

The principle of the 3rs between past and future

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Development of alternative methods responds both to the need to overcome some intrinsic limitations linked to the animal model and to the need to avoid unethical procedures. In this context, the 3Rs principle (Replacement, Reduction, Refinement) represents an important EU legal framework for minimizing animal use and suffering supporting at the same time high level of scientific research. In a modern vision animal testing should be the last resort, only used after all the other scientifically reliable methods have been explored. Since the early 2000s, an impressive speed up in efforts to develop non-animal approaches for investigating hazardous properties of chemical substances and drugs took place. These efforts went hand in hand with the new exciting possibilities offered by human-biology based innovative technologies and approaches. For this reason, researchers and legislators now prefer to address their attention on “New Approach Methodologies” (NAMs) instead of *simple* alternative methods. Mainly NAMs include: i) *in vitro* and *in silico* approaches connected to modern technologies and “bigdata”; ii) human relevant *in vitro* models, and iii) mechanism-based models. To date, the replace of traditional toxicity testing with NAMs for determining human hazard and risks is constantly increasing but it still needs to be consolidated.