A response to the British Heart Foundation

Peter Hollins, the Chief Executive of the BHF, has written to several Animal Aid supporters defending the charity’s funding of animal experiments. A BHF leaflet entitled ‘Animals and Heart Research’ was enclosed with his reply. What follows is some information that may help supporters who wish to reply to Mr Hollins. Much is abstracted from the Victims of Charity (VoC) report (http://www.animalaid.org.uk/images/pdf/booklets/victims.pdf, page references given). A hard copy is available on request from the Animal Aid office.

1. The BHF’s letter argues that the ‘strict peer review system’ of funding for animal experiments is evoked as a measure of the rigour with which the BHF vets its grant applications. It is also stated that their researchers are reducing the number of animals used.

Unfortunately, there is evidence that the entire peer-review process is flawed, secretive and biased – at all stages (p 39 VoC).

Furthermore, as noted by the British Union for the Abolition of Vivisection, the regulatory framework for animal experiments is ‘permissive, cloaked in secrecy and offers little meaningful protection to animals’. (See http://www.politics.co.uk/opinion-formers/buav-british-union-for-the-abolition-of-vivisection/political-challenges)

The BHF claims it is reducing the numbers of animals used but it has so far refused to provide evidence of this or confirm how many animals it uses or what species they are. And across the UK, the number of animal experiments conducted continues to rise. The Home Office (HO) is sanctioning more and more curiosity-driven ‘fundamental’ research (up 10 per cent in 2010), which by law need have no application to human medicine. According to the HO’s own statistics (see link below), nearly a million such procedures were ‘not relevant’ to any human body system in 2010. Universities, often funded by grants from medical charities, are now playing the lead role in this area of research, which is still largely devoid of proper scrutiny.

For more about the recent rise in animal use, see http://www.animalaid.org.uk/h/n/NEWS/news_experiments//2519//

2. The letter and leaflet state that there is no alternative method that can reproduce the complicated workings of our hearts and circulatory systems. It is claimed that the BHF only funds research involving animals where there is no feasible alternative.

There is, in fact, a wealth of alternative approaches in cardiovascular research (Animal Aid has produced a briefing on this issue http://www.animalaid.org.uk/images/pdf/factfiles/Nonanimalresearch.pdf) and yet progress away from animal experimentation has been far too slow, partly because of the endlessly repeated mantra of ‘no alternative’.
Purely experimental and irrelevant cardiothoracic surgery on animals continues, and a good deal of it is funded by the BHF. The charity has funded thousands of terminal experiments (procedures which result in the death of the animal) in the name of ‘basic’ research. One of the most damning, though by no means isolated, examples of BHF-supported research is the long-running series of dog experiments carried out at Leeds Medical School. The experiments involved opening the chests of anaesthetised dogs, cutting their spinal cords, draining and re-circulating their blood and cutting nerves to the brain, gut and diaphragm. The repetitive and self-justifying programme has been roundly condemned by a former Harvard Medical School Faculty member (and former dog researcher) John Pippin (p19 VoC).

Animal Aid agrees that some of the experiments cannot be replaced by non-animal alternatives. Testing the effects of DNA alterations on the hearts of laboratory mice, or performing open-chest surgery on dogs, clearly have no direct facsimiles in human cell culture or computer models. But as Victims of Charity shows, the results of such experiments are often not transferable to humans anyway and, in other cases, are simply irrelevant. Medical research must lead to medical benefits, and animal research in this area is simply not delivering. If phasing out the cruelty of animal experiments leaves some scientific stones unturned, so be it.

3. The letter and leaflet state that medicines are not allowed to be tested in humans before they have been shown to be safe in animals.

This is misleading as the BHF is funding research, not drug testing (which is a regulatory process driven by commercial interests. There is no requirement to use animals in basic or applied research. There is no legal requirement to conduct the kind of appallingly invasive experiments we describe in Victims of Charity – destroying the vital organs of dogs in esoteric physiology experiments (p19 VoC), inducing heart attacks in rabbits, grafting pigs’ leg veins into their necks, or putting pacemakers into goats. In fact, there is no regulatory requirement at all to use ‘animal models’ in disease research. And where there is a statutory requirement to use animals in the discovery, development and testing of commercial pharmaceutical products, the animal data often prove unreliable – as indicated below.

4. The BHF cites examples of cardiovascular drugs that have been developed using animal research, including beta-blockers, ACE inhibitors and cholesterol-lowering drugs (statins). The BHF claims that ACE inhibitors were discovered by testing snake venom on rats.

These assertions suggest that using animals to test such drugs yielded clear benefits when in reality the data obtained often differed significantly from those found in humans. Artificial heart valves, beta-blockers, digitalis, the statins and other medications and treatments were kept off the market because animal models raised concerns that did not manifest in people.

For example:

* In the history of ACE inhibitor research, Tigerstedt discovered the kidney extract renin in 1898. He found it constricted arteries without altering cardiac output, and subsequently showed that renal extracts caused a marked effect on the circulation of
animals from whom he had removed the kidneys. However, other investigators in the field were unable to repeat his observations, and the studies were abandoned. Little further interest was shown in the biological effects of renal extracts until 1934, when Goldblatt showed, in dogs, that clipping the renal artery raised blood pressure with effects similar to those of human hypertension. When plasma renin levels were subsequently measured in human patients with essential hypertension, it was found that, in contrast to Goldblatt’s experiments, the plasma renin levels were normal or low. They were elevated in fewer than 10 per cent of patients, and so Goldblatt’s renin hypertension hypothesis was rejected. Only serendipitous discoveries from elsewhere restarted a research programme. The blood pressure lowering effect of the snake venom in question (from a South American pit viper) was known in humans long before the substance was tested in rats. (References supplied on request.)

* Mevastatin was one of the first statins (cholesterol-lowering drugs) to be researched. In the development of most cholesterol-lowering agents, effectiveness has been evaluated predominantly in rats. During initial investigations in early 1974, researchers gave mevastatin orally to rats and measured blood fat levels three to eight hours later. Initial results, which showed a cholesterol-lowering effect were, however, difficult to reproduce, and, unexpectedly, the feeding of rats with a diet supplemented with mevastatin for seven days had no effect. Plasma cholesterol was not lowered even when the agent was given to the animals at high doses for five weeks. Furthermore, mevastatin was ineffective in mice, producing no detectable effects. Researchers felt that mevastatin should be evaluated in animal models more comparable to humans. At that time, however, such an animal model was not available. Fishing around for a species that their drug would work in, they finally tried hens, found efficacy, and moved on to dogs and monkeys.

In 1979, clinical trials of mevastatin were carried out in patients with severe hypercholesterolemia by more than 10 groups in Japan. In mid 1980, however, most of these clinical trials were suspended, because mevastatin had been found to produce toxic effects in some dogs at higher doses in a long-term toxicity study. It was only the beneficial effects observed in humans that caused researchers to persevere. (References supplied on request.)

* Beta-blockers were developed for the treatment of heart conditions, and one of the first agents to be administered to human patients was pronethalol. This drug had been ‘well tolerated’ by rats and dogs in prolonged toxicity tests at high doses, except for occasional effects on the central nervous system. Shortly after small-scale clinical trials on people, animal toxicity tests revealed that the drug caused thymus gland tumours in a certain strain (Alderley Park) of mouse bred for laboratory use. Consequently, when the drug was marketed in late 1963, its use was limited to patients whose lives were seriously at risk. However, no carcinogenic effects were ever found in rats, guinea pigs, dogs, monkeys or other types of mouse.

In an attempt to improve beta-blockers, ICI produced practolol, which after undergoing animal tests and clinical trials was marketed in 1970. The drug led to many severe adverse reactions: by the end of 1974, 187 adverse eye reactions, several hundred cases of skin reactions, and 25 complaints of deafness had been recorded. There were an estimated 7,000 victims of reactions to the drug in the UK alone. The Department of Health said at the time that an additional long-term animal study had
shown no such effects. In 1980, a joint publication by the UK Office of Health Education and the Association of the British Pharmaceutical Industry reported that ‘the practolol adverse reactions have not been reproducible in any species of animal, except man’.

* With regard to cardiovascular drugs, Victims of Charity uses many examples to show that non-correlation of animal studies with human trials is the rule rather than the exception (p15 VoC). Useful drugs have been developed in spite of, not because of, animal models.

5. Examples are cited of surgical techniques, such as heart transplants and bypass surgery that have been developed using animal research. The claim is made that ‘without animal research, many of today’s life-saving treatments for heart and circulatory disease could not have been developed’.

This categorical assertion is impossible to prove or to disprove retrospectively. It is certainly the case that treatments in use today have employed surgical experimentation or drug trials on animals. Whether the use of animals was essential, however, is mere speculation. We cannot know whether the use of non-animal techniques instead may have brought benefits of equal or greater medical value. Nor is it known how many potentially useful treatments have been lost due to misleading animal data.

Undoubtedly, many surgical techniques developed during the last century involved animal experimentation. But it is striking how often the first human trials led to a dramatic acceleration in progress, in a way that cannot simply be ascribed to technological improvements. Victims of Charity (p13) uses the examples of heart transplants, bypass surgery and interventional cardiology to illustrate this point.

The first Starr-Edwards heart valves, when transplanted into dogs, were severely compromised by fatal thrombus (blood clot) formation, and the necessary post-operative anticoagulation caused many dogs to bleed to death. Modifications to the design improved canine survival figures – but it was the original, simpler design that was chosen for placement in people. The researchers knew that humans were much less likely to develop thrombi than dogs; one commented: ‘humans will tolerate this surgery much better than dogs... dogs, for some reason, don't like to have their blood bubbled through a pump oxygenator’.

6. The leaflet claims that ‘more than eight out of ten people felt that – where there is no alternative and researchers follow strict rules for animal welfare – research that aims to reduce human suffering should be allowed’.

This question is clearly loaded in order to elicit a pro-vivisection answer. An Australian poll a year earlier found that only 18 per cent of respondents indicated that they would donate to health or medical research charities if they knew they were funding animal experiments. Other polls have shown that if people are given details about the reality of animal experiments, only a minority would continue to support them.
7. The leaflet quotes Professor Peter Weissberg, the Medical Director of the BHF, as saying: ‘Research using animals, predominantly mice, is providing an understanding of the workings of the heart and circulation that we could not have gained in any other way.’

The methods used to model heart disease in mice are crude, cruel and irrelevant (p14-15 VoC). The coronary arteries of mice are tied off to simulate a heart attack in a person, with up to half of the mice dying within the hour. Researchers have developed transgenic varieties who are programmed to be born with or to develop diseases. These include mice liable to die spontaneously due to rupture of their major vessels, or who will develop dilated and dysfunctional heart muscle.

Whether surgically or genetically created, the research community readily admits that these models do not accurately reproduce human pathology. The animals used are unlike humans in their basic physiology and anatomy. Rodents, for example, have a resting heart rate five times higher than humans, with different electrical impulses and muscle composition. In addition, the damage ‘induced’ in healthy animals is fundamentally different from the diseases found in humans. A 2010 review from the National Institute for Medical Research (NIMR) noted the obvious: ‘[in the animals] heart failure occurs suddenly post-surgery in the context of a relatively young heart, whereas in humans, the onset may be insidious over several years in the context of comorbidities and age-related changes... The major disease burden of heart failure in the future is expected to come from patients with the complex phenotype cluster of hypertension/hyperlipidaemia/obesity/diabetes... it is not obvious how closely [it] resembles the current animal models’. (p15 VoC)

8. The leaflet mentions that BHF researchers are looking at the way the heart and circulation develops in zebrafish embryos, and claims that a better understanding of how hearts are formed and grow in animals will lead to new ways of repairing human hearts damaged by heart attack.

This is pure speculation dressed up as science. There is no evidence whatsoever that studying zebrafish, who are often subjected to heart amputation studies, will ever translate into clinical benefit for humans (p18 VoC). There are a great many fundamental bio-evolutionary differences between zebrafish and humans. Importantly, the former have two-chambered hearts (compared with the four-chambered human organ), with different cardiac muscle, and can grow throughout most of their adult lives.

Cardiac progenitor cells are present in mammalian hearts, and it was thought until recently that zebrafish used these stem cells to regenerate cardiac tissue. However, zebrafish repair their hearts via a different mechanism (dedifferentiation), which has no functional analogue in human hearts. After this discovery, researchers stated lamely: ‘If we could mimic in mammalian cells what happens in zebrafish, perhaps we could be in a position to understand why regeneration does not occur in humans.’ This hardly suggests curative potential.

In humans, coronary artery disease is the most common cause of heart failure. It damages heart muscle both acutely and chronically via a lack of oxygen and nutrients. Heart attacks lead to large fibrous scars in an already diseased organ.
Heart failure is associated with a complex series of long-term physiological derangements. All these elements are absent in the animal ‘models’ whose hearts are instead surgically damaged.

9. The leaflet mentions that ‘more than ten years of research in animals has allowed the development of a gene therapy for heart failure that is now being trialled in humans’.

Gene therapies for heart failure, despite a mass of positive animal data, have to date been an almost unmitigated flop. The BHF neglects to mention that more than ten years of research on animals has led to numerous failed therapies (p17 VoC).

Dr Paul Williams, a BHF Clinical Researcher, commented in 2010: ‘... despite a huge amount of basic science research, promising animal studies, and numerous clinical trials, to date no gene therapy has demonstrated unequivocal benefit in the clinical setting... is all the hype and research expenditure unwarranted?’

The BHF should provide references for the animal research using this particular gene therapy, and for the relevant clinical trials.