(*formerly* Europeans for Medical Progress)

Safer Medicines Campaign

PO Box 62720, London SW2 9FQ - Tel: 020 8265 2880 - info@safermedicines.org - www.safermedicines.org

Newsletter Spring 2009

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

Safer Medicines Campaign/
Safer Medicines Trust
PO Box 62720
London SW2 9FQ
Tel: 020 8265 2880
info@safermedicines.org
www.safermedicines.org

INSIDE THIS ISSUE

Please send our postcard to your MP!

Historic Bill launched

A cross-party group of MPs is attempting to bring our revolutionary proposal to evaluate animal tests for drug safety into law. On 26th January, Dr Ian Gibson (Labour), David Amess (Conservative) and Mike Hancock, CBE (Liberal Democrat) launched the **Safety of Medicines (Evaluation) Bill**.

The Bill calls for a comparison of currently-required animal tests with a set of human biology-based tests.

A small but varied sample of drugs which have already been widely used in patients – so we know the problems they can cause – will be run through a suite of the latest tests, to see if they pick up those problems. Comparing these results with the results we already have from animal tests will reveal which methods are most predictive for humans.

The MPs also launched an Early Day Motion in support of the Bill (see p2) in order to allow parliament to show its strength of feeling on the issue.

250 MPs (a majority of those eligible to do so) signed EDM 92, calling for an evaluation, in 2006. Since then, the number of serious adverse drug reactions has risen still higher, to reach an astonishing one million Britons hospitalised by prescription drugs every year, at a cost to the NHS of £2 billion.

These figures simply cannot be ignored. Protecting the public from adverse drug reactions is an urgent priority, which demands an objective assessment of all aspects of the safety testing process. In light of such shocking figures, the evaluation called for in EDM 569 is the only responsible course of action.

A high level of parliamentary support will help to exert pressure on the Government to start listening to the rational, scientific case for the comparison we seek, which is supported by 83% of GPs surveyed.

ACTION

Your help in persuading MPs to sign EDM 569 is **vital! Please send the enclosed postcard to your MP today**. You can check our website or call us to find out whether they have already signed – if so, you could change the wording to thank them instead!

Please order further copies of the postcard and enclosed information sheet to distribute if you can.

For all our sakes, we must move the safety testing of medicines into the twenty first century.

'These impressive technologies deserve a fair trial, to see if they could do a better job of protecting patients.'

Dr Ian Gibson MP, Chair of the All Party Parliamentary Cancer Group, member of the Select Committee on Innovation, Universities, Science and Skills, the All Party Parliamentary Patient Safety Group and many other science and health groups.

'If replacing animal tests could benefit drug safety, who could fail to be happy?'
David Amess MP
Member of Health Select Committee 1998 - 2008

'It is astonishing that animal testing has never been scientifically evaluated. The process is long overdue.'
Mike Hancock CBE MP
Sponsor of EDM 92 in 2006

Early Day Motion 569

That this House believes the safety of medicines should be established by the most reliable methods available in order to reduce the large and increasing toll of serious adverse drug reactions and calls upon the Government to initiate an unprecedented comparison of currently required animal tests with a set of human biology-based tests, as required by the Safety of Medicines (Evaluation) Bill 2009, to see which is the most effective means to predict the safety of medicines for patients.

Media coverage

We are delighted that the launch of the Bill was reported in the Daily Telegraph on 26th January and will be covered by BBC1's Inside Out programme on 25th February in the Eastern region by an interview with our science consultant Dr Margaret Clotworthy. Viewers in other regions will be able to watch via the BBC website for one week following transmission.

Our director, Kathy Archibald, was interviewed on BBC Radio Scotland and we had letters published in the Herald and the Scotsman. Our conference (below) was also covered in an article in *The National* in Abu Dhabi! Visiting Reader in Science at Aston University, Robert Matthews, wrote:

'An international conference held last week at the Royal Society in London, organised by the UK-based Safer Medicines Trust, highlighted progress in a host of techniques which allow drugs to be tested directly on human cells. And in stark contrast to animal testing, a genuine effort is being made to gauge just how reliable such tests are in predicting the effect of the drugs in patients.

It will be some years yet before such techniques become the standard means of assessing new drugs. Until then, we can only hope that the lottery of animal tests does not lead to another medical disaster on the scale of thalidomide.'

Groundbreaking conference at the Royal Society

Safer Medicines Trust hosted an unprecedented scientific conference; **Speed and Safety in Drug Discovery** at London's prestigious Royal Society on 26th November. Eleven eminent scientists from around the world who work at the cutting edge of developing drug safety test methods that focus on *human* biology addressed an international audience

Science Consultant to the Trust, Dr Margaret Clotworthy, opened the meeting

on how to move drug safety testing into the 21st century. The scientists, pharmacists and doctors who attended represented pharmaceutical companies, academia, biotech companies and the Medicines and Healthcare products Regulatory Agency – the body responsible for licensing drugs in the UK.

A recurring theme throughout the day was how ethically donated human tissues, and cells derived from them which can be grown indefinitely in the lab, can bring unique advantages to the drug testing process: these tissues enable researchers to get human-specific answers to their questions. As some speakers commented, even a mouse engineered to have a 'humanised' characteristic is still a mouse in every other respect.

Delegates and speakers swap ideas over tea

A way of circumventing the vexing problem of how to test a drug in a whole human system – without actually exposing humans – was addressed by Hurel's (the name being derived from the words *Hu*man and *Rel*evant) biochip, which uses interconnected tissue pieces from the body's organs to represent the human body in miniature.

A 'clinical trial in a test-tube' using immune cells from blood donations to test vaccines greatly impressed the audience. Advanced computer models to predict drug effects were discussed, with examples of how they have already helped real patients. Two exciting technologies for taking drugs safely into humans for the first time, microdosing and microdialysis, were explained.

Finally, Dr Ian Gibson MP spoke about the economic value of these technologies, as well as their value to public health. He endorsed our proposed comparison and enthused about his new Bill in support of it. More detailed summaries of all the presentations may be found below.

The presentations generated many thought-provoking questions, with animated discussions continuing during the breaks and after the conference. Ideas flowed, and collaborations developed as a result of bringing the researchers developing new drugs together with the scientists designing the latest safety tests will hopefully move the field of drug safety testing forward, hastening the regulatory acceptance and widespread adoption of these groundbreaking technologies.

There was great interest in our idea of comparing a battery of these high-tech methods with the animal tests that are currently required by law. We hope that collaborations forged at our conference may contribute to realising the comparison at last. We are thrilled to have been instrumental in bringing such a diverse array of scientists together for the first time. The conference was buzzing and many people remarked on how unique and valuable it was – see some of their comments below:

'A conference which was long overdue! Excellent speakers and programme which highlighted the importance of developing drug testing methods incorporating human tissue' – Dr Philip Roberts, University of Central Lancashire.

'Thought provoking and stimulating' – Dr Alfred Thumser, University of Surrey.

'Excellent programme, eminent speakers, good presentations' – Dr Bob Sheldrick, Asterand.

'Excellent range of new and state-of-the-art technologies. Particularly good to see pharma, biotech, academia and even a politician together. Great talks, exciting prospects and challenging ideas. The field is moving rapidly and it is becoming increasingly difficult for industry to ignore these developments' – Professor Chris Hillier, Glasgow Caledonian University.

We are delighted that the event has been reported in two journals in February: *Alternatives to Laboratory Animals* and *Regulatory Affairs Journal Pharma*. The articles have been reproduced on our website with the very kind permission of both journals. The full proceedings will be published as a special supplement of *Alternatives to Laboratory Animals* in June, which we will make available to interested scientists who could not attend the event itself. We will also be pleased to sell copies of the proceedings.

Our science advisor, Dr Bob Coleman, was quoted in *Regulatory Affairs Journal Pharma* as saying:

'Frankly, it is only through a study such as that proposed by the Safety of Medicines Bill that the real strengths and weaknesses of human biology-based testing will become apparent. Having said this, I truly believe that with our present level of knowledge and technological strengths, if all animal testing was banned next week, all brains would be directed to how best to exploit human biology – *in vitro, in vivo* and *in silico* – and a more reliable testing paradigm would emerge.'

Recordings of the presentations along with the speakers' slides and biographies are available at www.drugtestingconference.com.

The conference was very expensive to organise, for such a tiny charity as ours, so we would greatly appreciate donations to help to plug the enormous hole that it has left in our finances!

Summary of presentations

'We should focus on the target species, ie man.'

The day began with Dr Bob Coleman, consultant to the pharmaceutical industry and science advisor to **Safer Medicines Trust** introducing the problems faced by companies attempting to bring new drugs to market. Dr Coleman went on to explain how our proposed comparison could help solve some of these pressing problems.

Dr Coleman founded the world's first human tissue research company, Pharmagene (now Asterand) and was keen to emphasise the need for better access to ethically donated human tissues, primarily through improved infrastructure to collect and deliver samples to researchers who need them.

Dr Paul Newbold from AstraZeneca explained the importance of being able to make the right decision about whether to pursue a drug as early as possible in the drug development process, and guided the audience through examples of where AstraZeneca has successfully employed an exciting range of the latest tests to do this. He pointed out that it is particularly difficult to predict how patients will respond to novel types of drug, such as those designed specifically to interact with the *human* immune system (e.g. the Northwick Park Hospital clinical trial drug from March 2006) and that in this area it was unwise to rely too heavily on animal test results.

'The animal data… often bears no resemblance whatsoever to the ultimate human data.'

Professor Chris Hillier gave an inspiring account of the breadth of tests that Biopta, a company he co-founded, has established using exclusively human tissues obtained by taking biopsies (tiny samples) from donors. His talk focussed particularly on tests they have developed to assess drugs' effects on cardiovascular tissues around the body.

Dr Greg Baxter introduced Hurel's revolutionary human-on-a-chip technology. Hurel's chip is about the size of a postage stamp and comprises tiny compartments, each containing a sample of tissue from various parts of the human body, linked by a circulating blood substitute to which drugs can be added to find out their effects on a whole system – something that it is often claimed only animal tests can provide.

'No more place for animal studies.'

Professor Johannes Doehmer, from the Technical University of Munich and biotech company BioProof, impressed upon the audience the fundamental importance of evaluating how drugs are metabolised in a *human* context rather than in animals. He specialises in developing rapid, *predictive*, cost-effective tests using cells engineered to contain the major genes responsible for determining what happens to drugs in the body. He was at pains to point out that using animals to try to predict what would happen in humans was simply not scientifically valid.

Dr Quin Wills, founder of Cambridge company Simugen, explained how their tests use a combination of human cells, genetic analysis and advanced computer models to determine whether a new drug is dangerous. The tests they have developed are fast and inexpensive enough to use very early in drug development whilst being surprisingly accurate and easy to interpret.

Professor Zvia Agur, founder of Israeli company Optimata, astonished listeners with the ability of their mathematical models (virtual patients) to predict safe drug dosing levels in real individual patients, hastening an era of truly personalised medicine.

'Animals can never offer completely predictive results of a new vaccine or therapy.'

Professor Russell Higbee wowed the audience with his account of the 'clinical trial in a test-tube' that Florida company VaxDesign has developed, using donated blood to grow up mini versions of hundreds of human immune systems for testing vaccines.

Dr Katya Tsaioun, founder of Apredica, entertained the audience with her witty cartoon depicting the pitfalls of inappropriate pre-clinical testing (please see our website for a link to the cartoon). Apredica's expertise lies in testing new drugs as early as possible in human cell-based assays covering a variety of tissues, from airways to kidneys.

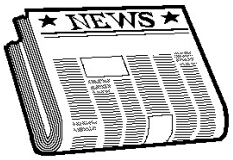
Professor Markus Mueller from the Vienna Medical University spoke authoritatively about the use of microdialysis to test new drugs very safely, using tiny localised doses in humans. He likened methods of looking for drug toxicity wherever it is most convenient (frequently in animal tests) to hunting for lost keys under a street light simply because that was where the light was!

'The best model for humans is human.'

Dr Mark Seymour from Xceleron revealed how microdosing can be used to find out, with supreme accuracy, how humans metabolise new drugs, but very safely and much earlier than would otherwise be possible.

'Maybe next time, Wembley Stadium won't be big enough to take all the people who are interested!'

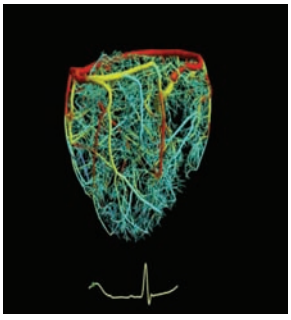
We were delighted that Dr Ian Gibson MP managed to take time out from his parliamentary duties to speak about his Safety of Medicines (Evaluation) Bill. He discussed how it takes a long time for the law to change but that after forty years, the time has come for these new technologies. He said it is now up to politicians to sit up, listen and deliver on such an important issue.



Medical Research in the News

Virtual humans a step closer

Dr Peter Kohl, a researcher at Oxford University, where Professor Denis Noble pioneered the virtual heart (see our film, *Safer Medicines*) is driving research into the use of computer models to improve heart surgery. His team aims to use heart scans combined with modelling to investigate surgical options before the patient is operated on, to ensure they receive the best treatment first time. His research is part of an international drive to model the human body known as the Virtual Physiological Human initiative.



Meanwhile, the US Food and Drug Administration, the world's largest drug regulator, has entered into a partnership with Entelos, a company which specialises in modelling patients and even whole clinical trials. Their advanced computer simulations, which they liken to 'flight simulators' for predicting how a drug will react, will be used to focus particularly on risks associated with the heart, to try to improve the safety of drugs released onto the market. It is believed that had the Entelos system been available at the time, the Vioxx painkiller tragedy, where tens of thousands of patients died of heart attacks and strokes, could have been avoided. James Karis, CEO of Entelos remarked:

'Currently, it is a trial and error process to try and predict clinical response, but given the high failure rate [of investigational drugs], clearly it doesn't work very well.'

References: BBC News online 12th January 2009, Outsourcing-pharma.com, 23rd Decemeber 2008, Pharmalot.com, 12th Decemeber 2008.

Test to prevent another Northwick Park

Using a mixture of human immune cells, scientists have developed a test that replicates the devastating side effects seen in six young volunteers who almost died while testing a new drug that had been shown to be safe at 500 times the dose in monkeys. The test is already being used by drug companies working on other drugs that may interfere with the human immune system.

'We have made significant progress in designing new in vitro tests that hopefully will avoid the consequences that occurred with TGN1412 (the Northwick Park Hospital drug); indeed such tests could prevent harmful drugs of this type even reaching the animal testing stage' – Dr Stephen Poole, National Institute for Biological Standards and Control

Reference: *British Medical Journal* 337:a3061, 18th December 2008.

Stem cell breakthrough

'The animal models are pretty useless, to be honest' – Professor Clive Svendsen, University of Wisconsin-Madison, USA

Spinal Muscular Atrophy (SMA) is a devastating condition that kills nerve cells controlling muscles, causing paralysis and death, usually by the age of two. American scientists have now been able to recreate nerve cells affected in the same way, using skin cells from an affected child. The skin cells were 'reprogrammed' to turn into stem cells and then prompted to become nerve cells, meaning that a limitless supply of these cells will now be available for study.

Professor Svendsen explains: 'Now you can replay the human disease over and over in the dish and ask what are the very early steps that began the process.'

The cells have already been used to test two potential treatments, and should be available for large scale drug screening within a couple of years. According to Professor Chris Mason, a leading stem cell researcher at University College London, these cells will 'play a major role in future drug discovery.'

Reference: *Nature,* 22nd December 2008.

New drugs more likely to harm than help

'Drug disasters are literally built into the current system of drug testing and approvals in the United States' – Donald Light, Professor of comparative health policy at the University of Medicine and Dentistry of New Jersey

Professor Light's study shows that whilst one in seven new drugs is superior to existing treatments, two in every seven result in serious side effects. Thus new drugs are twice as likely to harm some patients as to provide them with benefits superior to existing drugs. Professor Light believes this is partly due to the fact that drugs are approved based on superiority to a placebo, rather than to existing drugs. Another reason is that clinical trials are too short and use volunteers who are not representative of the populations who will actually use the medicines.

The European Commission has estimated that across the EU, adverse drug reactions cost 197,000 lives and €79 billion each year. Hopefully this situation will be improved by new EU regulations mandating enhanced monitoring of drugs for side effects after they have been marketed.

References: American Sociological Association press release, 3rd August 2008, Outsourcing-pharma.com, 15th December 2008.

Drugs double risk of death

A large study of newer treatments for schizophrenia, autism and dementia, such as Risperdal, Zyprexa and Seroquel, has found the drugs double the risk of death from sudden heart failure in patients over the age of 30. Previous research showed that three out of four new drugs tested were no more effective than their older and much less expensive predecessors for treating schizophrenia, and no better than placebos for dementia-related psychosis.

A study funded by the Alzheimer's Research Trust reveals that up to 23,500 dementia patients are being killed by the drugs each year. A report from the all-party parliamentary group on dementia stated last year that almost three quarters of those taking the drugs were given them inappropriately – at a cost of more than £60 million a year.

References: *New York Times*, 14th January 2009, *The Times*, 9th January 2009.

New study blames animal tests for thalidomide

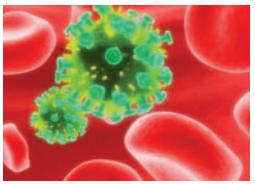
'The rapid and fatal approval of thalidomide at that time ultimately was a consequence of the sole use of thalidomide-insensitive species in animal toxicity tests.'

Fifty years after the thalidomide tragedy, a new paper was published in December that reveals why rats and mice are resistant to the terrible effects of thalidomide in humans.

This knowledge could help scientists to make thalidomide safer for those who depend on it today for conditions including leprosy and multiple myeloma.

The supreme irony of thalidomide is that while the tragedy prompted worldwide regulations demanding animal tests for drug safety, those same animal tests would still fail to alert us to the hazard of thalidomide even today.

Reference: *Molecular Pharmaceutics*, 1st December 2008.



Resistance to HIV

By studying people who have been exposed to HIV and yet do not go on to develop AIDS, scientists have discovered what makes these lucky few resistant. Using genetic techniques on blood samples, they found that such people have cells that produce more of a particular protein. When cells from patients with AIDS were stimulated in the laboratory to produce more of the same protein, they too were much more successful at killing virus-infected cells. It's hoped that this discovery will lead to vaccines that could stimulate everybody's immune systems to behave in the same way.

Refs: *The Scientist*, NewsBlog 4th Dec 08, Migueles et al, *Immunity* **29 (6):** 1009, 4th Dec 08.

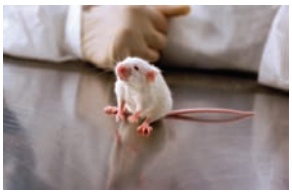
Cancer genetic blueprint revealed

Scientists have decoded the complete DNA of a cancer patient and traced her disease to its genetic roots.

Dr Francis Collins, former director of the US National Human Genome Research Institute, called the study a 'true landmark in cancer research.' He said:
'In the past, cancer researchers have been 'looking under the lamp-post' to find the causes of malignancy - but now the team from Washington University has lit up the whole street.

This achievement ushers in a new era of comprehensive understanding of the fundamental nature of cancer, and offers great promise for the development of powerful new approaches to diagnosis, prevention and treatment.'

Reference: BBC News online, 6th November 2008.



Call to study humans, not mice

'Mice are lousy models for clinical studies' – Professor Mark Davis, Director of the Stanford Institute for Immunity, Transplantation and Infection, California.

Prof Davis calls for a national or even international effort to collect information from human blood and tissue samples. He says:

'We can't depend on the mouse for all the answers, because in some cases it's not giving us the right answers. But think about what we can do with people. People come to hospitals, get vaccinations, give blood and tissue samples for routine lab tests and clinical trials. We're not learning nearly as much as we could from these samples.

We seem to be in a state of denial, where there is so much invested in the mouse model that it seems almost unthinkable to look elsewhere.'

Reference: *Immunity* 29: 835, 19th December 2008.

Personalised Medicine

Blood test for lung cancer treatments

Lung cancer still kills 30,000 people every year in the UK alone. By looking at patients' blood, scientists have discovered that they can predict which patients are most likely to be resistant to treatment. This could help doctors to decide what sort of treatment a patient needs early on, help monitor progress and perhaps select patients for particular clinical trials.

Reference: BBC News online, 31st December 2008.

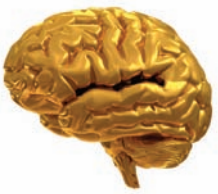
Test for Tamoxifen resistance

'Previously our understanding of why this occurred could be compared with trying to fix a broken car without knowing how the engine worked' – Dr Jason Carroll, Cambridge Research Institute

Research has previously shown that only women with certain genetic features will respond to anti-breast

cancer drug Herceptin, and this finding has now been extended to another important treatment, tamoxifen. By studying tissues donated by cancer patients, scientists in Cambridge have discovered that they can predict the quarter of patients whose tumours will become resistant to tamoxifen, meaning that those patients can be treated with a more suitable drug from the start. The new test, which should be available within five years, stands to benefit thousands of women. Meanwhile, understanding how some tumours become resistant to drugs could help researchers to develop new anti-cancer treatments.

References: BBC News online, 13th November 2008; *New York Times*, 29th December 2008.



Childhood brain tumour clue

'We think this important finding will be vital in guiding our future research' –Dr Lesley Walker, Cancer Research UK

The genetic root of an aggressive form of childhood brain cancer, pilocytic astrocytoma, has been uncovered by another group of Cambridge scientists who conducted genetic scans of patients' brain tumours. It should now be possible to tailor treatments to patients more accurately, as scientists now have a way of differentiating between certain types of cancer. Also, because researchers know what genetic fault triggers the development tumour development, they can begin to construct treatments designed to specifically target the cause of the tumour.

Reference: BBC News online, 1st November 2008.

Personalising brain tumour treatment

'This is a hugely important development for the patients in terms of morale' – Dr Willie Stewart, head of Institute of Neurological Sciences

Doctors from Glasgow's Southern General Hospital have identified a way of profiling patients' tumours in order to identify who would benefit most from radiotherapy, and who from chemotherapy. The researchers have discovered that tumours have different molecular 'signatures' or profiles that identify them as being more responsive to one treatment. This discovery means that many patients will be spared unnecessary side effects, and receive the most effective treatment as early as possible. More centres plan to offer the same tailored service soon.

Reference: BBC News online, 6th November 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

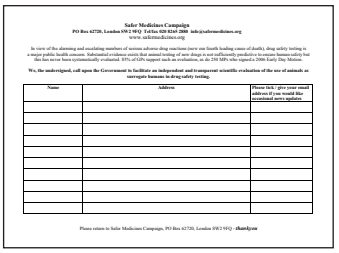
Watch ***Safer Medicines*** on our website or buy a copy: **only £5!** If you know any secondary school teachers or lecturers please encourage them to ask us for a free copy. An order form is on our website.

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 ___A3 Sheet ___Postcards ___Booklets ___Petitions

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

Please make cheques payable to either 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 would prefer to receive our twice-yearly newsletter by email - please write your email address clearly.

Name:_____

Address:_____

_____

Email:_____

❑ Please tick if you are eligible and wish to *gift aid* your donation to the Trust (*only* the Trust is eligible for gift aid).

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

Printed on recycled paper

Safer Medicines Campaign/ Safer Medicines Trust, PO Box 62720, London SW2 9FQ
Tel: 020 8265 2880 - info@safermedicines.org - www.safermedicines.org