Select Committee on Health Minutes of Evidence

Memorandum by Richard Horton (PI 108)

THE PHARMACEUTICAL INDUSTRY AND MEDICAL JOURNALS

The Lancet is a weekly general medical journal that publishes clinically oriented research about common diseases. A substantial part of the research that we publish concerns drugs manufactured by the pharmaceutical industry. Most of these research studies—notably, the gold standard means of assessing the efficacy and safety of a product, the randomised clinical trial—are paid for by the makers of the drug. There are many safeguards in place to protect the integrity of this research endeavour, from ethics committees to good clinical practice guidelines to journal peer-review systems. The standards set by the pharmaceutical industry in the conduct of clinical trial research are second to none. However, the extent of the commercial sponsorship of medical research and its intrusion into the academic sphere is one of the gravest threats to the independent evaluation of new medicines—indeed to the notion of an independent science base. Without greater scrutiny of the interaction between private and public sectors, the health of our population will continue to be put at risk by biased, over-interpreted, and misreported research findings. At present, our population is part of a largely unregulated experiment involving poorly investigated new medicines that have been licensed on the basis of insufficient data.

In my own very narrow area of interest—medical publication—I would draw attention to 10 especially damaging practices that distort the evidence base of medicine today.

1. Manipulation of research findings: In August, 2004, The Lancet published an important and rigorously conducted trial called ACTION, which was designed to investigate the effectiveness of a drug—nifedipine—in patients with heart disease. The results were presented at the European Society of Cardiology in Munich. The authors considered that the drug had "no effect" according to its predetermined criteria for judging effectiveness. The sponsor was Bayer. In the copious marketing material distributed to over 10,000 doctors in Munich, Bayer stressed that ACTION was "proving safety and improving outcomes...adding even more for hypertensive patients." The marketing claimed "primary endpoints significant in hypertensive patients", a total distortion of the actual result. Doctors were seriously and deliberately misled. This is not an uncommon practice.
2. Bias in sponsored studies: Research has demonstrated clearly that sponsored studies are more likely to produce a positive result for a company than an independent study of their product. The inherent biases in design, conduct, analysis, and reporting of research all reveal this pervasive undermining of scientific excellence. Examples include calcium channel blockers for heart disease and trials of drugs for myeloma.
3. Undisclosed adverse data: Research sponsored by industry is sometimes published at an early stage when there is a positive result for a new drug. But longer term follow up may yield an unwanted negative result. This finding may not be reported even when it is known at the time of publication of the early report. *JAMA* suffered a particularly egregious example of this deception. In another recent case, a journal was forced to reject a negative article after objections from its marketing department—an outrageous incursion into scientific integrity.
4. Hiding negative data: The classic recent example concerned Paxil (GlaxoSmithKline). The hidden trials showed a pattern suggesting limited efficacy of the drug and risks of potentially fatal adverse effects. The available published evidence indicated a very different story. Under severe reputational threat, GSK was forced to reveal these hidden results—leading to a $2.5 million US legal settlement and an unequivocal FDA warning about the risks of the drug. In response, the International Committee of Medical Journal Editors has called for all trials to be disclosed and registered at an early stage in their development.
5. Supplement publishing: Journal supplements often represent little more than information-laundering operations for industry. A company will sponsor a promotional meeting, pay a pharma communications company to convert the lectures of paid experts into articles, and then seek to publish these papers as a non or lightly peer-reviewed supplement to an established journal. The company will pay the publisher a large sum to secure publication, thereby buying, not earning, the imprint of the journal on its marketing-driven symposium. In one email that The Lancet has seen about a supplement, the sponsor argued that the more the article was peer reviewed the less value the supplement would be to the company—showing clearly the marketing goals rather than the scientific endeavour that lies behind supplement publishing. Multiple research studies confirm the scientific weaknesses of such supplements.
6. Undisclosed conflicts of interest: The escalating problem of industry payments to scientists—stock options, consultancy fees, research grants, staff costs, entertainment, conference fees, hospitality—has been recognised for several years. The International Committee of Medical Journal Editors (which includes the editors of the *New England Journal of Medicine, JAMA,* and *The Lancet*), has tried to force such competing interests into the open through tough disclosure requirements. But the continuing privatisation of much of science (science in the service of wealth creation rather than health improvement) threatens to make independent research almost impossible to do.
7. Editorial kick-backs: The Lancet has been offered substantial sums of money in exchange for publishing certain

research studies. In all cases, we have declined such offers and these papers have been rejected. The mechanism of this intended exchange is commonly through the explicit promise by the company of a large order of commercial reprints in return for publication of a research paper. The impression left is that if editors reject the paper or try to alter its message, there will be an often major loss of income to the journal.

8. Ghost-writing: It is standard operating procedure for pharmaceutical companies to seed the medical literature with ghostwritten editorials, reviews, and opinion pieces emphasising off-label indications of licensed drugs. These papers are commissioned to a specific marketing-driven brief and are written by non-specialists. A company friendly expert is then paid to have his or her name appear on the article, facilitating publication in a respected journal and thus enhancing the impact of the message.
9. Continuing medical education: Industry is now a major sponsor of medical "education". As a former editor of the NEJM, Marcia Angell, has argued in her powerful book, The Truth About the Drug Companies, this leap into education is driven more by a desire to lever messages concerning prescribing opportunities than it is about truly educating doctors about the prevention and treatment of disease. She estimates that about 60% of CME in the US is paid for by industry.
10. Failure to align commercial with public interests: Pharmaceutical companies clearly have a legal requirement to earn as much return as they can for shareholders. But their untrammelled power in shaping the research priorities of medicine means that national and international gaps in knowledge remain unfilled—eg, concerning the relative efficacy and safety of one product versus another (the damaging dominance of placebo-controlled trials), drugs for neglected diseases, health systems or health services research, and in returning a fair proportion of profit back to the public sector where many of the scientific ideas fuelling drug development have originated.

It is perfectly true to say that industry plays a vital part in developing new medicines to ameliorate suffering and to cure disease. Modern medicine needs a dynamic, innovative, and robust pharmaceutical industry. But it is also the case that the for-profit motive of the pharmaceutical sector clashes with the public-health values of NHS clinical care and independent scientific research. The compromised integrity of medicine's knowledge base should be a serious concern to politicians and public alike. It is surprising and disappointing that this danger does not seem a serious priority within medicine itself.

Previous Contents Next

Commons Parliament Lords Search Enquiries Index

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