Comment on the Talking Points in *EMBO reports*, June 2007

Frank Gannon's introduction to the Talking Points about the use of animals in scientific research (Gannon, 2007) underestimated the burgeoning field of animal replacement techniques. Although it is clearly important to be aware of the philosophical arguments against animal research, it is also vital to discuss the scientific issues that surround the debate.

Non-animal research methods have enormous potential to replace animal experiments both now and in the future; furthermore, these cutting-edge techniques often outperform the animal experiments that they replace. The British government now recognizes non-animal techniques as 'advanced methods' that broaden the scope of animal models and overcome some of their limitations.

The article mentions that the implementation of the European Union's REACH (Registration, Evaluation and Authorisation of Chemicals) directive will lead to the use of up to 45 million animals in toxicity tests. This was the original figure suggested by the European Commission; however, recent expert analysis has reduced this figure to an estimated 8–9 million animals (EC, 2006). Approximately half of this massive reduction is due to the application of alternative non-animal techniques; indeed, both UK and European laws require the use of non-animal replacements whenever they are available (UK Government, 1986; EEC, 1986). This huge contribution is made possible by the development of groundbreaking techniques such as Q(SAR)s—quantitative structure–activity relationships—as well as various *in vitro* methods, which have saved the lives of millions of animals and improved safety for humans.

The acceptance of replacement tests by regulatory agencies is slow, but it is occurring. The European Centre for the Validation of Alternative Methods (ECVAM; Ispra, Italy) has validated more than 18 full or partial replacement methods, 8 of which have gained regulatory acceptance. In May 2007, four new tests to replace animals—mainly rabbits—in skin and eye irritancy tests were validated at the European level. The skin tests, which use reconstructed

human skin, will completely replace whole-animal tests in all skin irritation studies and save an estimated 20,000 rabbits in Europe alone (ECVAM Scientific Advisory Committee, 2007).

Non-animal replacement methods in toxicology are not just cell-based tests. A whole range of non-animal tests are now available to regulators, and these can be combined or used in isolation to make test results more far-reaching and relevant to humans than the animal studies that they replace.

Computer modelling techniques can predict the likely effects of a drug on a range of cells and organs, before specific human cells are selected for *in vitro* studies. These tests represent progress towards improving safety for humans. The largest survey of drug testing data so far showed that the results of only 43% of toxicity studies of pharmaceuticals using rodents were concordant with human clinical trial results (Olson *et al*, 2000). Overall, 92% of the drugs that pass animal toxicology studies go on to fail in clinical trials (FDA, 2004). Clearly, we need more effective methods and non-animal replacements are providing the solution.

Of course, cell-based tests and modelling techniques do not "represent a whole-body system", as pointed out by Simon Festing and Robin Wilkinson (Festing & Wilkinson, 2007), but they have the advantage of representing human cells and tissues, and not those of a different species. In addition, whenever it is safe and ethical to use them, studies of healthy volunteers and patients provide gold-standard data on the whole human organism.

Animal experiments are also being replaced by human-based methods in medical research. During the 1990s, the Dr Hadwen Trust (Hitchin, UK) funded groundbreaking research at Aston University (Birmingham, UK) in human brain imaging. This work showed that a new type of non-invasive brain scanner—magnetoencephalography (MEG)—could be used to study human brains both safely and reliably. MEG detects electrical activity in the human brain with a spatial discrimination of approximately 2 mm and a temporal resolution of 1 ms (Hall *et al*, 2005), and is increasingly being used to replace invasive experiments on non-human primates and cats. This is just one example of the huge potential of non-animal replacement techniques in medical research.

There is only one solution that ensures the safety of humans while maintaining our ethical obligation to animals, and that

is to develop and apply more non-animal replacement techniques. This requires an increased commitment and investment at the highest level, but we are already seeing the benefits of these applications.

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Comment on 'The ethics of animal research' by Festing & Wilkinson

Simon Festing and Robin Wilkinson's scientific defence of animal research rests on their claim that the development of new medicines and treatments is "all made possible by animal research" (Festing & Wilkinson, 2007). Yet the Advertising Standards Authority (ASA; London, UK) has ruled that such claims are misleading (ASA, 2005).