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Response by Festing & Wilkinson

The commitment of the scientific community to developing alternatives to refine, replace and reduce the use of animals in scientific research and regulatory toxicology has been shown many times. New methods have revolutionized high-throughput screening for the pharmaceutical industry, and thus reduced the need for tens of thousands of animals. From simple advances like pregnancy tests, to complex brain imaging techniques, scientists—not anti-vivisectionists—are continually developing new methods to replace the use of animals.

In some cases these new tests can outperform animal studies and their use should be applauded, but to make the generalization that non-animal methods are therefore ‘superior’ in all areas of biomedical research, or to make a broad judgement as to ‘relative efficacy’, is scientifically meaningless. Scientific methods can only be assessed on a case-by-case basis. For example, computer modelling is good at predicting protein folding, but isolated human cells will never be able to tell us the full story about the regulation of blood pressure.

The Dr Hadwen Trust might make a small contribution to the field of replacement techniques; nonetheless, Gill Langley is a well-known anti-vivisectionist who uses the debate about alternative methods to undermine the use of all animals in research wherever possible. It is true that

non-animal methods can sometimes overcome the limitations of animal studies, nevertheless, in many cases, animal studies are needed to overcome the limitations of alternative methods—as with the blood pressure example just given. *In vitro* studies can actually have a much higher failure rate than animal studies in predicting what will happen in humans. The Ames test to assess the mutagenic potential of a chemical, for example, is riddled with false positives. There are also strict ethical limitations about what can be studied in humans. This is why, as responsible scientists, we must use all available research methods, as long as they are humane and well-considered. The strong ethical reasons to minimize studies in animals are incorporated in the 3Rs approach, which we discussed at length in our original article (Festing & Wilkinson, 2007). We agree with the Dr Hadwen Trust that the development and application of more non-animal replacement techniques is important; however, until these are available, some animal research will still be necessary.

As in any field of scientific controversy, there are pressure groups, some of which will deliberately and systematically distort scientific arguments to their own ends. The organization Europeans for Medical Progress (EMP; London, UK), is an animal rights group that purports to speak on behalf of patients. In fact, nothing could be further from the truth. The reality is that patient organizations in the UK overwhelmingly support the use of animals in biomedical research; more than 100 medical research charities supported an ethical statement on the use of animals in research (AMRC, 2006).

It is worth looking in some detail at the verdicts made by the Advertising Standards Authority (ASA; London, UK) about several complaints made about animal research-related advertising. In 2005, the ASA upheld five complaints (ASA, 2005a) against a leaflet by EMP for claims that were unsubstantiated and untrue. The ASA also commented that, “citing specific cases where animal tests had proved misleading or unhelpful did not, in itself, show that the general approach was misconceived, as implied by the claim” (ASA, 2005a).

In a separate adjudication (ASA, 2005b), to which EMP refer in their correspondence (Archibald & Clotworthy, 2007), the ASA rejected two complaints made by the EMP against a scientific leaflet by the Association of Medical Research Charities

(AMRC; London, UK). The ASA agreed that “at some stages of research there is no alternative to using animals” and that many medical advances were “made possible with animal research”. The ASA did uphold one complaint: they requested that the claim of the leaflet should be amended to state that “some of the major advances in the last century relied on animal research”, rather than the original—“would have been impossible without”—because the burden of proof required by the word ‘impossible’ was too great. This complaint was upheld on semantics, not as an indictment of the scientific validity of animal research.

Contrary to the claims of EMP, the Research Defence Society (RDS) has long argued for independent verification of the validity of animal studies. Our website contains an article (Macleod & Sandercock, 2005) explaining why systematic reviews are important and useful, and calling for more. We have liaised with the teams involved in the recently published systematic reviews to which the EMP refer in their Correspondence. The views of these teams are that improvements are needed both in the design and conduct of clinical trials, as well as in animal studies. These groups do not agree with the interpretation by EMP that all animal studies are scientifically invalid.

To suggest that the use of animals to test medicines means that animal tests are responsible for any side-effects is nonsense. It is primarily human clinical trials that are intended to identify adverse side-effects in new drugs. In the case of the drug Vioxx®, for example, it was extensively studied during clinical trials using many thousands of patients before being approved by more than 70 regulatory agencies around the world. Many took Vioxx® in these studies for more than a year and severe toxicity was not reported—a testament to the success of animal and other pre-clinical tests at protecting those early volunteers.

EMP quote Michael Goodyear (Dalhousie University, Halifax, Canada) to remind us that a lack of severe toxicity in animal models should never be construed as a guarantee of safety in man (Archibald & Clotworthy, 2007). Our response is that of course scientists accept the limitations of animal studies—but they do provide real, useful, life-saving data. Just because seat belts do not guarantee car safety does not mean that you should not use them. In any case, Goodyear in fact argues for the

status quo, that we need to consider a parallel process, using human tissues and other *in vitro* methods, as well as animal studies. Our cautiousness about—not “criticism” of—microdosing, reflects the views of the experts in that field (FRAME, 2005; Rowland, 2006). Microdosing is not designed to elicit toxicity and will therefore never be able to guarantee safety. It is not a question of using either animal studies or alternatives; good science is about getting the best information from all the available methods.

Anti-vivisection groups make a great deal of the supposed failings of animal testing highlighted by the US Food and Drug Administration (FDA, Rockville, MD, USA). However, the FDA report was not actually about animal testing *per se*, but rather about the generally high attrition rate in drug development and the need for new techniques to counter this (FDA, 2004). It has long been the case that all potential new medicines given to humans in clinical trials must undergo extensive testing beforehand, including animal tests and all available alternatives, such as computer modelling and cell culture. There has always been a very high rate of drop-out at all stages of drug development because pharmaceutical companies only seek to market the most effective medicines with the best safety profile. The role of safety tests is mainly to identify severely toxic compounds that should not be tested in humans. Animal and other studies have proven extremely effective in this regard and without them it is likely that the TGN1412 tragedy of last year would be a common occurrence.

The suggestion that 92% of medicines that work in animals do not work in humans is not only factually incorrect—many do work in humans but are not taken forward for business reasons—but is also a misleading distortion of the role of animals in research. We would also point

out that the alternative methods, which the anti-vivisectionists always point to, have a much lower success rate.

The FDA report does not suggest that animal testing is ineffective. On the contrary, it advocates the use of animals and encourages the use of new technology to improve animal models. The FDA's summary gives the first example of an opportunity for improvement as the “[d]evelopment of good animal models for many conditions, including SARS and anthrax infection.” Furthermore, they state that, “New genetic technologies may make it possible to develop animal models that are more predictive of human responses to vaccines and treatments for these diseases” (FDA, 2007).

Researchers and doctors overwhelmingly support well-regulated animal research, and—as we previously noted with approval (Festing & Wilkinson, 2007)—have a healthy scepticism that guards against over-reliance on any single research method. We can find no credible scientific or medical organization anywhere in the world that supports the views of EMP. In fact, EMP frequently abuse isolated quotes from organizations such as Cancer Research UK (London) to give a distorted and misleading impression (Archibald, 2004; ASA, 2006). In this particular case, EMP quote Cancer Research UK out of context and without acknowledging that Cancer Research UK carries out substantial animal research that is essential in the fight against cancer.

EMP's scientific ignorance is further displayed by citing “the story of thalidomide” as evidence for the supposed failings of animal testing. In fact, the thalidomide tragedy arose owing to a lack of animal safety testing, and was the main impetus for the legislative requirements we have today. Finally, to suggest that the response of the viewers of Sky News to an internet questionnaire is equivalent to a rigorously conducted opinion poll of public opinion

is absurd. Thankfully, anti-vivisectionists remain isolated in their extreme aims to abolish animal research.

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