

Europeans *for* Medical Progress

Europeans for Medical Progress is a non-profit research and educational institute dedicated to improving human health by modernising biomedical research. We focus on rigorous scientific analysis of animal experimentation to assess the balance of help or harm to human health. We oppose animal modelled research as a method for seeking cures and treatments for human disease based on overwhelming scientific evidence that findings from animal models cannot be reliably extrapolated to humans. When such findings are extrapolated to humans, patients, consumers and research volunteers are harmed and medical progress is hampered. We communicate the urgent need to focus on methods of research that truly serve the interests of patients, rather than corporate finances.

Our educational work functions as a separate charity: EMP Trust.

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Newsletter Winter 2005/06

House of Commons Debate

Late 2005 saw an extraordinary discussion meeting in the House of Commons, entitled “Is animal experimentation helpful to medicine?” EMP’s science director, Dr Jarrod Bailey and science consultant, Dr John Pippin – Senior Medical Advisor to the Physicians Committee for Responsible Medicine – opposed Professor Colin Blakemore, Chief Executive of the Medical Research Council and Dr Simon Festing, Executive Director of the Research Defence Society.

As always on such occasions, EMP presented scientific data making a compelling case against the medical value of animal experimentation, while our opponents’ case rested on the notion that experimenting on animals is better than eating them or hunting them. They present no data in support of their position, relying instead on hyperbole such as “all medical advances of the past 100 years have depended on animals” – a claim for which we request evidence each time but which is never provided. In fact, the Advertising Standards Authority upheld a complaint made by EMP when it ruled in October that the claim made in a

leaflet by the Association of Medical Research Charities that “Some of the major advances in the last century would have been impossible without animal research” is misleading and told the AMRC not to repeat it.

Our opponents were completely unable to refute such devastating indictments of animal research as the fact that 30 AIDS vaccines successful in primates have failed in clinical trials, or that out of 700 stroke treatments successful in animals, not a single one of more than 150 tested in humans has emerged as safe and effective, or that Vioxx, which caused an estimated 320,000 human heart attacks and strokes was marketed partially on the strength that it is cardioprotective in mice, rats and monkeys. Instead – predictably – they resorted to personal attacks, including the favourite tactic of labelling opponents as animal rights activists. Dr Festing’s recent exploits in this vein include telephoning colleagues of Dr Bailey at Newcastle University to ‘inform’ them that Dr Bailey is ‘involved in animal rights’ in a desperate attempt to tarnish his standing.

It was a pity that a larger audience could not have been treated to this revealing display of the contrast between the two sides in this debate but many more people were able to get a flavour of the event from an article in the Independent, reproduced with permission here:

The Independent, 16 Jan 2006
Life&culture: The Green Pages
The Green Goddess:
Julia Stephenson
(j.stephenson@independent.co.uk)



Dr Jarrod Bailey & Dr John Pippin

While the debate rages on, lab rats are still suffering

The last time I visited the Houses of Parliament was seven years ago to have tea with my then romantic interest, who was a member of the House of Lords. It was a comforting occasion, with homely waitresses, toasted teacakes and lashings of "your lordships". This antiquated vision has fortunately been swept away and replaced by Blair's hand-picked cronies. Far more democratic!

I only share this blast from my past because my most recent visit wasn't so comforting. For a start, the queues! It's easier to get through customs at Tel Aviv airport these days than through security at the House of Commons.

This time I was attending a debate: "Is animal experimentation helpful to medicine?" Pro-vivisectionists Professor Colin Blakemore, chief executive of the Medical Research Council, and Dr Simon Festing, executive director of the Research Defence Society were ranged against Dr Jarrod Bailey, science director of Europeans for Medical Progress, and Dr John Pippin, consultant to the Physicians Committee for Responsible Medicine.

Drs Bailey and Pippin explained how human tissue, imaging, computer models and microdosing offer more reliable data than can ever be obtained from animals.

Exciting developments like pharmacogenomics that use human DNA chips allow the right medicines to be prescribed for the right patients. This reduces adverse drug reactions, which kill thousands of people and cost the NHS £500m every year.

Owing to habit and cost, most companies still rely on animal tests - even though they often fail to predict hazards for humans. The arthritis drug Vioxx was linked with fatal heart attacks and strokes, though tests in mice and monkeys had shown it was "safe".

Testing on animals tells us about animals, not people. Aspirin can be fatal to cats; penicillin kills guinea pigs; arsenic poisons humans but not sheep; lemon juice poisons cats and rabbits; thalidomide can be hazardous to humans but is safe for most animals; 30 HIV vaccines worked well in monkeys but all have failed in human trials; 700 stroke treatments have succeeded in animals but not one has succeeded in patients.

I was shocked that instead of refuting any of these arguments, Dr Festing (who has never been a research scientist) suddenly began accusing Dr Pippin of being a radical animal rights campaigner and connected to Peta. Dr Pippin reiterated he had no

links with any animal rights groups or charities, that he was a fully paid-up scientist and committed to proving the ineffectiveness of animal testing through scientific means only.

It makes me livid that anyone who argues against vivisection is branded a radical (some of us are quite reasonable). This tarnishes the fair-minded guardians of animal welfare and makes it harder for them to get a fair hearing.

Interestingly, Dr Festing's father is a consultant for Harlan UK, which is one of the world's largest suppliers of animals to research laboratories. He also holds financial interests in a number of pharmaceutical companies, including GlaxoSmithKline and Celltech.

The tragic thing is that while we humans bicker and pharmaceutical companies line their pockets, in laboratories all over the world animals are suffering unimaginably agonising deaths when there are already far more effective testing methods available.

It is refreshing to see such an honest account of a debate about the scientific validity of animal experimentation printed in a national newspaper; having become more accustomed to the kind of dishonest version of events produced by the Observer (see our last newsletter). George Orwell observed that "In times of universal deceit, telling the truth becomes a revolutionary act." We hope that other newspapers will follow the Independent's courageous lead and that the ramifications of this article will be far-reaching.

We were pleased to observe a boost in support for EDM 92 following the debate: there were 149 signatories as we went to press.

Action – EDM 92

149 MPs have already signed Early Day Motion 92: "Animal testing of drugs", revealing that there is substantial parliamentary support for the idea of a scientific evaluation of animal testing. However, in order to turn that support into action, we would like to double the number of signatories and for that we need **your** help. If your MP has not already signed, please ask them to do so before late November 2006. We have produced a postcard (enclosed) in order to enable you to do this with the minimum of effort. Every MP has received a briefing from us, setting out several compelling reasons to assess the efficacy of animal tests, as itemised on our website at www.curedisease.net/news/050525.shtml.

You can find the name of your MP at www.locata.co.uk/commons or the House of Commons information line 020 7219 4247.

EDM 92 reads: "That this House, in common with Europeans for Medical Progress, expresses its concerns regarding the safeguarding of public health through data obtained from laboratory animals, particularly in light of large numbers of serious and fatal adverse drug reactions that were not predicted by animal studies; is concerned that the Government has not commissioned or evaluated any formal research on the efficacy of animal experiments, and has no plans to do so; and, in common with 83 per cent. of general practitioners in a recent survey, calls upon the Government to facilitate an independent and transparent scientific evaluation of the use of animals as surrogate humans in drug safety testing and medical research."

Please contact us if you are able to distribute further copies of the postcard: maybe your local library, health food shop or GP surgery would display them for you. We also have a petition to gather public support for an independent scientific evaluation of animal testing – please print a copy from our website or request a copy from us by post. You can also add your support on our website.

Review of Primate Use Published

It is very rare for papers critical of animal experimentation to achieve publication in the scientific literature. It is therefore particularly important that EMP has succeeded in gaining publication of a critical review of primate research in the December issue of the journal *Biogenic Amines*: "Non-human primates in medical research and drug development: a critical review": *Biogenic Amines*, Vol. 19, No. 4-6, pp. 235-255 (2005). Copies of the paper are available from EMP for £3, including postage. You can also view the paper on our website. Here are the opening and closing paragraphs:

There is much current debate surrounding the use of non-human primates (NHPs) in medical research and drug development. This review, stimulated by calls for evidence from UK-based inquiries into NHP research, takes a critical view in order to provide some important balance against papers supporting NHP research and calling for it to be expanded. We show that there is a paucity of evidence to demonstrate the positive contribution or successful translation of NHP research to human medicine, that there is a great deal of often overlooked data showing NHP research to be irrelevant, unnecessary, even hazardous to human

health and to have little or no predictive value or application to human medicine. We briefly discuss the reasons why this may be so, reflect upon the consequences for future medical progress and, on the basis of our findings, suggest a more scientifically robust and promising way forward.

For the benefit of human medical progress, it is surely time for objectivity, transparency and honesty in the assessment of NHP models and their contribution to medical science. Only by ensuring this can we be confident that we are utilizing scientific technology to the full, performing the best translational research possible, and making real progress towards the relief of human suffering and disease.

Reaching Major Science Journals

The most popular science journals reach a huge audience and wield substantial influence not only over scientists but also over policy-makers, so getting our message heard in leading journals is a very important goal. Publication of the following editorial (co-authored by Dr Bailey) in the *British Medical Journal (USA)* is immensely gratifying:

Animal Tests Yield Misleading Results

BMJ USA: Education and debate

Which drugs cause cancer?

Despite President Nixon's War on Cancer, launched in 1971, and billions of dollars spent since then, cancer remains the second-leading killer of Americans. Around 40% of us will get cancer, and half of us will die from it. This ceaseless tide of human suffering starkly questions the effectiveness of our strategies, including the accuracy of our methods for identifying human carcinogens.

Millions of laboratory animals have been sacrificed for this purpose. Thousands of chemicals, including ever-increasing numbers of therapeutic drugs, are consequently described as potentially carcinogenic. Yet, are animal experiments really predictive of human carcinogenicity?

The agency most responsible for protecting Americans from environmental contaminants is the Environmental Protection Agency (EPA), and the chemicals of greatest public health concern are described within its Integrated Risk Information System (IRIS) toxic chemicals database. We recently surveyed this database to assess the human utility of animal carcinogenicity data. Most chemicals lack human exposure data and possess only animal carcinogenicity data. In the majority of cases,

however—58.1% (93/160)—we found that the EPA considered the animal data inadequate to support the useful human carcinogenicity classifications of probable carcinogen or non-carcinogen.

But at least the animal data were predictive for 42% of chemicals. Or were they? A comparison of EPA carcinogenicity classifications with those assigned by the World Health Organization's International Agency for Research on Cancer (IARC) yielded disturbing results. For the 128 chemicals with human or animal data assessed by both agencies, human carcinogenicity classifications were similar only for those 17 possessing significant human data. For the 111 primarily reliant on animal data, the EPA was far likelier than the IARC to assign carcinogenicity classifications indicative of greater human risk.

The IARC is widely recognized as the world's leading authority on carcinogenicity assessments. Such profound differences in carcinogenicity classifications of identical chemicals between the IARC and the EPA appear to indicate that in the absence of human data the EPA is over-reliant on animal carcinogenicity data. Consequently, the EPA tends to over-predict carcinogenic risk.

The questionable reliability of EPA carcinogenicity assessments was also the topic of a 2000 Congressional investigation. It concluded that despite being advertised as quantitative, science-based classifications, some were, in fact, more grounded in EPA policy favoring classifications indicative of greater human risk.

No agency responsible for protecting public health is ever likely to be sued for excessive caution. As every medical professional is acutely aware, however, the converse in the case of medical mishap is not true. One cannot help but sympathize with the concerns of EPA policy-makers in the world's most litigious nation. Nevertheless, the resultant EPA carcinogenicity classifications cannot be regarded as generally correct.

On the face of it, the EPA's heavy reliance on animal carcinogenicity tests seems understandable. There is a longstanding tradition of animal testing, and virtually all human carcinogens, when tested in sufficient animal species, have generated positive results. However, if enough animal testing is conducted, it appears that carcinogenesis will eventually occur in some species regardless of human risk. Of 20 human non-carcinogens studied in animals, 19 produced carcinogenic effects.

The problem with animal carcinogenicity tests is not their lack of sensitivity for human carcinogens, but rather their lack of human specificity. A positive result

has poor predictive value for humans. Reasons for this include the predisposition of chronic high-dose bioassays for false-positive results due to the overwhelming of natural tissue repair mechanisms, and the unnatural elevation of cell division rates during ad libitum feeding studies. Such factors render accurate extrapolation from animals to humans virtually impossible.

The protracted time frames of animal carcinogenicity studies, and their substantial drain on human, financial, and animal resources, present other important disadvantages. Standard rodent bioassays take at least three years to plan, execute, and interpret. They have cost hundreds of millions of dollars and have consumed millions of skilled personnel hours. They also account for many of the animals reported to be experiencing the highest levels of pain and distress in laboratories.

Modern alternatives exist, such as quantitative structure-activity relationship (computerized) expert systems, which predict biological activity based on chemical structure; enhanced in vitro assays; and cDNA microarrays, which allow detection of genetic expression changes long before the development of macroscopic lesions. These methods have the potential to yield superior human specificity results, in greatly reduced time frames, with greatly reduced demands on financial, personnel, and animal resources.

Inexplicably, however, regulatory agencies have been frustratingly slow to accept modernized testing protocols. With some 400 new drugs now introduced annually, a radical rethinking of our reliance on prolonged animal testing is required. The development and implementation of rapid and predictive non-animal assays will minimize cancer losses to society, and might even restore our faith in the accuracy of the neoplastic warnings metastasizing throughout our medical formularies.

Andrew Knight, *research scientist*¹; Jarrod Bailey, *medical scientist*²; Jonathan Balcombe, *research scientist*³

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An Awful Lot of 'Heretics'

A heretic is defined as 'A person holding an opinion at odds with what is generally accepted.' This doesn't mean

that heretics are automatically wrong: a view being widely held is no guarantee of its validity. Throughout history heretics have been pivotal in accelerating scientific discovery, and have frequently been 'before their time,' establishing groundbreaking truths about science and the natural world decades before their acceptance by the societies that derided them.

Supporters of animal experimentation have dismissed opponents as heretics for over a century. But, as with Copernicus' suggestion that the Earth was *not* the centre of the universe, and the postulation of the 'Big Bang' theory of the origin of the universe, the number of scientists moving camp to side with the heretics is growing substantially. A sense of this, and the direction in which things are moving, can be gleaned from two events that took place in the summer of 2005.

At the end of August, almost 1000 people attended the 'Fifth World Congress on Alternatives and Animal Use in the Life Sciences' in Berlin, the majority of whom were scientists. Many of the delegates have worked for years to develop scientific methods that can exceed the stringent 'validation criteria' set for them, in the hope that they will be accepted and used in preference to the animal tests that could never reach the same standards – and indeed have never been required to do so.

Despite being chronically under-funded, the scientists presented evidence of amazing developments and progress that promise to revolutionise our approach to the testing of drugs and chemicals, and the use of animals in medical research. Examples include computer programmes that can predict the toxicity of drugs and chemicals with unprecedented accuracy; the use of human stem cells to assess the hazards posed by these substances; new models of the skin to test for harmful absorption and corrosion properties; enhanced use of 'genomic' technologies to screen drugs and to elucidate the causes of human disease, and many more.

But for the first time there was also a widespread frustration at the attitudes of scientists in industry and the regulatory authorities for their inertia and resistance to these validated and better-performing methods. There was indignation that no matter what is done, no matter how well an 'alternative' achieves its stated aims, the status quo will remain... simply because those whose job it is to actually use these methods are comfortable with the animal-based approach. How can such an outlook be justified? Why are these individuals beyond reproach? How can anyone seriously defend the animal-based tests that are clearly unscientific, and object to the proposed alternatives because they're not perfect?

A comment by Dr James Watson (co-discoverer of the structure of DNA) is appropriate here: "The fact is most scientists act as though they are stupid because they are wedded to some approach they can't change, meaning they are moving sideways or backwards."

Frustrations at these attitudes were commonplace and vociferous. Demands were made that both approaches be treated equally: can it be right that animal tests have an in-built 'safety factor' of a one hundred-fold margin of error, when non-animal methods don't? Can it be right that non-animal methods are criticised for being less than perfect, when the animal tests they're intended to replace are so poor?

Fortunately, frustration has already been channelled into action. While scientists continue to do sterling work to provide tests that will ensure human safety and drug efficacy better than ever before, work is underway to address the inequitable treatment of animal and non-animal methods. It seems logical that if validating non-animal methods is not enough, then we must turn our attention to the animal tests and invalidate them... and this is precisely what is happening.

In fact, the presentation of a study invalidating animal-based testing of potential human carcinogens, co-authored by our Science Director Dr Jarrod Bailey, won one of only two conference prizes for its scientific merit, beating off competition from 350 others. Dr Bailey was also invited to present his study on the futility of animal testing for substances that can cause birth defects, which was very well received.

And there were 'heretics' in abundance... esteemed and experienced scientists showing that human-specific in vitro (test-tube) tests can predict human toxicity better than tests in live rats, alongside drug development specialists stating unequivocally that there is no place for animal studies in drug discovery or development – that they are scientifically unsound – that making an effort to 'refine' and 'reduce' such animal experiments is futile and that replacement is the only option. And what's more, that this is now starting to become major drug company thinking...

The theme of invalidation continued in September as Dr Bailey formed part of the committee at a meeting of the European Centre for the Validation of Alternative Methods (ECVAM) in Italy, to discuss the prospect of a formal invalidation process for the long-standing, commonly accepted, widely used though never validated animal-based methods. It is expected that ECVAM will soon begin to formally evaluate the scientific validity of the animal tests that continue to be required by the regulatory bodies that oversee drug and chemical approvals in Europe. This is a

groundbreaking move, and one that will surely be the final nail in the coffin of animal experiments in this field, helping to ensure the safety of European citizens in a way that animal testing never could.

But the evaluation of animal experiments doesn't stop there. There has been a recent surge in the interest of many scientists to broaden the scope of this evaluation process to animal models of human diseases, used in universities and other research establishments all over the world. Building on the preliminary work just completed by Dr Bailey and his colleagues in the fields of cancer and teratology (birth defects), a huge, multi-centre raft of work is about to get underway to tackle this issue. It is in society's interest to ensure that this work goes ahead unmolested: an objective, transparent and comprehensive assessment of animal research is long overdue, and will help to ensure that the testing of drugs and chemicals, and research into the diseases that affect us all, will be the most effective it can possibly be. No-one with honourable motives and without conflicting vested interests can object to this assessment...but support from those who champion animal experimentation is conspicuous by its absence.

NICE Conference

In December, we exhibited again at the annual conference of the National Institute of Health and Clinical Excellence (NICE) in Birmingham. This is a great opportunity to speak to people involved in shaping healthcare policy and its delivery. Once again, we were delighted by the level of interest in our organisation and by the overwhelming encouragement and support for what we are seeking to achieve. Doctors, nurses, researchers, lecturers, professors and representatives of patient groups and primary care trusts could not have agreed with us more.

School Talk Successes

EMP's director, Kathy Archibald, gave talks to several hundred students at colleges which were also receiving speakers from Merck, Sharp and Dohme. It was interesting to learn that the Merck speakers were quite unable to answer questions put to them by the students, following their session with EMP. It was very pleasing that substantial numbers of students revised their opinions about the necessity of animal experimentation in light of the evidence presented to them. This is always an unexpected bonus, simply because the prospect of undoing a lifetime of

brainwashing in under an hour is challenging, to say the least! Jarrod Bailey also gave a talk to his old school in Newcastle, which was very well received by students and teachers alike, who were keen to ensure that his return visit would not be his last!



Kathy Archibald

Widespread Media Coverage

In our last newsletter, we commented on the woefully unbalanced coverage of the issue of animal experimentation in the media. It is a pleasure to report that the past few months have seen a small but significant improvement in the balance, starting with coverage of the statement orchestrated by the RDS and signed by 500 scientists in support of animal research. Predictably, most of the media presented the story as though those 500 scientists represent the entire scientific community – and neglected to mention that, simultaneously, 1,000 scientists were in Berlin at the 5th World Congress on Alternatives and Animal Use in the Life Sciences, as mentioned above. Channel 4 News commendably broke the mould and interviewed Kathy Archibald as well as RDS director Simon Festing, as did BBC News 24 and BBC Radio Scotland. Interestingly, Simon Festing said on Channel 4 News that he would support an independent scientific evaluation of animal testing: in fact, he has been campaigning hard against EMP's initiative and told the Scientist magazine that he will write to every MP who has signed EDM 92 to inform them of their mistake! On the subject of the 500 scientists, EMP cannot improve on the comment made by Dr Robert Matthews in The First Post; "If you want to know the future of animal experiments, forget the 500 scientists. Their arguments are as scientific as organ-grinders insisting they must keep their monkeys. Watch instead the pharmaceutical companies, whose patience with the farce of animal experiments can't last much longer."

An unusually fair and balanced article in the Guardian on August 27th quoted EMP's survey of GPs, which found that 82% of doctors are concerned that animal data can be misleading when applied to humans and 83% would support an independent scientific evaluation of the clinical relevance of animal experimentation. BBC Radio 4 presented a refreshingly balanced pair of "You and Yours" programmes on animal experimentation in September. Jarrod Bailey featured in the first programme and Kathy Archibald spoke in the follow-up debate.

A September article in the Financial Times, entitled "Small dose of our own medicine" reported encouragingly; "With its potential to speed up drug development and cut the risk of nasty shocks during clinical trials, microdosing may be just the tonic that big pharma needs." BBC Focus magazine ran a 5-page article; "What are the alternatives?" in October, featuring a Q&A with Dr Bailey.

The Times published an article in December; "The human guinea pigs", posing the question, "Could animal testing become redundant? Some scientists believe technology has the answer." The article quotes Dr Bob Coleman, chief scientific officer of Pharmagene, asking "If two different species give you different answers to the same question about a drug's action, how confident can you be that either one of them will be predictive of humans?" The article goes on to describe microfluidics chips, just 2cm wide, which have etched into them a series of tiny chambers, each containing a sample of tissue from different parts of the body. The compartments are linked by microchannels through which a blood substitute flows. "What we are trying to do is to mimic what goes on in the body on a micro scale," says Leslie Benet, Professor of biopharmaceutical sciences at the University of California and chairman of the scientific advisory board of Hurel, the Californian corporation making the chips, which originated at Cornell University. The test drug is added to the blood substitute and circulates around the device. Its effects on the cells in each compartment can be measured by sensors in the chip and fed back for computer analysis. The article then discusses microdosing, revealing its unsurpassed predictivity of drug metabolism in humans which is, bizarrely, rebuffed by Simon Festing, who claims "Animals are hugely predictive of toxicity in humans. There is no conceivable alternative."

Unethical Clinical Trials

The winner of the 'best film of 2005' at the BAFTAs was the dramatisation of the book "The Constant Gardener" by John le Carré. This thriller about big pharma exploiting African HIV victims may be fictional but according to le Carré it is "as tame as a holiday postcard" when compared with reality. The scandal at the heart of the film is that a British company is using poor Kenyans as expendable guinea pigs in unethically conducted trials of its potential new international blockbuster drug and – crucially – covering up its serious side effects. Mark Henderson, the ill-informed science correspondent of the Times, took exception to

the criticism and wrote a column entitled "Inconsistent Gardener" on December 17th. He accuses le Carré of misrepresenting reality and asserts that pharmaceutical companies do not exploit poor, deprived or ill-educated people as expendable guinea pigs in clinical trials as it would be folly to do so.

Unfortunately, such optimism betrays profound ignorance of harsh realities, such as the fact that in 1996 Pfizer, the world's biggest drug company, tested its potential western blockbuster drug on children in Nigeria, against the fervent protestations of its own childhood diseases specialist, whose contract was hastily terminated. This story, along with other disturbing examples, was told by Channel 4 in the 2003 documentary "Dying for Drugs." 16,000 volunteers in Thailand were recruited in 2004 to a farcical trial of another AIDS vaccine (the failed Aidsvax in combination with another unproven vaccine) widely regarded by scientists as having no chance of success. The US FDA, in response to lobbying by pharma, has even proposed to bypass the Declaration of Helsinki – drawn up in 1964 to protect human test subjects – in order to approve certain drugs by testing them in India and other poor countries. Conducting clinical trials in India, for example, is 60% cheaper for pharmaceutical companies, which are flocking to 'outsource' much of their business there for this reason.

In America, more than 75% of clinical trials financed by pharmaceutical companies are conducted by private, for-profit centres comprising a \$14 billion industry, with poor immigrants comprising the overwhelming majority of subjects recruited. The enterprise is poorly regulated and riddled with conflicts of interest, with secretive review boards – charged with protecting participants' safety – funded by the same drug companies that fund the test centres they are supposed to be regulating. The net result is that every year, trial participants are injured or killed.

Ken Goodman, director of the Bioethics Programme at the University of Miami, says pharmaceutical companies are shirking their responsibility to safely develop medicines by using poor, desperate people to test experimental drugs. Marcia Angell, former editor in chief of the New England Journal of Medicine, says the fundamental problem is that testing companies have more incentive to satisfy pharmaceutical companies wanting speedy results than they have to ensure the safety of participants or integrity of research data.

Sadly, it appears that the opinions on scientific matters offered by the Times cannot always be trusted. EMP has noted that Mark Henderson frequently uses his column to write about animal experimentation; a

subject about which he is even more ill-informed. Of course, one of the main reasons that clinical trials are risky for participants is that very often, the only information about the safety of the experimental drug pertains to animals, and nothing at all is known about its safety in humans before it is administered to the clinical trial volunteers. This is precisely the situation that EMP seeks to change, via EDM 92.

US and EU Back Microdosing

Dr Elias Zerhouni, director of the US National Institutes of Health, wrote an article in the *New England Journal of Medicine* in October entitled "Translational and Clinical Science — Time for a New Vision." One of the concerns he addresses is that "it has also become clear that available animal models of human disease are often inadequate, necessitating even more research on human populations and biologic samples."

The US regulatory agency, the FDA, issued new guidance in January 2006 to encourage pharmaceutical companies to speed the development of new drugs by utilising safe low-dose studies (such as microdosing) in humans. The FDA launched its Critical Path Initiative in 2004 and issued guidance endorsing the use of microdosing in 2005. The agency is clearly impatient with pharmaceutical companies for being so slow to take advantage of these opportunities to hasten progress towards clinical trials. The new guidance points out that "Many resources are invested in, and thus wasted on, [animal studies of] candidate products that subsequently are found to have unacceptable profiles when evaluated in humans" – which, it hastens to add, is more than 90% of candidate products. It emphasises that because low-dose human studies present fewer potential risks to participants than do traditional phase 1 studies, such exploratory investigations in humans "can be initiated with less, or different, preclinical [animal] support than is required for traditional studies." Now that they have spelled it out in capital letters, it is to be hoped that the beleaguered pharmaceutical industry will seize this lifeline, to the benefit of all concerned.

Carl Peck, director of the University of California, San Francisco's Center for Drug Development Science and former head of the FDA's Center for Drug Evaluation and Research, welcomed the new guidance.

Commenting on the FDA's historic requirement to test drugs on animals before humans, he said; "There's no scientific basis for it...sometimes it works and sometimes it doesn't." The safety of clinical trial participants will surely be better protected by a battery of 'Phase 0' human-based tests, including microdosing, than by traditional animal studies.

Professor Colin Garner, Chief Executive of Xceleron, the York University-founded microdosing company, wrote in a letter to the *Guardian* in September that, "One might have thought that approval by regulators would be a green light to try this new approach, particularly as microdosing information is obtained in the best animal model for humans. Sadly the number of studies conducted so far by the drug industry is in single figures." The FDA's new guidance should help to improve the fortunes of microdosing companies. In November, Xceleron signed a three-year deal with GlaxoSmithKline, shortly after commenting that "Currently, preclinical studies can take up to 18 months at a cost of \$3–5m (€2.3-3.8m). Microdosing techniques could reduce the time to four to six months and the costs to \$0.35m (€0.26m) per new molecule."

Xceleron will also lead the new EU Microdose AMS Partnership Programme (EUMAPP), which has been awarded €2.1 million under the Sixth Framework Programme. The 30 month programme, beginning in January 2006, aims to harness the promise of microdosing tools to improve predictability and efficiency in the drug development process. EUMAPP will also develop *in silico* modelling applications to predict metabolic parameters of new drugs from data derived from microdosing studies, thus improving the safety of human clinical studies, while reducing animal testing.

EMP Seeks Temporary Assistant Director

Financial reward will be small but personal reward could be immense. If you are a qualified doctor or scientist (PhD required as a minimum) and may be interested, please write in the first instance to:

EMP, PO Box 38604, London W13 0YR

or, preferably, email info@curedisease.net, detailing your qualifications and experience and explaining why you are interested.