papers point out a number of advantages. The minipig model has utility in reproductive toxicology studies, though the lack of placental transfer of antibodies may limit its role in reproductive testing of some biotechnology products. For safety pharmacology studies, minipigs are considered an advantageous model in particular for cardiovascular safety pharmacology tests. The immune system of the pig is better characterized than some of the other conventional large animal models, however consideration toward potential limitations of availability of appropriate reagents/assays for this species exist.

Conclusion

The minipig has become recognized as a suitable alternate nonrodent species and because there is a sufficient body of historical data that enables unequivocal data interpretation. Continued consideration should be given to use of the minipig as an alternate model of choice for safety assessment studies.

References


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