Adverse reaction reports may be vulnerable to manipulation

Liza Gibson *London*

Pharmaceutical companies may be involved in manipulating reports of adverse drug reactions to generic drugs that are in competition with their own branded products, say drug regulators at the World Health Organization.

Experts at WHO's Uppsala Monitoring Centre, a body responsible for international drug monitoring, believe that systems for monitoring adverse drug reactions may be vulnerable to manipulation, after a case in Poland in which an unusually large number of reports of adverse drug reactions were filed for a generic psychiatric drug.

The doctors who filed the reports with the Polish regulatory agency may have been prompted to do so by the manufacturer of the branded version of the drug.

Professor Ralph Edwards, the director of the WHO centre, said: "This kind of underhand dealing for commercial competition is appalling."

The pharmacovigilance unit of Poland's Office of Medicinal Products, Medical Devices and

Biocides, says it received more than 100 "suspicious" reports of adverse drug reactions from 90 doctors for the generic drug. Most of the reports described lack of efficacy of the generic product and some serious side effects.

The Polish regulator does not identify the product or company, as it does not have "any proof" of its suspicions, but it believes the reports may be part of a marketing strategy of the manufacturer of the brand name drug.

It informed the WHO centre, which manages a database of adverse drug reactions called Vigibase, that it had received 36 "suspicious" spontaneous reports for the generic drug in 2003 and 92 in 2004. The second figure represented 29% of reports of adverse drug reactions for all drugs in Poland for that year (312 reports in total). The case is highlighted in the April 2005 issue of *Uppsala Reports* (No 29), the journal of the WHO monitoring centre.

The Polish regulatory body tried to investigate the reports with the doctors concerned, but they were unwilling to provide

any further information. It also assessed the quality of both products and found that they both proved to be good.

Some of the questions to the doctors related to the date of treatment, the basis for the diagnosis, the outcome of the adverse reaction, and the batch number of the product used.

A letter was sent to all of the reporting doctors, who were mostly psychiatrists, within 10 working days of their report being received. One doctor made six reports.

"We tried to contact each reporting physician in writing and sometimes by telephone," the regulator said. "The telephone contacts were extremely difficult, as some respondents claimed that they did not have time at that moment and some phone numbers were the hospital contact. We received two answers to our letters, which in fact did not clarify the cases a lot."

The WHO centre asked the regulator to investigate the matter, as WHO did not want to keep alleged "fraudulent" case reports in its database. On the other hand it could not dismiss the reports unless it knew for sure that they were invalid. As it could not prove they were invalid, it processed them but warned its staff to be particularly

alert to any potential signals relating to the drug.

Five months later the national subsidiary of the multinational company that is marketing the original brand name drug asked the WHO centre for a list of Polish adverse drug reaction reports for this drug. This search clearly distinguished between reports for the generic and brand name products. The WHO centre told Poland of the company's request.

Although the WHO centre says it does not have any proof of manipulation by the drug company, it wants to use the case to show that adverse drug reaction reporting programmes are "vulnerable to manipulation."

Professor Edwards said that although the issue is important, he believes that pharmacovigilance centres have the tools to pick up these sorts of trends. He was not surprised by the case, as it was not the first time he had encountered such manipulation, he said. There was a case in the United States in the 1990s that was not made public at the time but was resolved between the two companies concerned.

"The major reason we have not been talking about this before is it may give people ideas. I don't think it is a big problem. It is an occasional problem," said Professor Edwards. □

Dutch GPs strike over reforms

Tony Sheldon *Utrecht*

Ninety per cent of Holland's roughly 7500 general practitioners went on strike last week over fears that plans to boost competition among health insurance companies will damage primary care.

For three days normal surgeries and home visits were cancelled, and telephone answer machines directed urgent cases to hospitals.

Exceptions were made for seriously ill patients, however, when strikers volunteered to help reduce the increasing pressure on emergency departments.

The national strike came after the collapse of months of negotiations between the health minister Hans Hoogervorst and the GPs' national association (Landelijke Huisartsen Vereniging).

Negotiations, which began over pay, have grown into an ideological dispute over the benefits of competition in health care and the authority of family doctors to decide appropriate care.

From 1 January 2006 a single basic health insurance package will be introduced for everyone, allowing insurance companies to compete for patients.

For GPs this will mean a cut in the guaranteed income they get for each patient, while 6% of their budget—€90m (£62m; €113m) overall—will instead go first to insurance companies. GPs could then be reimbursed as a result of negotiations of contracts with insurers over plans to offer services such as minor surgery and specialist care for chronic patients.

But insurance companies will also be free to spend this money on other services, such as on-call centres, nurses, or specialist treatment centres.

Mr Hoogervorst believes that competition will encourage

insurance companies to get the best deal for patients. But the GPs' association believes that quality and GPs' income will suffer as insurance companies seek cheaper alternatives.

The insurers' umbrella body insists that the concerns of the GPs are unwarranted. Insurers are obliged to seek good deals

for their clients on quality and price, it says.

The minister has now written to all GPs to "remove any misunderstanding" and warning that patients must not become the victims of strike action. The association, of which 95% of GPs are members, has in turn accused the minister of intimidation. □

GPs in the Netherlands protest, hands tied, outside The Hague, at proposed changes in insurance payments