(*formerly* Europeans for Medical Progress)

Safer Medicines Campaign

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Newsletter Autumn 2008

Welcome to our joint Safer Medicines Campaign/Safer Medicines Trust newsletter.

Kathy Archibald

Director

Safer Medicines Campaign is an independent organisation of scientists and doctors whose aim is to ensure the best methods are used to assess the safety of medicines. We campaign for sophisticated human biology-based tests to be compared with the animal tests currently required by law. A million Britons are hospitalised by medicines every year, costing the NHS £2 billion. We believe 21st Century science can do better.

Our educational wing, Safer Medicines Trust, is a registered charity: Number 1039411

Help us put patient safety first

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INSIDE THIS ISSUE

Our new name

As you can see, we have changed our name, which has been quite an upheaval but we are sure it was worth it and have already begun to reap the benefits.

The reason for the change was to make it clearer what we are about – something that was not always obvious from our old name. We feel that Safer Medicines Campaign communicates our raison d'être very simply and effectively. This will help politicians, journalists and the public to engage with us more readily.

This certainly seemed to be the case at the recent annual party conferences, where we attracted a great deal of interest from MPs, ministers, journalists and party members.

We hope our supporters will find our new name more conducive to spreading the word about us and explaining what we stand for. Please see the back page for resources to help you do this.

Please recycle any stocks you have of literature in our old name, as the contact details are no longer valid.

Party conference progress

We attended the Labour, Conservative and Green party conferences in September and were delighted with the contacts we were able to make. Many MPs and ministers were very interested to learn that sophisticated human biology-based methods of research are available and could reduce the serious problem of adverse drug reactions.

We gave them copies of our short film, ***Safer Medicines***, which showcases some of the exciting technologies that we believe could supplant animal tests in drug development to benefit humanity.

The Rt Hon Alan Johnson MP, Secretary of State for Health, with Dr Clotworthy

Public Health Minister Dawn Primarolo MP with Communications Director, Shelly Willetts

Michael Foster MP with Science Consultant Dr Margaret Clotworthy

BBC admits bias but defends lies

In our last newsletter we reported that the BBC had upheld our complaint of bias concerning the programme 'Monkeys, Rats and Me' which was screened in November 2006. The BBC admitted that the programme suffered from an unacceptable lack of balance and must not be aired again.

We further pressed the BBC Trust (the BBC's watchdog, defending its independence in the public interest) to uphold our complaint regarding accuracy, since the central premise of the programme – that treatments such as deep brain stimulation (DBS) for Parkinson's disease and dystonia resulted from experiments on monkeys – is false. DBS was actually pioneered in patients, not monkeys.

We had to wait just over a year for the BBC Trust's verdict, which was – astonishingly – that the programme was not inaccurate. Even more disappointing than the ruling itself was the fact that the BBC Trust ignored our central complaint (that DBS was pioneered in patients, not monkeys) just as BBC management had done. We pointed this out in a series of correspondence both before and after the ruling but to no avail.

We have spent almost two years negotiating the entire BBC complaints procedure only to find that the process is a charade. We spelled out our key complaint and requested a response on six separate occasions but still the point has never been addressed.

Our complaint is legitimate and important. Public opinion on the acceptability of animal experimentation – particularly its most controversial element, i.e. brain research in primates – is influenced overwhelmingly by the magnitude of its purported value to human health. Producing treatments for distressing disorders like Parkinson's disease provides a powerful argument in defence of such controversial research. However, if such claimed successes are actually the fruit of research in humans, those seeking to justify research in monkeys are left, like the emperor, without any clothes.

Why the BBC should wish to defend animal experimentation deserves explanation. The BBC is a public service broadcaster charged with a statutory duty to inform and educate the public – who own and pay for it – with the highest standards of honesty, accuracy and impartiality.

The BBC proudly accepts this role and has its own stringent guidelines defining its responsibilities. The guidelines state, for example:

We should not distort known facts, present invented material as fact, or knowingly do anything to mislead audiences.

Clearly the BBC is prepared to defend animal research to the extent of making a mockery of its own guidelines. The position they have adopted in order to defend the false claim that DBS was discovered in monkeys is that programme makers and contributors are 'entitled to their view' – whether true or false – and may present it as fact, even as part of a supposedly factual documentary.

It is thus fair to conclude that what passes for truth at the BBC cannot be trusted – in blatant contravention of its obligations to the public, as laid down in its Royal Charter. Furthermore, there is little point complaining about mistakes since, if the BBC does not like a complaint, they will simply ignore it. In this case, BBC policy appears to be:

'See no facts, hear no facts, speak no facts.'

We are still waiting for the BBC to respond to our criticism of the intervention in the complaints process by powerful organisations with enormous commercial and intellectual vested interests in defending animal experimentation. One of the BBC Trust's major roles is 'to ensure that the BBC remains independent, resisting pressure and influence from any source.'

Yet the programme team, with the approval of BBC executives, joined forces with pro-animal testing lobby group RDS (Research Defence Society) to solicit letters from eminent pro-animal testing spokesmen professors Colin Blakemore and Clive Page. The purpose of the letters was an attempt to overturn the ruling that the programme was biased. Happily, the attempt was unsuccessful, presumably because the bias is so overt that it simply cannot be denied.

However, it is reasonable for us to speculate that such heavyweight intervention may have exerted some influence on the BBC's continuing refusal to address our key complaint: striking, as it does, at the heart of the Establishment's defence of animal experimentation.

It would be illuminating to see Professor Blakemore's letter but the BBC has refused to show it to us. They did, however, send a copy of Professor Page's letter by mistake, which can be viewed on our website, along with all of our letters of complaint and the BBC's responses (which reveal a catalogue of lies on the part of the programme maker).

Professor Page's letter contains a barrage of false and defamatory allegations against us and is a blatant attempt to undermine our credibility in order to persuade the BBC to dismiss our concerns. It illustrates the lengths to which those who feel threatened by our position are prepared to go in an attempt to suppress coverage of the scientific challenges to animal experimentation that we represent.

House of Lords meeting

Professor the Lord McColl of Dulwich, CBE with Dr Bob Coleman, DSc (Hon).

It was a great pleasure for us to meet Lord McColl and to learn that he shares our conviction that the answers to human health problems will be found by studying humans and their tissues, rather than animals. Lord McColl is a Conservative Shadow Minister for Health, as well as Professor of Surgery at the University of London and a Fellow of the Royal College of Surgeons. He is Chairman of MercyShips UK, for whom he is a regular volunteer surgeon, among many other active roles in a number of charitable organisations.

We were delighted to be invited to address a meeting of the Associate Parliamentary Group on Surgical Services, of which Lord McColl is Chair.

Dr Bob Coleman, one of our scientific advisors and a pioneer of the use of human tissue in drug discovery and development, gave a very enlightening talk on the merits of human tissue and the advantages to be gained by making wider use of it.

Our director, Kathy Archibald, then explained why we believe a comparison of currently required animal tests for drug safety with a set of human biology-based tests is necessary. To illustrate this point, we showed a ten minute version of our film, ***Safer Medicines***, which was followed by a lively question and answer session.

We are deeply indebted to Lord McColl for such an excellent opportunity to present our arguments to MPs and peers and to distribute copies of our film to them, as well as to members of the Royal College of Surgeons.

Drug Innovation conference

'We'll never have an animal model that is really predictive of what is going to happen in humans.'

Dr Philippe Menasché

A conference on innovation in drug discovery and development was hosted in London by the Drug Information Association at the end of September. Representatives from the UK, European and US bodies responsible for regulating new drugs, academics, and many of the pharmaceutical companies responsible for bringing drugs to the market gathered to discuss how to better bring drugs to market, as well as the impact of the latest legislation and initiatives such as the EU's Innovative Medicines Initiative, which will fund €2 billion of research over the next ten years.

The conference was an excellent opportunity for us to meet regulators and pharma executives and discuss with them our proposal for a comparison of the effectiveness of human biology-based tests with currently required animal tests for drug safety. Many speakers and attendees were very interested in our initiative and encouragingly supportive of the idea.

An interesting perspective on the utility of animal tests (particularly the use of rodents) for testing new cell-based treatments came from a surgeon in France who works at the forefront of research in this area:

'We don't have a single animal model that can really mimic the very complex situation in humans.'

Dr Philippe Menasché, Department of Cardiovascular Surgery, European Hospital Georges Pompidou, France

Although Dr Menasché uses animals in his research, he pointed out that in a decade of work on animals to test the idea of giving stem cells to patients who have suffered heart attacks, no sign of heart arrhythmia, a dangerous heart disturbance, had been found. Yet when this procedure was tried in patients for the first time, four people suffered this complication. This underlines the fact that it is only in clinical trials that we really find out what will happen in people.

Promoting our message

Our talks to schools and universities continue to be very well received, generating a great deal of discussion and debate, and we continue to receive requests for copies of our film, ***Safer Medicines***.

Several radio discussions in which we have participated have prompted listeners to call in, adding their support.

We contributed to an OECD consultation on human biobanks, a Nonhuman Primates in Science strategy team consultation and a European Commission consultation on the use of primates.

Medical research in the news

Mouse models 'nearly useless'

The use of mice as 'models' for testing drugs intended for use in humans is 'nearly useless', according to an article in the prestigious science journal *Nature*.

In the past year alone, three major potential new drugs for Alzheimer's disease that appeared very promising in mouse 'models' of the disease failed in clinical trials. Although scientists can create mice with deformities resembling those seen in patients' brains, the mice do not have dementia, and drugs that target these deformities have repeatedly failed in human trials, causing scientists to question whether the mice truly mimic what happens in the human brain.

Worse, almost a dozen drugs that helped mice with amyotrophic lateral sclerosis (ALS), a progressive, usually fatal disease of the nerves, to live longer have failed or even harmed humans:
'In the most recent and spectacular of these failures, [a drug] which had seemed modestly effective in four separate ALS mouse studies since 2002, was found last year to have *worsened* symptoms in a clinical trial of more than 400 patients.'

There are no good mouse models for Parkinson's disease, and even the mouse model for Huntington's disease, which has a simple genetic cause, does not suffer from all the same symptoms. This shows yet again how recreating even a seemingly straightforward genetic fault in another species cannot be relied upon to mimic the human condition, because the background biology of each species is just too different and complex.

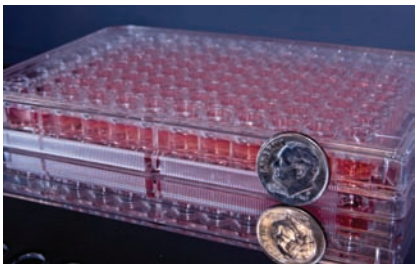
According to neurologist Dr Michael Benatar, from Emory University School of Medicine in the US:

'I think there's a sense of desperation that we need a convenient model for bringing drugs to clinical trial. But desperation is an inadequate justification for the continued use of a poor model.

It's a bit like the proverbial drunk who keeps looking for his lost keys under the lamp post, simply because the light's better there.'

Reference: *Nature* **454:** 682

'Clinical trial in a test-tube'



Credit: VaxDesign Corporation

An exciting breathrough in providing human-relevant vaccine testing in the safety of a lab has been made by a Florida company called VaxDesign (www.vaxdesign.com).

According to Dr William Warren, president, CEO and co-founder of VaxDesign:

'We know animal models do not translate to human responses...Animal models of treatments for HIV to psoriasis and flu are not representative of human responses.'

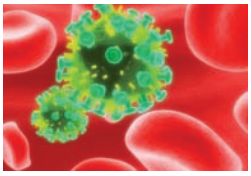
The scientists at VaxDesign saw this and built a test using plastic dishes containing almost 100 wells in which cells from different human blood samples are grown. This means that you can effectively test the impact of a new vaccine on hundreds of humans, safely and rapidly, before a single volunteer has to be exposed! Michael Rivard, vice president of corporate development at VaxDesign points out that:

'The information you get from this type of test is far and beyond what you'd get out of a mouse study, both because it's humans and because you can see the effect across a spectrum of genotypes (different genetic make-ups).'

In March, the International AIDS Vaccine Initiative (IAVI) bestowed its first ever Innovation Award on VaxDesign, whose approach is supported by Dr Wayne Koff, senior vice president of research and development at the IAVI, who commented:

'In the end, you can only extrapolate so much from a monkey model.'

References: *Time* magazine, 27th March 2008 and *TechJournal South*, 2nd October 2007.



AIDS vaccine research

Meanwhile, many AIDS vaccine researchers (and their funders) appear determined to keep their heads buried in the sand. In the wake of several high profile vaccine failures, some of which actually *increased* the risk of infection with HIV, many have called for a change in direction:

'"I think we should pull the plug on vaccine research. Do we have any other enterprise that has been studied for 25 years and for which we've spent billions of dollars where we have no results?' Michael Weinstein, President of the AIDS Healthcare Foundation.

Dr Anthony Fauci, director of the US National Institute of Allergy and Infectious Diseases (NIAID) admitted that:

'We've learnt a few important things [from the clinical trial]. We've learnt that one of the animal models, the SHIV [an artificial virus meant to mimic the human virus but capable of infecting monkeys] model, really doesn't predict very well at all. At least we now know that you can get a situation where it looks like you are protecting against SHIV and you're not protecting at all in the human model – that's important.'

Yet despite accepting that the major animal model for AIDS is not predictive for humans, he has vowed to continue to fund and promote much more basic research… in animals.

'We will not discontinue research, period. Not only will we not decrease it, we will in fact try to increase it.'

Surely it should be clear by now that the focus needs to be on patients and human biology-based research, rather than on attempting to improve animal 'models' whose record to date is of complete failure.

'When it comes to testing HIV vaccines, only humans will do.' Alison Tonks, *British Medical Journal*, 2007; **334:** 1346.

A Canadian team has used virus extracted from the blood of people with HIV, in combination with their own immune cells grown in the lab, to produce individually tailored treatments for each patient. Early results using the treated immune cells have been very promising, with eight out of nine recipients seeing an improvement. Larger trials are now being planned by the researchers from the McGill University Health Centre and University of Montreal, in collaboration with biotechnology company Argos Therapeutics.

'Our approach is unique in the world: no one else has yet developed customized immunotherapy using the virus from individual patients.' Dr Jean-Pierre Routy, McGill University Health Centre.

References: *The Washington Post,* 26th March 2008, *The Baltimore Sun*, 26th March 2008, *the Independent,* 24th April 2008.

Heart drug blunder revisited

An article in the prestigious science journal *Nature* discussed the now discredited use of anti-arrhythmia drugs after heart attacks. These drugs were supposed to save lives by reducing irregular heart beats. Subsequent reviews of the outcomes for patients who had received these drugs, compared with those who had not, caused consternation when it was discovered that the drugs more than doubled the risk of death or heart attack:

'Everyone was so confident that if you quieted the extra heartbeats, the patients would do better, but people died.' Dr Harlan Krumholtz, Yale University.

'It is not easy to think of a greater medical error, since the practice of therapeutic bleeding, than the use of antiarrhythmic drugs in patients after myocardial infarction.' Robert Temple, director of the Office of Medical Policy at the US Food and Drug Administration (Clinical Measurement in Drug Evaluation, 1995).

The author reminded readers that the use of the drugs:

'depends principally on tradition, on an unproven expectation that antiarrhythmic effects are likely to be beneficial for potentially lethal arrhythmias as well as for less malignant conditions, and on *extrapolation from animal experiments*.' (Chamberlain, *Heart* 1998; **80:** 408).

Reference: *Nature* **452**, April 2008: 510.

Adverse drug reactions cost NHS £2bn

Compass, a London-based thinktank, has revised the latest estimates for the cost of adverse drug reactions dramatically upwards. According to Health Minister Dawn Primarolo, 6.5% of hospital admissions (well over a million) are as a result of bad reactions to prescription drugs. When the cost of caring for patients who become ill whilst already in hospital as a result of drugs they are prescribed is factored in, Compass estimates that the cost to the NHS is £2billion.

With the NHS coming under ever increasing pressure to provide expensive drugs to patients, it is imperative that the burden of adverse drug reactions be reduced. Part of the solution would be to introduce more personalised medicine (making use of genetic and other testing techniques to check whether a drug is suitable for a patient). Also, to ensure that only drugs with the best safety profiles are marketed, more extensive clinical trials need to be carried out, preceded by the most human-relevant laboratory tests.

Reference: *the Guardian*, 3rd April 2008.

Every cloud has a silver lining?

Researchers writing in the journal *Science* have found, using test tube-based experiments, that unexpected uses for drugs may be identified by comparing the side effects they cause with those of other, unrelated drugs. This finding makes it even more important that accurate information about the side effects patients experience is collected and analysed.

Reference: *Science,* **321**: 263, July 2008

Brain donors worth their weight in gold

The Parkinson's Disease Society Tissue Bank, at Imperial College London opened five years ago to provide a vital resource to any researcher wishing to study Parkinson's Disease. The bank has since received more than 250 brains. However, perhaps unsurprisingly, the majority of donors have been patients with Parkinson's Disease, leaving only 17 'control' brains, which are needed for comparisons between the brains of sufferers and non-sufferers of this debilitating disease.

'Alzheimer's, Parkinson's and other neurodegenerative diseases occur in humans and it is in human tissue that we will find the answers to these diseases.' Dr. John Xuereb, Director, Cambridge Brain Bank Laboratory (BBC Radio Cambridgeshire, 2002).

For more information on becoming a donor, contact the UK Parkinson's Disease Society Tissue Bank: 0207-594 9732, pdbank@imperial.ac.uk or visit www.parkinsons.org.uk.

Reference: *the Times*, 30th August 2008.

Mice are *not* men

A study published in the prestigious journal, the *Proceedings of the National Academy of Sciences*, in May has found that although humans and mice share about 85% of their genes, 22% of genes known to be essential in humans are not at all essential in mice. This casts serious doubt over the relevance of using mice to find out the roles of genes in humans.

Another study published in the *Proceedings of the National Academy of Sciences* (*PNAS*) in July showed that a gene which promotes colon cancer growth in mice has the opposite effect in human colon cancer cells. So a drug designed to suppress this gene or its protein product - based on its function in mice - might actually speed the growth of colon cancers in people.

References: *PNAS* **105**:6987 and **105:**9697

Virtual children

'We now have a tool which allows complex clinical scenarios to be explored in the safety of a computer.' Professor Amin Rostami

Testing medicines in children has always been difficult as they cannot give consent to participate in trials and parents are, naturally, wary of exposing their children to unknown risks. However, thanks to a computer model developed by Sheffield-based company Simcyp, it should now be much easier to calculate safe doses. This development could not have come at a better time after a new EU regulation demanding that medicines destined for children must now have been tested especially for them. This makes sense as it is now acknowledged that children cannot simply be treated as scaled-down adults:

'In particular, children under two years old are the most physiologically different to adults, so it can be too simplistic to scale back from adult values when determining appropriate doses for children, as currently happens.' Amin Rostami, Professor of Systems Pharmacology at the University of Sheffield and director of research and development at Simcyp.

Reference: *The Times*, July 28 2008.

Animal pain research criticised

'In my research, animal models don't represent human patients sufficiently well, and that's a problem that extends across pain research as a whole.

New and highly sophisticated brain-imaging technology is providing vital insights that animal research has failed to produce. I would like to see far greater uptake of these and other human-relevant approaches to pain research to help us develop the effective treatments that patients so desperately need.' Professor Qasim Aziz, Barts and the London School of Medicine and Dentistry.

A report in the journal *Neuroimage* has criticised the use of animals in pain research.

The report's authors encouraged scientists to make better use of the latest technologies, such as MRI scanning, in ethically conducted studies in people who actually suffer from the pain they are trying to treat. The role of human tissues grown in the lab was also emphasised.

Pain research experts from leading institutes across the UK made these recommendations at a workshop organised by Focus on Alternatives, a coalition of not-for-profit organisations promoting non-animal research, including the UK Human Tissue bank and chaired by the Dr Hadwen Trust.

Reference: *NeuroImage* **42**:467.

Animal studies contribute very little to human healthcare

A review of the contribution of animal-based studies has failed to find significant agreement between the results seen in animals and in humans. The author examined an extensive list of published research, including experiments conducted on chimpanzees, and found that they were generally very poor at predicting human outcomes and contributed little to the development of successful human treatments.

Reference: Knight, *Reviews on Recent Clinical Trials*, 2008; **3(2):** 89.

Animal tests miss liver poisons

Scientists have reviewed the ability of animal tests to predict which drugs will harm patients' livers and found that they miss dangerous chemicals around half of the time.

Perhaps surprisingly, non-rodents (such as pigs or monkeys) predicted human toxicity in many cases only 19% of the time, which is even less often than rodents (such as mice or rats), which can correlate as poorly as 46% of the time! These astonishing figures go some way towards explaining why 92% of drugs fail in human trials, despite undergoing extensive animal tests.

The pharmaceutical researchers who wrote the report, *Species Concordance for Liver Injury,* are part of an initiative known as the Safety Intelligence Program. They are currently trying to understand why the animal tests translated so poorly to humans; hopefully they will now look at human biology-based methods for predicting liver toxicity as a means of improving this abysmal track record.

Reference: *Nature Reviews Drug Discovery* **7:**719, September 2008.

ACTION

Leaflets

If you can help by distributing our leaflets we will be delighted. Donations to help with postage and printing costs will be greatly appreciated.

Newsletters

Please order further copies of this newsletter to distribute if you can.

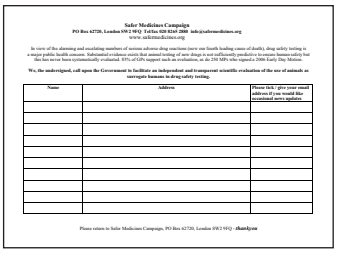
DVDs

Watch ***Safer Medicines*** on our website or buy a copy: **only £5!** If you know any secondary school teachers or lecturers please encourage them to ask us for a free copy. An order form is on our website.

Booklets

Order *A Critical Look at Animal Experimentation*:
a booklet examining the impact of animal experimentation on research into cancer, AIDS, neurological disorders and others, as well as outlining more valid human-based methods of research.

Petition



Sign our petition in support of an independent and transparent scientific evaluation of the use of animals in drug safety testing

- on our website
- on our petition sheet – which you can print from our website or order by email, post or telephone
- on the form below.

Donate

Please make a donation to help us cover the costs of producing these resources and distributing them free of charge to teachers, lecturers and MPs.

You can donate to the Trust on our website or to the Campaign or the Trust by post – please see below.

Regular gifts by standing order help us to plan ahead with confidence – if you would like to help us in this way, we will be delighted to send you a standing order form: please contact us for one or download one from our website.

We rely completely on your generosity. We receive no corporate or government funding and have no expensive overheads: all of our office space is donated without charge. 100% of your donation will go directly towards our vital work.

If you want to see real progress towards a future where medical research is based on studying humans rather than animals, please give generously today.

Please copy this section or cut it off and return to us – thank you

❑ Please tick if you wish to see an independent scientific evaluation of animal tests for drug safety

Please send ___Leaflets ___Newsletters ___DVDs ___Booklets ___Petitions

I enclose ❑ £10 ❑ £20 ❑ £50 ❑ £___ to support your vital work

Please make cheques payable to Safer Medicines Campaign OR Safer Medicines Trust.

We can keep costs to a minimum by not sending receipts.
❑ Please tick if you would like a receipt.
❑ Please tick if you do not wish to receive our twice-yearly newsletter.

Name:_____

Address:_____

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❑ Please tick if you are eligible and wish to *gift aid* your donation to the Trust

Thank you for your invaluable support – none of the progress we are making would be possible without it.

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