

Safer Medicines Trust Safer Medicines Campaign

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Newsletter Autumn 2011



Welcome to our newsletter

Kathy Archibald

Director

Safer Medicines Campaign is an independent patient safety organisation of scientists and doctors. Our aim is to protect human health by promoting human-focused medical research and to ensure that 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. Every year, a million Britons are hospitalised by their medicines, 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

"We don't have to look for model organisms any more because we are the model organism" - Nobel laureate Sydney Brenner CH FRS

OUR PATRONS

Tony Benn
Mat Fraser
Dr Caroline Lucas MP
Carol Royle

15,000 signature petition delivered to 10 Downing Street

Former Minister of Technology Tony Benn joined actors Mat Fraser and Carol Royle, plus Green MP Dr Caroline Lucas, to present a 15,000 signature petition to Number 10 Downing Street. The Safer Medicines patrons, alongside other MPs, including David Amess (Conservative), Dr Julian Huppert (Liberal Democrat) and Grahame Morris (Labour), are calling for sophisticated new tests based on human biology to be compared with the animal tests currently used to assess the safety of new medicines.

"No other area of science is still relying on the flawed methodologies of 40 years ago. Now is the time to bring the science into the 21st century"

Dr Caroline Lucas MP

"We hope the Government will listen because this is a really big issue of public safety"

Tony Benn

You can watch a 5 minute clip of the petition presentation, including interviews with our Patrons and some of the MPs on our website.



Carol Royle and Mat Fraser



Dr Caroline Lucas MP and Tony Benn



Tony Benn, Dr Julian Huppert MP, David Amess MP, Grahame Morris MP

Safety of Medicines Bill progress

Senior Conservative MP David Amess presented the Safety of Medicines Bill on 20th July 2010 with a ten minute speech to the House of Commons, which can be viewed via our website.

The Bill calls for a comparison of the ability of a suite of the the latest human biology-based tests with that of currently-required animal tests to predict side effects in people.

Mr Amess said: [“A combination of these approaches promises to predict the effects of new drugs in humans more accurately than animals ever could.”](#)

The second reading of the Bill has been postponed a number of times and is currently awaiting a new date to be scheduled.

Early Day Motion 475



[“We must move safety testing into the 21st century for all our sakes”](#)
Bob Russell MP (Liberal Democrat), primary sponsor of EDM 475

MPs are strongly in favour of the Safety of Medicines Bill. More than 150 MPs have already signed EDM

475: Safety of Medicines, in support of the Bill. We hope that many more MPs will sign the EDM before it closes at Easter 2012.

Open letter to the Prime Minister and Health Secretary

Safer Medicines Trust joined forces with 22 senior scientists to call on the Prime Minister and Health Secretary to compare animal tests for drug safety with newer tests based on human biology. Our letter was published in the world’s leading medical journal, *The Lancet* on 4th June 2011 and is reproduced opposite. The published version can be viewed via a link from our website.

Sky News covered the story with an excellent report and *The Daily Mail* also reported on the story. All coverage can be viewed from our website.

Predictably, the pro-animal-research lobby attacked our letter with a response published in *The Lancet* on 9th July, which can also be viewed via a link from our website. They wrongly accused us of making misleading claims, while making several false claims themselves and seriously misrepresenting our position.

Bizarrely, the authors declared that they have no conflict of interest, yet all of them are members of Understanding Animal Research; a lobby group whose sole purpose is to defend and promote animal experimentation.

Their position seems to be that there is no cause for concern about the safety of medicines and that animal tests should not be criticised. This view contrasts sharply with most of the world’s pharmaceutical companies, which are seeking to address these problems, as well as the medical profession and the US Food and Drug Administration (FDA), the world’s largest drug regulator:

[“The current animal models and human cell lines are inadequate. There is a real need to more accurately model human physiology”](#) – Dr Jason Gardner, GSK Vice-President and Head of Stem Cell Drug Performance Unit (*Bloomberg News*, 23 September 2010)

[“This big rise in serious and fatal adverse drug reactions should be a wake-up call to all doctors... patients may be given drugs that are more harmful than helpful”](#) – Dr Peter Maguire, deputy chairman, BMA Board of Science (*The Independent on Sunday*, 21 October 2007)

[“Currently, nine out of ten experimental drugs fail in clinical studies because we cannot accurately predict how they will behave in people based on laboratory and animal studies”](#) – Mike Leavitt, Secretary of Health and Human Services, FDA (FDA press release 12 January 2006)

[“We want to migrate away from animal testing. We also want to see drug development become more efficient so that fewer resources are wasted”](#)
– Dr David Jacobson-Kram, executive director for pharmacology and toxicology, FDA (*Bloomberg News*, 5 August 2010)

However passionately one supports a particular method, such reluctance to allow it to be scrutinised suggests a fear that it will not stand up to that scrutiny. If animal tests really are the best method we have, then surely its advocates should welcome the opportunity to prove it. That they oppose such a small and inexpensive comparative study speaks volumes. It is high time that the government called their bluff.

Our letter to David Cameron and Andrew Lansley, published in The Lancet on 4th June 2011

We are writing to you as a group of clinicians and scientists to express our concern about the escalating problems of drug failures and adverse drug reactions. The UK pharmaceutical industry is in crisis, as the departure of Pfizer from the Sandwich site makes plain. Likewise, healthcare is in a web of crises, many of which are intimately linked to the pharmaceutical industry's major problems.

Adverse drug reactions have reached epidemic proportions and are increasing at twice the rate of prescriptions. The European Commission estimated in 2008 that they kill 197,000 EU citizens annually, at a cost of €79bn. The cost of new medicines is rising unsustainably, creating an ever-increasing burden on the National Health Service. Meanwhile, many increasingly prevalent diseases, such as Alzheimer's disease, diabetes, many cancers, and stroke, remain without adequate treatments.

The major reason for the rising cost of new drugs is the fact that more than 90% of them fail in clinical trials. Companies need to recoup the cost of development not only for the drug that succeeds, but for the nine others that fall by the wayside.

It is increasingly clear that an important factor contributing to these problems is the over-reliance of the pharmaceutical industry on the use of animals to predict drug behaviour in man. The stark differences not only in the diseases of different species but also the ways that they respond to drugs are now well known. Many studies have shown that animal tests frequently fail to translate to the clinic, with estimates of their ability to predict effects on people as low as 37-50%, or no better than the toss of a coin.

Our reliance on animals to establish safety results in the exposure of clinical volunteers and patients to many treatments that are at best ineffective, and at worst, dangerous. Take for example the notorious Northwick Park clinical trial drug, TGN1412, that left six young men in intensive care in 2006. This drug was demonstrably safe in monkeys at doses 500 times higher than those that nearly proved fatal to the volunteers. Soon after the disastrous trial, an assay that used human cells was developed to predict such an immune system over-reaction. Had this been in use before human beings were exposed, the trial would never have taken place. Surely the time has come for there to be a rigorous assessment of the ability of such human-based tests to improve on the deeply flawed, animal-based approaches in current use?

We call on the Government to initiate a comparison of a set of human-biology-based tests with those currently used, as proposed in the Safety of Medicines Bill 2010-11, to see which are more effective at predicting the safety of medicines for patients. Several new technologies promise increased clinical predictability as well as substantial improvements in efficiency and cost. The Bill does not propose any replacement of animal tests, merely their evaluation of fitness for purpose. 148 Members of Parliament have already signed a motion in support of this proposal.

Some of us recently made representations to the Department of Health, and were told that the Government believes that human-biology-based systems have not been established as being more predictive than are animal studies for developing safer medicines. We agree, but that is because no rigorous examination of such systems has been undertaken. The very purpose of the proposed comparison is to initiate such an examination, which is urgently necessary for the sake of the NHS, the pharmaceutical industry and, most importantly, patients.

We urge you to act now to ensure that the best technologies currently available are used to establish the safety of medicines for patients.

Signatories to the open letter

Kathy Archibald, Director, Safer Medicines Trust, London

Dr Anthony D Baxter (PhD), Chief Executive Officer, Cyprotex plc, Macclesfield

*Dr Kelly BéruBé (PhD), Director, Lung & Particle Research Group, Cardiff University

Dr David Bunton (PhD), Chief Executive Officer, Biopta, Ltd, Glasgow

Dr Margaret Clotworthy (PhD), Director, Human Focused Testing, Cambridge

Dr Bob Coleman (PhD), DSc, Drug Discovery Consultant & Adviser to Safer Medicines Trust

Dr Ann Cooreman (PhD), Chief Operating Officer, Tissue Solutions Ltd, Clydebank

Professor Anne Dickinson, Director, Alcyomics Ltd, Newcastle upon Tyne

*Professor Christopher S. Foster (DSc, FRCPath) Professor of Pathology, Liverpool University

Professor Barry Fuller, Department of Surgery, UCL Medical School, London

Dr B J Nathan Griffiths (PhD), Commercial Director, Abcellute & Abcellute Tissue Bank, Cardiff

*Professor Chris Hillier (PhD), Professor of Physiology, Glasgow Caledonian University

Dr Morag McFarlane (PhD), Chief Scientific Officer, Tissue Solutions Ltd, Clydebank

*Anup Patel, Consultant Urological Surgeon, St. Mary's Hospital, Imperial College Healthcare NHS Trust and Chairman of Clinical Studies Committee, European Association of Urology Research Foundation

*Professor Barbara Pierscionek, Head of Vision Science Research, University of Ulster

Dr Cathy Prescott (PhD), Director, Biolatris Ltd, Cambridge and Chair of the UK National Stem Cell Network Advisory Committee

James Root, Senior Scientist, Pfizer, Sandwich

*Professor Gerry Thomas, Chair in Molecular Pathology, Imperial College, London and Director of Scientific Services, Wales Cancer Bank

*Dr Katya Tsaioun (PhD), Chief Scientific Officer, Cyprotex plc, Macclesfield

Dr J Malcolm Wilkinson (PhD), Chief Executive Officer, Kirkstall Ltd, Sheffield

*Professor Sir Ian Wilmut FRS FRSE, MRC Centre for Regenerative Medicine, University of Edinburgh

Dr Amanda Woodrooffe (PhD), General Manager, Asterand UK Ltd, Royston

Dr Karen L Wright (PhD), Peel Trust Lecturer in Biomedicine, Lancaster University

*Signatories marked thus are honorary Advisers to patient safety charity Safer Medicines Trust.

Our second letter, published in The Lancet on 28th October 2011

Frances Balkwill and colleagues' response to our letter shows the intense resistance of entrenched interests to new technologies that could improve pharmaceutical safety.

Our letter called for the UK Government to invest in an assessment of new technologies for safety testing. Balkwill and colleagues take the position that not only should this research not be done, but that even to question whether animal testing best assures pharmaceutical safety means the questioner is opposed to all animal research and is therefore standing in the way of progress towards new life-saving cures.

Nothing could be further from the truth. We are calling for a paradigm shift in which new models of pharmaceutical safety testing are allowed to compete on their scientific merits against old models. The only thing we have against animal testing is the attitude that it is the only and the best technology for assessing safety. We are in favour of whatever best assures safety. Therefore, we are in favour of assessing which particular *in vivo* or *in vitro* tests are best.

Animal research is far more expensive and labour-intensive than *in vitro* research. Since pharmaceutical safety testing is regulated by the Government, the market forces that would otherwise cause costly and inferior technologies to be naturally supplanted by superior technologies are impaired. We call on the Government to support research to assess the performance of new *in vitro* and other technologies relative to the old *in vivo* technologies so that progress towards safer and more economical new pharmaceuticals can be accelerated.

We are very grateful to The Lancet for publishing a further letter from us on 28th October, which can also be viewed via our website and which is reproduced (in our own format) above.

The following observation seems particularly apposite: "When honest human beings have a vested stake in seeing the world in a particular way, they're incapable of objectivity and independence" – Dr Max H. Bazerman, Professor of Business Administration, Harvard Business School (*New York Times*, 21 March 2007)

Response from the Government

It is extremely disappointing that, even after we have met with key members of the Government to explain the purpose of the Bill, their official position is to deny that the human-based technologies we have presented to them could, in fact, be superior.

Despite Safer Medicines Trust providing evidence that a number of the technologies we are recommending have already demonstrated an ability to identify adverse drug reactions that preclinical animal studies failed to identify, the Department of Health insists that: "human biology based tests are not better able to predict adverse drug reactions in humans than animal tests" (personal communication).

Professor Michael Balls paraphrased the Government's lamentable attitude in his Editorial for ATLA 39, 201–202, 2011: "We can't accept new procedures, because we cannot escape from our belief in the old ones, whatever evidence is put before us."

The Department of Health is not just being badly advised – it is being *wrongly* advised. The consequence is that, as our Lancet letter says: the market forces that would otherwise cause costly and inferior technologies to be naturally supplanted by superior technologies are impaired – to the detriment not only of the pharmaceutical industry but also, and more importantly, of patients and the NHS.

Our dialogue with key Government officials is ongoing and we hope very much to have better news to report in our next newsletter.

However, we may meet with even greater opposition now that Olly Grender MBE is the Government's acting Deputy Director of Communications. Her previous role was Associate Director of Political Lobbying and Media Relations, who represent Understanding Animal Research, among other clients such as the Association of Brazilian Beef Exporters. It would be interesting to know what measures, if any, have been taken to ensure that Political Lobbying and Media Relations' clients, who until very recently were paying Ms Grender to represent them, do not have undue influence on government policy.

Introducing our newest Science Advisers

We are delighted to welcome and introduce our newest Science Advisers, who bring a wealth of expertise from their vast experience across academia and industry.



Professor Sir Ian Wilmut, FRS FRSE

Sir Ian is a pioneering embryologist renowned as the ‘father’ of Dolly the sheep, the world’s first mammal cloned from an adult cell. This accomplishment opened the door to the field of therapeutic cloning, to which Professor Wilmut turned his attention in 2005, in the search for treatments for Motor Neurone Disease. Professor Wilmut is currently the Chair of Reproductive Biology at the Medical Research Council Centre for Regenerative Medicine in Edinburgh. He believes that induced pluripotent stem cells adapted from adult cells hold greater promise than embryonic stem cells for the treatment of degenerative conditions such as Parkinson’s disease, and to treat stroke and heart disease patients, and this is his current focus of study. In 2008, Ian Wilmut was knighted for his services to science.



Professor Chris Hillier PhD

Chris is Professor of Physiology at Glasgow Caledonian University. He has founded, and run as CEO, two successful biotechnology companies: Biopta Ltd, a CRO specializing in human tissue-based drug screening tests utilizing innovative approaches to drug development; and Sistic, a high growth R&D company focused on using epigenetic biomarkers, particularly miRNA, for drug profiling and toxicology screening. Both companies have won Best Company Awards in Scotland. From 2006 to 2007 he was Visiting Professor with Integrated DNA Technologies (Iowa, US), the world’s largest manufacturer of nucleic acids. Professor Hillier has published and presented extensively internationally in both science and business and has won many awards including a Royal Society of Edinburgh Enterprise Fellowship and a John Logie Baird Award for Innovation.



Anup Patel MS, FRCS (Urol)

Anup is a Consultant Urological Surgeon at St. Mary’s Hospital, London. He qualified with CCST, FRCS (Urol) and MS, after gaining MBBS and BSc at St. Bartholomew’s Hospital. He then completed double certified supra-specialty fellowships at UCLA in Complex Endourology-Laparoscopic Urology and Uro-Oncology, which he established as specialist interests on returning to NHS practice in London. Mr Patel chairs the Clinical Studies Committee of the European Association of Urology Research Foundation and is a Member or Board Member of 10 national or international Urology Associations. He is a Journal Reviewer or Editorial Board Member for 20 urology and surgical journals, a Scientific Adviser to the Prostate Cancer Charity and the Pro-Cancer-Research Fund and has been a Reviewer to the National Cancer Research Network and St. Peter’s Trust. He has over 100 publications to his name, as well as many visiting professorships and is regularly invited onto specialist panels at international congresses.



A warm welcome to our newest Patron

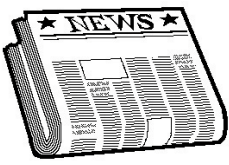
We are delighted that actress Carol Royle has joined us as a Patron. As Carol said when we presented our petition at 10 Downing Street:

“Animal testing is totally illogical, when you realise how far removed from people the results from animal tests can be. It is time for the government to test the tests and find which are the best ones to discover the safety of medicines for people.”



Farewell to Dr Margaret Clotworthy

After 5 years with Safer Medicines Trust, Margaret has left to establish Human Focused Testing (www.humanfocusedtesting.com): a searchable online database to connect providers of human tissues and assays with end-users, such as pharmaceutical and academic researchers. This is an excellent initiative to encourage the use of technologies superior to traditional animal tests. Since our aims are so closely aligned, we are pleased that it keeps us in regular contact. We thank Margaret for 5 great years and wish her every success with her new venture.



Medical Research in the News

What price our medicines?

As the number of clinical trials conducted in India by western pharmaceutical companies continues to grow (due to costs as much as 80% lower), so too does the death toll. The Indian government records that 1,725 people have lost their lives in drug trials in the last four years: rising from 132 deaths in 2007 to 688 in 2010. Dr Chandra Gulhati, who has led several clinical trials in the UK, says that because of gross under-reporting, the actual number of deaths would be much higher than we will ever know.

The purpose of the Safety of Medicines Bill is to protect not just patients but also – and especially – participants in clinical trials, who are currently used as guinea pigs to test drugs for which there is often no prior evidence of safety in humans. The most dramatic example we have seen in the UK of ‘proof of safety’ in animals meaning nothing for people was at Northwick Park Hospital in 2006. Perhaps the reason we have not seen more ‘Northwick Parks’ is because most of them happen on the other side of the world.

In response to Safer Medicines’ concerns about the inadequacy of preclinical testing, the UK Department of Health says, in its standard letters, that: “Without animal testing it is highly likely that a large number of potentially dangerous medicinal products would have to be tested in healthy volunteers and patients in clinical trials. This would be quite unacceptable.”

We agree that it is unacceptable but the fact is that this is currently standard practice. Much of the blame for this can be laid at the door of government regulations that require evidence of safety in animals but *do not* require evidence of safety in the most sophisticated human-biology-based assays currently available.

Ref: Aditi Tandon, www.tribuneindia.com 8 August 2011

Mice an obstacle to heart disease research

Researchers at Washington University in the US studied two drugs to treat heart rhythm disorders, using mouse hearts. What they found was so promising that if it translated into humans, it would have been a major breakthrough. However, rather than put patients at risk in a clinical trial, so many of which end in failure, Dr Igor Efimov and Professor

Colin G. Nichols decided to test the drugs using human hearts, which had been donated for research but were considered unsuitable for transplantation.

In human hearts, the drugs behaved completely differently, and the results suggested that they would have caused fatal arrhythmias had they been administered to people.

“The problem is that at least in the cardiac arrhythmia field, this [animal model] paradigm has had very few successes. Clinical trial after clinical trial has ended in failure... A mouse’s heart beats about 600 times per minute, so you can imagine it is a little different from humans, whose hearts beat on average 72 times per minute... You can mutate in mice the gene thought to cause heart failure in humans and you don’t get the same disease, because the mouse is so different. Since we’ve begun to work with human hearts, we’re finally starting to catch up with animal physiology”
– Dr Igor Efimov, Distinguished Professor of Biomedical Engineering, Washington University

Ref: Diana Lutz, Washington University News, 3 August 2011



Call for “non-furry immunology”

Vaccine researchers in Australia are calling on their government to invest in research into *human* immunology, rather than continuing to invest huge resources in transgenic mouse models.

“Use of murine models to study the immunobiology of infectious diseases, such as malaria and herpes simplex virus, has severely skewed our understanding of immune control of these pathogens in humans, and it could be argued that over reliance on these model systems may have slowed progress in the development of effective vaccines against many human pathogens”
– Dr Rajiv Khanna and Dr Scott R Burrows, Australian Centre for Vaccine Development, Queensland Institute of Medical Research

They anticipate that the large-scale collaborative human-focused studies they are proposing will be opposed by those who study immunology in animal models but they ask:

“How long can we justify investing millions of dollars of taxpayers’ funds on delineating the murine immune system, which in most cases has limited application for human diseases?”

Ref: *Immunology and Cell Biology* (2011) 89, 330–331; doi:10.1038/icb.2010.173

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. The DVD is also free for MPs.



Information for MPs

This double-sided A3 sheet is designed for MPs and is also excellent to display on stalls.



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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.

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.



Booklets

Order *A Critical Look at Animal Experimentation*: a free 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.

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