Experts say research on primates is vital to fight disease

Michael Day *London*

Medical experiments on non-human primates will be vital in the fight against AIDS, tuberculosis, and malaria "for the foreseeable future," a group of leading scientists has concluded.

Their report, sponsored by the Academy of Medical Sciences, the Royal Society, the Medical Research Council, and the Wellcome Trust, adds that a ban on the use of monkeys would jeopardise important research into neurological diseases such as Parkinson's disease and dementia.

The ban on research involving apes should remain, the scientists say.

The report's chief author, David Weatherall, the leading malaria expert and professor of medicine at Oxford University, said the "huge discrepancy" between the number of monkeys used in medical experiments and the number of people who stood to benefit, particularly in the developing world, justified such research.

He noted that "even with the money pouring in from people like Bill Gates," the vast cost of large scale clinical trials meant that the world could not afford to squander money for research into AIDS on human vaccines that had little or no hope of succeeding.

"Pre-testing in a small number of non-human primates can ensure we proceed into human trials with vaccines that are likely to succeed," he said.

Professor Weatherall said that advances in medical technology, including improving scanning and the development of new genetically engineered rodents, would see the need for experiments involving monkeys decline over time.

He warned, however, that "there will be a need for these experiments for the foreseeable future."

His group's 18 month study found that about 400 monkeys a year are used in the United Kingdom. An additional 3000 are used, however, in drug company toxicology tests—a branch of study that was deemed largely beyond the remit of the investigation.

SAM OGDEN/SPL

The "huge discrepancy" between the number of monkeys used in experiments and the number of people who stand to benefit justifies research using primates, the report says

Professor Weatherall added that ministers needed to tackle urgently the problem of intimidation and harassment of scientists, which he said was driving many leading researchers abroad.

Another of the report's key recommendations was that about six centres of excellence be formed to improve the standards of research and guarantee the best possible welfare of animals. □

The full version of this article is available at bmj.com.

The Use of Non-Human Primates in Research: a Working Group Report is available at www.mrc.ac.uk.

Drug eluting stents are safe for licensed indications, says FDA

Susan Mayor *London*

Drug eluting stents (DES) are safe when used within their licensed indications, a panel of the US Food and Drug Administration advised at a special meeting last week. But the possibility that stents may be associated with increased risk of death and myocardial infarction caused by late stent thrombosis when used off label should be investigated further, it says.

The panel suggested that the increased risk may be related to use of antiplatelet therapy for too short a time in higher risk patients and called for further research to clarify the optimal duration.

The FDA's circulatory systems devices advisory panel held a two day hearing last week to review recent data that indicate a small but significant increased risk of death and myocardial infarction associated with stent thrombosis in patients with drug eluting stents.

A statement released at the end of the hearing said, "At this time, the FDA believes that coronary drug-eluting stents remain safe and effective when used for the FDA-approved indications. These devices have significantly reduced the need for a second surgery to treat restenosis for thousands of patients each year."

The panel heard that at least 60% of procedures using drug eluting stents are carried out in patients outside the licensed indications.

The FDA panel said it intends to more formally evaluate the studies suggesting increased risk.

It is also interested in the long term follow-up of patients enrolled in the original pivotal stent randomised trials and in patients with more complex conditions (patients with diabetes, acute myocardial infarction, or multiple vessel disease) and lesions (lesions involving arterial bifurcations, the left main coronary artery, and long arterial segments) who are currently being treated in "real world" randomised and registry studies.

The FDA statement said that the panel was also evaluating information on the duration of treatment with clopidogrel, an antiplatelet drug used in combination with aspirin to reduce and prevent clotting in patients given drug eluting stents. □

The full version of this article is available at bmj.com.

The FDA statement is at www.fda.gov/cdrh/news/091 406.html.

In brief

Australia relaxes ban on stem cell research: After impassioned debate, Australia's politicians have passed a bill lifting a four year ban on somatic cell nuclear transfer for generating stem cells. Lawmakers used a rare vote of conscience to side with scientists, voting 82 to 62 in favour.

Long term statin use reduces risk of heart attack: Patients who persist with the use of statins have a 30% reduced risk of hospitalisation for acute myocardial infarction, a study has found. Of 59 094 new users of statins, 31 557 discontinued use within two years. "Results show that statins are suboptimally used in real life for having the maximum benefit in terms of preventing acute myocardial infarction," say the authors (*European Heart Journal* 2006 Dec 7, doi: 10.1093/eurheartj/ehl391).

Chlamydia cases rise in Netherlands: Diagnosed cases of the Netherlands' most prevalent sexually transmitted infection, chlamydia, have risen by 15% to 5146, say the latest Dutch statistics from the Institute of Public Health.

Finger complaints more likely in orthopaedic surgeons: Orthopaedic surgeons have a larger glove size than gynaecologists, drink more, are more likely to use vibrating tools outside work, and suffer numbness of the fingers. The study was based on a questionnaire sent to 2040 members of the British Orthopaedic Association and 1797 members of the Royal College of Obstetricians and Gynaecologists (*Occupational Medicine* 2006 Dec 6, doi: 10.1093/occmed/kql141).

Canada's leading medical journal gets new editor: *CMAJ*, the journal of the Canadian Medical Association, has appointed a new editor. Paul Hebert is a critical care physician at the Ottawa Hospital and vice chair of medical research at the University of Ottawa. The dismissal of the journal's previous editor in chief, John Hoey, last February led to claims that the CMA had breached the journal's editorial independence.

NHS told to make £250m surplus

Michael Day *London*

The NHS has been ordered to end the next financial year with a surplus of £250m ($490m; €370m) even though many clinical posts and services face cuts.

Senior health service officials said that a cultural change was needed in which the health service aimed for surpluses instead of settling for debts. The announcement came as part of the NHS framework for 2007-8 set out by the NHS chief executive, David Nicholson.

Jonathan Fielden, chairman of the BMA's consultants' committee, warned that trying to make a surplus would cause problems. "While it may be good business practice to have a financial surplus, the NHS will struggle to meet the challenge at a time when hospitals are already cutting back on services.

"Operations are being delayed, jobs are being frozen, and trained doctors and other healthcare staff are struggling to find jobs, while the NHS attempts to get its finances sorted."

Mr Nicholson admitted that he had not worked out how different parts of the NHS would contribute to the surplus. Some parts of the NHS are in good financial health—while some are virtually bankrupt.

But he denied that the planned £250m surplus was a public relations stunt: "This is not politically motivated. I agree that we should focus on improving patient care," he said.

The health secretary Patricia Hewitt has staked her job on getting the NHS to break even by April next year.

Next year's NHS framework sets out other "key milestones," saying that 85% of patients needing admission to hospital should be treated within 18 weeks by March 2008. In addition, by March 2008 90% of outpatients should be treated within 18 weeks. Providers that failed to meet the targets would be subject to a financial penalty, with up to 2% of their overall income withheld.

Mr Nicholson said that the introduction of local targets would provide better care and better value for tax payers. These targets would see health authorities spending according to the needs of their communities. As an example he said that in areas with high levels of heart disease, health authorities would spend more on anticholesterol drugs.

But Gill Morgan, of the NHS Confederation, warned that accounting regulations known as resource accounting and budgeting were adding to the NHS's financial woes. She said that many trusts were being penalised because when they reported a deficit their income was reduced by the same amount next year, trapping them in a cycle of debt.

Dr Fielding of the BMA agreed, "This artificial accounting measure has imperilled many NHS trusts unnecessarily and forces short term cuts directly impacting on patient care." □

The full version of this article is available at bmj.com.

The NHS In England: the Operating Framework for 2007/8 is available at www.dh.gov.uk.

Staff costs are to blame for NHS deficits, say MPs

Adrian O'Dowd *London*

Good standards of health care have been jeopardised by financial pressure on NHS trusts to balance their books, says a report by MPs that was published this week.

The parliamentary health select committee's final report from its inquiry into NHS deficits says that the need to reduce deficits, rather than a desire to improve services, is driving changes currently taking place in the NHS.

The MPs said that trusts were damaging the quality of care of patients and staff morale by cutting training budgets to solve their cash flow problems. Failures in financial management had occurred at all levels of the NHS, they said.

Tackling deficits by cutting training budgets is "unacceptable," says the report.

UPPTOPFOTO

Committee chairman Kevin Barron said weaknesses in financial structures had been exposed by greater transparency

The report says that the evidence of a failure of financial management within the NHS is compelling. It says: "The most basic errors have been made."

The report says, "Many [deficits] are associated with the extraordinary growth in staff costs arising from pay rises and the large increase in staff numbers. The pay rises have far exceeded the Department's estimates and the numbers of new staff are far higher even than the figures proposed in *The NHS Plan*."

The government's estimates of the costs of the new pay systems, such as the new GP and consultant contracts, were "hopelessly unrealistic," says the report, and central targets such as all patients being seen at emergency departments within four hours had been imposed without regard to cost.

It says that the expectation that the whole NHS will be in balance by the end of 2006-7 is misguided and that it is unlikely that trusts with the biggest deficits will get into the black within five years.

The government's resource accounting and budgeting regime should be replaced or refined, it adds, to give trusts more flexibility and a suitable period to get out of debt. □

The full version of this article is available at bmj.com.

NHS Deficits is available at www.parliament.uk.

Researcher received undisclosed payments of $300 000 from Pfizer

Jeanne Lenzer *Boston*

Pearson "Trey" Sunderland III received $300 000 from Pfizer for providing spinal fluid samples, and $311 000 for lectures organised by Pfizer's marketing team

A federal research scientist working for the US National Institute of Mental Health (NIMH) pleaded guilty last week to a charge that he had not declared a conflict of interest to his employers.

Pearson "Trey" Sunderland III pleaded guilty to a misdemeanour charge that he failed to report about $300 000 (£150 000; €230 000) worth of consulting fees and expense payments from Pfizer. Under the plea agreement, Dr Sunderland will pay back the $300 000 to the federal government, and prosecutors say they plan to recommend that he also serve 400 hours of community service and be placed on probation for two years.

Dr Sunderland's activities came under scrutiny when Susan Molchan, a former NIMH researcher, blew the whistle on him when she suspected that he had diverted samples of cerebrospinal fluid that she had obtained during a study of 25 subjects.

When Dr Molchan left the NIMH in 1997, the samples came under the control of Dr Sunderland. Dr Molchan became suspicious when in 2004 she tried to obtain some of the samples, but Dr Sunderland was only able to account for 2-3% of the cerebrospinal fluid that should still have been in storage. When Dr Molchan asked for the linked clinical data, Dr Sunderland told her that it had been purged because it was more than 5-7 years old.

Dr Molchan's charges triggered a Congressional inquiry. A report issued by the House Committee on Energy and Commerce in June concluded that Sunderland had transferred more than 3200 samples of cerebrospinal fluid and plasma to Pfizer.

According to the report, cerebrospinal fluid samples from 538 subjects, who participated in 14 studies at NIMH, were sent to Pfizer, including subjects from Dr Molchan's study. The committee found that there were "reasonable grounds" to conclude that Dr Sunderland received compensation from Pfizer "for activities that were derived directly from his official acts in providing Pfizer access to spinal fluid samples … and linked clinical data and that Dr Sunderland used NIH employees and resources to provide such access."

The samples were considered "extraordinarily valuable" because they were obtained at several points over a period of years. The samples were prized for their ability to aid in the identification of biomarkers in early Alzheimer's disease.

Dr Sunderland also endorsed cholinesterase inhibitors, including donepezil (Aricept, Pfizer), as a treatment for Alzheimer's disease in medical journal articles. For example, in the *Journal of Clinical Psychiatry* he wrote, "Donepezil, recently approved for use in mild to moderate Alzheimer's disease, appears to be less toxic and better tolerated than tacrine," again without explaining his financial ties to Pfizer (1998;59(suppl):s31-5).

The report also found that separate from his undeclared consulting fees with Pfizer, he received $311 150 in lecture fees between 1996 and 2004, for talks that were, the committee observed, "arranged by Pfizer's marketing team charged with promoting Aricept."

The report raised questions about the nature of informed consent from the human subjects who donated their tissue samples because most subjects, according to the report, were not told about the Pfizer "collaboration."

The NIH did not respond to inquiries at this time. □

The full version of this article is available at bmj.com.

The report, *Human Tissues Samples: NIH Research Policies and Practices*, is accessible at http://energy-commerce.house.gov/108/home/staff%20report.pdf.

Pfizer stops clinical trials of heart drug

Janice Hopkins Tanne *New York*

Pfizer, the world's largest drug company, suddenly halted phase III clinical trials of torcetrapib on 2 December. Torcetrapib is a new agent that increases concentrations of "good" high density lipoprotein (HDL) cholesterol.

Only two days earlier, Pfizer executives had said that they hoped to ask the US Food and Drug Administration for approval next year.

Pfizer said that "in the interests of patient safety" it was stopping the clinical trials of torcetrapib (called Illuminate) because the independent data safety monitoring board found more deaths and cardiovascular events in patients taking the drug. The trials included 7500 patients who were taking a combination of torcetrapib and atorvastatin (marketed as Lipitor) and 7500 patients who were taking atorvastatin alone. There were 82 deaths in the group taking the combination, compared with 51 in the group taking atorvastatin.

The trial investigators were instructed to tell patients to stop taking the combination, and Pfizer also notified the FDA.

Torcetrapib inhibits cholesteryl ester transfer protein. In patients with low HDL cholesterol, torcetrapib markedly increased HDL cholesterol and lowered "bad" low density lipoprotein (LDL) cholesterol, in a small trial reported in the *New England Journal of Medicine* (2004; 350:1505-15)

Pfizer began trials of torcetrapib in combination with atorvastatin, which inhibits the production of LDL cholesterol. In October, Joseph Falco, Pfizer's chief medical officer, said that the combination increased HDL cholesterol by 55-60% and decreased LDL cholesterol by 50-60%.

On 30 November, John LaMattina, president of Pfizer Global Research and Development, said, "We are first in class, and we intend to remain best in class in a category that has the potential to change the face of cardiovascular medicine."

Then Philip Barter, director of the Heart Research Institute in Australia and chairman of the steering committee overseeing the Illuminate study, told Pfizer that the data safety monitoring board had found higher mortality and morbidity in the torcetrapib-atorvastatin group and recommended ending the study. Dr Barter said, "We were very surprised by the information received from the DSMB [data safety monitoring board], the only body with access to the unblinded safety data. We believed the study was coming along as expected, and this new information was totally unexpected and disappointing, given the potential benefits of the drug."

The company said it had invested about $800m over 15 years in developing the drug. After the announcement its shares fell about 10%. □

The full version of this article is available at bmj.com.

bmj.com news roundup

Full versions of these stories are available at: **bmj.com/content/vol333/issue7581/#NEWS_ROUNDUP**

Genetic tests and staff are cut to save money

The UK government's plans to make genetic testing more widely available in the NHS are being thrown into reverse by financial cutbacks, a survey by its own advisory body shows.

The Human Genetics Commission's survey of 14 of the United Kingdom's 18 regional genetics centres shows that most are being forced to make cuts, which vary from 3% to 9% of their total budget. Five have had to cut staff or leave vacancies unfilled.

This has led to restrictions in the number of genetic tests as well as longer waits at a time when referrals are rapidly increasing.

The commission's chairwoman, Helena Kennedy, will present the findings of the survey to health minister Andy Burnham when they meet early next year.

Speaking at the commission's December meeting, Frances Flinter, clinical director and consultant clinical geneticist at Guy's and St Thomas' NHS Foundation Trust, said that primary care trusts were artificially restricting the number of referrals to centres through demand management. "It's frustrating to know there are things we could and should be doing but know we're not allowed to in order to balance the books."

Andrew Cole *London*

Woman in PVS can die, rules judge

A woman in a persistent vegetative state is to have artificial nutrition and hydration withdrawn to allow her to die with "dignity" after failing to respond to a drug which is said to have woken up some unconscious patients.

England's senior family judge, Sir Mark Potter, ruled last week that doctors could lawfully withdraw all life sustaining treatment from the 53 year old mother, named only as J, who has been in a persistent vegetative state after she had a brain haemorrhage on a family holiday in August 2003.

Her husband, mother, and two daughters wanted her to be allowed to die, arguing that she would not have wished to be kept alive in such a state. But the outgoing official solicitor, Laurence Oates, after reading a report about the effects of the sleeping pill zolpidem on three patients said to be in a permanent vegetative state and consulting an expert, said that the drug be tried for three days.

J only fell asleep when given the drug in mid-November. Afterwards, Sir Mark gave the go ahead to withdraw artificial life sustaining treatment from J.

Clare Dyer *legal correspondent, BMJ*

COURTESY ROYAL INFIRMARY EDINBURGH

PFI contributes to large deficits of Scottish health boards, warns a report from Edinburgh University

Money will have to be diverted from patient care throughout the United Kingdom to pay for hospitals constructed under the government's controversial private finance initiative (PFI), a report from the University of Edinburgh has warned.

It says that the schemes (now known as public-private partnerships) are already a key factor in NHS deficits and the problem will escalate as more of projects are completed. Under PFI, the private sector builds and pays for new hospitals and in return, the NHS pays an annual charge to the private sector—often for 30 years or more.

The study by the University's Centre for International Public Health analysed data from the Scottish Executive. It shows the NHS will have to pay more than £2.4bn (€3.5bn; $4.7bn) in charges to private companies over the next 30 years for schemes that cost £602m to build. One of the first such schemes was the Royal Infirmary of Edinburgh (above).

Scotland's health minister Andy Kerr said the report betrayed a lack of understanding of how public finance works.

Bryan Christie *Edinburgh*

The report, *The Impact of PFI on Scotland's NHS: a Briefing*, is available at www.health.ed.ac.uk/CIPHP.

Dutch doctors call for action on drug safety

Doctors, pharmacists, and patients' groups in the Netherlands are demanding government action on drug safety after a national study has concluded that drug related problems were responsible for twice as many hospital admissions as road traffic crashes.

The hospital admissions related to medication (HARM) study found that 41 000 hospital admissions a year in the Netherlands were caused by either the incorrect use of or adverse reactions to drugs (www.nvza.nl).

These admissions accounted for 5.6% of acute admissions and were twice as likely to involve patients older than 65 years.

Almost half—19 000 admissions—were deemed "possibly avoidable" and cost the health services €85m (£57m; $112m) a year. They were thought to have a role in an estimated 1254 deaths a year.

Tony Sheldon *Utrecht*

Sponsorship of patients' groups by drug companies should be made transparent

Drug companies are sponsoring more and more groups for patients in Germany to increase demand for their products, but many members remain unaware of their involvement, a study has found.

The firms are also advertising their products on what seem to be independent websites, despite laws that ban advertising prescription medicines to the public.

The study, by the Zentrum für Sozialpolitik of Bremen University, was commissioned by Germany's state health insurance companies and focused on funding of groups for patients with chronic diseases, such as Alzheimer's disease and eczema.

At present, health insurance companies are the main sponsor of patients' groups, spending a total of €28m (£19m; $37m) in 2005, but drug companies are increasingly moving into the area.

Currently, there are about 300 national support groups for patients with chronic disease or disabilities, about 800 groups and 270 contact offices within the 16 federal states, and about 70 000 regional groups.

"Pharmaceutical firms have recognized that patient groups have a large influence," said Kirsten Schubert, joint author of the study with Gerd Glaeske. "Members are often not aware of the involvement of the pharmaceutical industry."

The authors of the study recommend that all sponsorship be made transparent.

Annette Tuffs *Heidelberg*

GPs should use "premier" sources when prescribing

GPs should not use internet search engines, such as Google or Medline, when seeking advice on what to prescribe, say senior NHS officials.

Instead they should stick to "premier" information sources, such as the National Institute for Health and Clinical Excellence (NICE), the Cochrane Collaboration, or national service frameworks.

Experts from the National Prescribing Centre told this week's annual NICE conference that this would eliminate waste and improve patient care.

"Most start at Medline, when we should be starting with the most useful sources that have been sifted for usefulness," said the centre's medical director, Neal Maskrey.

GPs were ill equipped to make rational prescribing decisions based on complicated medical research papers or obscure reports.

Jonathan Underhill, the centre's assistant director of education and development, said the sheer quantity of medical research published every week meant that GPs could not be expected to keep abreast of all relevant developments by themselves.

Michael Day *London*

NICE requires primary care trusts to tackle obesity

All primary care trusts must ensure that systems are in place to allow health professionals to implement interventions to prevent and treat obesity, the first national guidance from the National Institute for Health and Clinical Excellence (NICE) on obesity in adults and children in England and Wales says.

The guidance was developed by the National Collaborating Centre for Primary Care, a group of healthcare professions based at the Royal College of General Practitioners, and NICE's Centre for Public Health Excellence. It aims to stem the rising prevalence of obesity and associated diseases, to increase the effectiveness of interventions to prevent overweight and obesity, and to improve care provided to adults and children with obesity, particularly in primary care.

James McEwan, emeritus professor of public health at the University of Glasgow and chairman of the guidance development group, said: "This guidance recognises the scale of the problem and the need for coordinated efforts to reduce its impact. Its scope is ambitious but this is going to be a major public health problem if nothing is done."

Susan Mayor *London*

NICE clinical guideline 43 is available at www.nice.org.uk/CG043.

Review of drug subsidy delayed as test case looms

A review of the pharmaceuticals provisions of the Australia-United States free trade agreement has been deferred until after the announcement of the outcome of a landmark appeal.

The appeal by Eli Lilly Australia against the decision not to include the osteoporosis drug teriparatide (Forteo) in the Australian government's Pharmaceutical Benefits Scheme will be decided upon by an independent reviewer and is expected early next year.

The decision is seen by the drug industry as a test case on the effectiveness of concessions won when the agreement was concluded in 2004 (*BMJ* 2004;328:604).

Following US claims that Australia's use of reference pricing, which benchmarks the price paid for a patented drug against a generic comparator, was a trade barrier, the Australian government agreed to establish a review process when drugs were not included in the scheme.

Thomas Faunce, lecturer at the Australian National University law faculty, questioned the future of the scheme and said, "The drug industry is progressively whittling away at the core features of the scheme until, sooner or later, it will fall over."

Bob Burton *Canberra*

Cooksey recommends central coordinating body for research

Andrew Cole *London*

The long awaited report by Sir David Cooksey on UK healthcare research has proposed a new model of structured coordination between the NHS, the Medical Research Council (MRC), and the healthcare industry to ensure more research is translated into tangible benefits for patients.

But the report, commissioned by the chancellor, Gordon Brown, has decided against merging the two main funding bodies, the MRC and the NHS's National Institute for Health Research (NIHR).

Instead the report proposes a central coordinating body, the Office for Strategic Coordination of Health Research, which will oversee all health research funding, determine strategy, and monitor progress against targets.

In addition, a joint MRC-NIHR Translational Medicine Funding Board will direct money towards projects that promise "health and economic benefits."

But the MRC and NIHR will continue to operate independently. Indeed, the report wants to see a clearer demarcation of their roles. And it says that the institute should move from a virtual organisation, with no physical headquarters, to a real body by April 2009 and become an executive agency of the Department of Health.

Healthcare research is failing to realise its potential, said Sir David, a former chairman of the Joint Healthcare Research Delivery Group, the coordinating body between the MRC and NIHR, because of "perverse incentives that value basic science more highly than applied research."

He confessed that he had felt frustrated with the joint delivery group because "although people were using the same words, they were speaking different languages. On a voluntary basis we couldn't break that down but this [report] puts in the architecture that makes it possible."

He proposes that an urgent review determines the United Kingdom's health priorities, focusing particularly on areas of unmet need. From this would emerge a list of priority research projects, which could be fast tracked through to implementation.

But some are concerned that the new arrangements could disguise a cut in funding, noting that when announcing the report Gordon Brown referred to a total health research budget of "at least £1bn [€1.5bn; $2bn]." The combined MRC and NIHR budget for 2007-8 was expected to be £1.3bn. (See Editorials, doi: 10.1136/bmj.39 059.444 120.80.) □

The full version of this article is available at bmj.com.

A Review of UK Health Research Funding is available at www.hm-treasury.gov.uk/independent_reviews/Cooksey_review/cookseyreview_index.cfm.

PA/EMPICS

Chancellor Gordon Brown announced publication of the Cooksey report in the House of Commons last week

Dispute over conflicts of interests leads to changes for medical society

Nina Vinther Andersen
Copenhagen

After a year of controversy over the influence of drug industry money, conflicts of interests and lack of transparency, members of the International Continence Society (ICS) last week decided to postpone an election for a new general secretary and to review and possibly rewrite the constitution of the society and its ethical guidelines.

"In three days we've made five years' worth of progress. We have managed to re-establish trust between the involved parties, and this should go a long way towards resolving our problems," said Hans Peter Dietz, associate professor in obstetrics and gynaecology at Sydney University, a vocal critic of industry influence.

The review comes as a result of a dispute within the society stemming from growing unease that industry money is influencing scientific discourse in the medical society.

Overactive bladder syndrome and its treatment, for example, has been fiercely debated. The syndrome covers everything from having an unusually strong and sudden urge to urinate—maybe combined with frequent urination in the day or night—to incontinence.

There are currently a handful of medicines used to treat overactive bladder syndrome, but, according to a review by the Cochrane Collaboration, their efficacy is questionable (*BMJ* 2003;326:841-4).

The review concluded, "Although statistically significant, the differences between anticholinergic drugs and placebo were small, apart from the increased rate of dry mouth in patients receiving active treatment. For many of the outcomes studied, the observed difference between anticholinergics and placebo may be of questionable clinical significance. None of these studies provided data on long term outcome." Up to nine out of 10 patients stop the drugs within a year.

The altercations in the society began last year with the election of a new editor in chief of the society's journal *Neurourology and Urodynamics*. The selection process was thought by some members of the editorial board to be so obscure that they resigned.

When, subsequently, certain members of the society asked that full disclosure be given by some of the society's office holders of any relevant conflict of interest, their request was denied. Instead an internal discussion document was prepared proposing that the society's advisory board be given a new, far reaching power to expel any member "if, in the opinion of the Board, he has acted or has threatened to act in a manner which is contrary to the interests of the Society as a whole or if his conduct … is likely to bring the Society, or any or all of its Directors or members into disrepute."

The proposal was never presented to the society's members and abandoned, but then an alternative was put forward: no member should be able to view or discuss the disclosure of another member's conflicts of interests unless the society's executive committee and the member permit it.

The rule said that every member would have to fill in a form annually showing their conflicts of interests, which would be held at the society's office.

"Any member wishing to view other members' disclosure forms must:

a) Complete and submit a form themselves

b) Put their request in writing indicating the reason for their request

c) Make a written commitment not to discuss or disclose any information contained in the disclosure form to a third party without prior consent of both the form's author and the ICS Executive Committee.

"The ICS Executive Committee will review and approve requests accordingly. Failure to adhere to this policy is likely to result in expulsion from the Society."

More recently, the society's executive has proposed another rule change, the effect of which, according to some members of the society, would be to remove the limit on the period of time trustees are entitled to hold office. This proposal has further aggravated the internal opposition.

At the annual meeting of the society last week in Christchurch, New Zealand, Professor Peter Dietz together with Danish professor Gunnar Lose, and Werner Schäfer, a biomedical engineer and director of the Continence Research Unit at Pittsburg University, led a push for transparency, new ethical guidelines, and a totally different structure of governance within the society.

A compromise solution was reached and a constitutional committee was established to review and, where appropriate, to rewrite the rules. All the matters will be voted on by the membership next year. □

Duff's report calls for changes in way drugs are tested

Michael Day *London*

Experts have called for major changes to the way new drugs are tested to avoid a repeat of the disastrous Northwick Park Hospital study that almost killed six volunteers.

The panel, set up by health secretary Patricia Hewitt and led by Gordon Duff, professor of molecular medicine at Sheffield University, investigated the incident in which all six recipients of the immune modulating drug TGN1412 had multiorgan failure at the private research wing of the Northwick Park Hospital, north London, in March this year.

In the light of events, the report makes 22 recommendations for pre-phase I, "first-to-human" trials using new drugs or drugs that alter the immune system.

It calls for independent expert advice to be sought before such high risk studies are allowed. It also calls on firms, universities, and hospitals to pool information from unpublished or abandoned trials that may provide clues about adverse reactions to new drugs.

The report also recommends that when drugs are tested in humans for the first time they be given to one volunteer at a time, in case there are rapid ill effects. Some drugs should also be given slowly, by infusion instead of a one-off injection, the report adds.

Ann Alexander of Irwin Mitchell, the law firm representing Ryan Wilson and Mohamed Abdelhady, the two men most seriously injured in the TGN1412 trial, largely welcomed the findings.

Of particular importance, she said, was the report's acknowledgment that the TGN1412 study had not considered what constituted a safe dose for use in humans—and had not been required to under current law.

"Going forward, it is now critical that the 22 recommendations made by the committee are implemented urgently to ensure the safety, rights and wellbeing of volunteers taking part in future clinical trials," she said. □

The full version of this article is available at bmj.com.

Expert Group on Phase One Clinical Trials: Final Report is at www.dh.gov.uk/PublicationsAndStatistics.

KIRSTY WIGGLESWORTH/EMPICS

Solicitor Ann Alexander said the recommendations should be implemented urgently