I-3-420

The value of non-human primates in the development of therapeutic monoclonal antibodies

P. J. K. van Meer[1], M. Kooijman[1], J. W. van der Laan[2], E. H. M. Moors[1] and H. Schellekens[1]

[1]University Utrecht, Utrecht, The Netherlands; [2]Medicines Evaluation Board, Den Haag, The Netherlands

p.j.k.vanmeer@uu.nl

The pharmaceutical industry is increasingly focusing on the development of biological therapeutics. These molecules generally cause no off-target toxicity and are highly species specific. Therefore, non-human primates (NHPs) are often the only relevant species in which to conduct regulatory safety testing to support clinical trials. However, species specificity and immunogenicity may negatively impact the predictive value of these ethically contentious animals and thus limits their value as a test species for drug development.

To study what the value has been of 30 years of NHP testing in drug development, we investigated the drug registration files of all therapeutic monoclonal antibodies (mAbs) which were approved in the European Union to date. We analysed 30 mAbs of which 5 were diagnostic agents. As the industry moved towards the development of more human proteins, we observed that the average use of NHPs also increased. 16 registration files described studies in which anti-drug-antibodies caused increased clearance of the therapeutic and potentially confounded the study. Post mortem analysis in repeated-dose toxicity studies rarely revealed new or unexpected findings nor did embryo-fetal and peri-postnatal developmental toxicity studies. These issues limited the value of NHPs in the safety assessment of new monoclonal antibodies. To reduce the use of less relevant NHP studies in the development of new biological drugs, regulatory demands might be decreased, and manufacturers should be given incentives for successfully evaluating the safety of biological therapeutics using alternative technologies.