

# Pre-Clinical Models in Implant Dentistry: Impact of the Legislation Underpinning the 3Rs Principle

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## Commentary

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## ABOUT THE STUDY

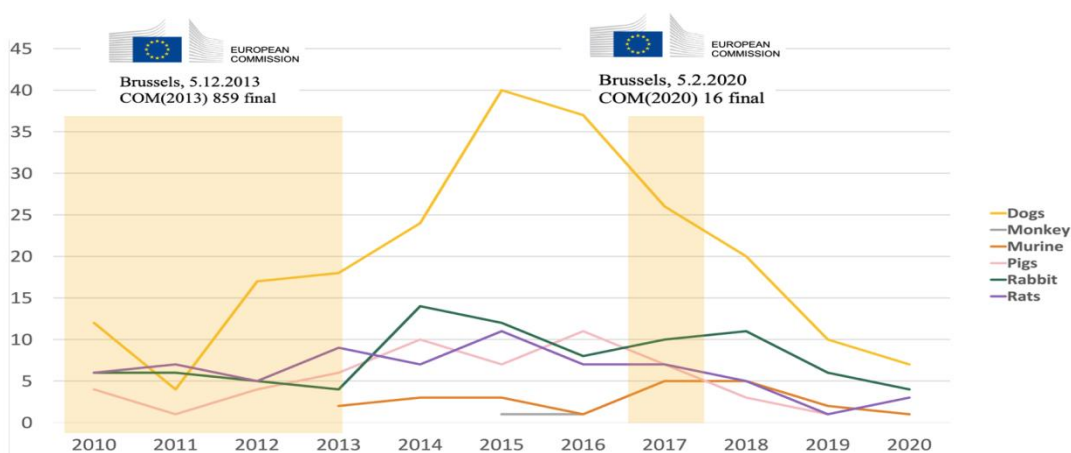
Translational application of experimental knowledge to clinical setting is the ultimate goal of biomedical research. In the field of dental implant research, protocols have been mainly developed to identify key processes of osseointegration failure or success, but also development of new surgical technics, new biomaterial or implant development (e.g. macro or micro surface). By mimicking biological conditions of dental implant osseointegration and in particular, the oral environment, pre-clinical researches investigate aspects of peri-implant tissue healing and peri-implant disease development and treatments.

Blanc-Sylvestre, et al. introduced a new level of decisional procedure based on species-specific characteristics and not only on the implant size. Over the last decade, the use of the rabbit model has dramatically decreased for dental implant research (from 39% to 18% of *in vivo* studies), in contrast to the huge increase in the number of studies using rat and mouse models. Minipigs appear as the model of choice for studies of bone regeneration around dental implants, whereas non-human primate models are no longer used in Europe, restricted to already accredited procedures. Finally, dog models, which were extensively used (45% of the procedures) in the past 10 years, should now only be used when pigs are not relevant for the question of interest.

A remaining question is the impact of the principles of the Replacement, Reduction and Refinement (the “3Rs”) embedded in national and international legislations on animal use in biomedical research, especially in implant dentistry. A major change occurred in 2010 with the establishment of the European (EU) Directive 2010/63/EU on the protection of animals used for scientific purposes. By superimposing government guidelines (developed until 2013) to our analysis, the implementation of this directive took three years to have a real impact on research protocols.

In 2020, the report from the commission of the European parliament and the council assessed the repercussions of the UE directive on the use of animal models from 2013 to 2017 (with now 4 years of insight of the new laws). The commission concluded in a “diminution of use in species of public concern”, demonstrating the direct impact of government rules on animal research. Interestingly, in 2017, mice, fish, rats, and birds represented 92% of the total number of animals used for the first time in research while dogs and cats classed as pets and non-human primates believed to have ‘higher’ mental abilities (i.e. enabling them to use tools, solve problems, and be self-aware) represented less than 1% of the total number of animals, regarding public attitudes to animal research. This year, no Great Apes were used for scientific purposes in the EU (Figure 1). As an indirect consequence, biomaterial, *in-vitro*, and *in-silico* researches have an increasingly important place among pre-clinical studies, which open new perspectives.

**Figure 1.** Impact of government guidelines on the use of animal models in the field of dental implant research (adapted from Blanc-Sylvestre et al.). **Note:** ( — ) Dogs; ( — ) Monkey; ( — ) Murine; ( — ) Pigs; ( — ) Rabbits; ( — ) Rats



At the dawn of the 2020s, although animal research remains essential to the discovery of the causes, diagnoses, and treatment of diseases, the development of new protocols should always be preceded by the question "Can animal testing be avoided?".