## Open letter to UK Prime Minister David Cameron and Health Secretary Andrew Lansley on safety of medicines

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

Adverse drug reactions have reached epidemic proportions and are increasing at twice the rate of prescriptions.[1] The European Commission estimated in 2008 that adverse reactions kill 197 000 EU citizens annually, at a cost of €79 billion.[2] The cost of new medicines is rising unsustainably, creating an ever-increasing burden on the National Health Service (NHS). Meanwhile, many increasingly prevalent diseases, such as Alzheimer's disease, diabetes, many cancers, and stroke, remain without adequate treatments.

The major reason for the rising cost of new drugs is the fact that more than 90% of them fail in clinical trials.[3] Companies need to recoup the cost of development not only for the drug that succeeds, but for the nine others that fall by the wayside.

It is increasingly clear that an important factor contributing to these problems is the over-reliance of the pharmaceutical industry on the use of animals to predict drug behaviour in man. The stark differences, not only in the diseases of different animal species, but also the ways that they respond to drugs, are now well known. Many studies have shown that animal tests frequently fail to translate to the clinic, with estimates of their ability to predict effects on people as low as 37–50%, or no better than the toss of a coin.[4]

Our reliance on animals to establish safety results in the exposure of clinical volunteers and patients to many treatments that are at best ineffective and at worst dangerous. Take for example the notorious Northwick Park clinical trial drug, TGN1412, that left six young men in intensive care in 2006. This drug was demonstrably safe in monkeys at doses 500 times higher than those that nearly proved fatal to the volunteers.[5] Soon after the disastrous trial, an assay that used human cells was developed to predict such an immune system over-reaction.[5] Had this assay been in use before human beings were exposed, the trial would never have taken place. Surely the time has come for there to be a rigorous assessment of the ability of such human-based tests to improve on the deeply flawed, animal-based approaches in current use?

We call on the UK Government to initiate a comparison of a set of human-biology-based tests with those currently used, as proposed in the Safety of Medicines Bill 2010–11,[6] to see which are more effective for predicting the safety of medicines for patients. Several new technologies promise increased clinical predictability as well as substantial improvements in efficiency and cost. The Bill does not propose any replacement of animal tests, merely their assessment of fitness for purpose. 148 Members of Parliament have already signed a motion[7] in support of this proposal.

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

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

We declare that we have no conflicts of interest.

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1 Lakhani N. Special report: prescription medicines. *The Independent* Oct 21, 2007.
2 Anon. Strengthening pharmacovigilance to reduce adverse effects of medicines. Brussels: European Commission, 2008. http://ec.europa.eu/health/files/pharmacos/pharmpack_12_2008/memo_pharmacovigiliance_december_2008_en.pdf (accessed May 10, 2011).
3 US Food and Drug Administration. Innovation or stagnation: challenge and opportunity on the critical path to new medical products. http://www.fda.gov/ScienceResearch/SpecialTopics/CriticalPathInitiative/CriticalPathOpportunitiesReports/ucm077262.htm (accessed May 10, 2011).
4 Perel P, Roberts I, Sena E, et al. Comparison of treatment effects between animal experiments and clinical trials: systematic review. *BMJ* 2006; **334:** 197–200.
5 Stebbings R, Findlay L, Edwards C, et al. "Cytokine storm" in the phase I trial of monoclonal antibody TGN1412: better understanding the causes to improve preclinical testing of immunotherapeutics. *J Immunol* 2007; **179:** 3325–31.
6 House of Commons. Safety of Medicines Bill. London: Stationery Office, 2010. http://www.publications.parliament.uk/pa/cm201011/cmbills/059/2011059.pdf (accessed May 10, 2011).
7 House of Commons. Early day motion 475: safety of medicines. http://www.parliament.uk/edm/2010-11/475 (accessed May 12, 2011).

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For a full list of signatories, see **Online** for webappendix

## Global trends in body-mass index

In a comprehensive assessment of trends in body-mass index (BMI) in 199 countries, Mariel Finucane and colleagues (Feb 12, p 557)[1] show that mean BMI and prevalence of overweight have increased since 1980, concluding that "interventions and policies that can curb or reverse the increase…are needed in most countries". Caution, however, is warranted in interpreting the country-specific or region-specific

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