Deaths prompt calls for drug control review

Tokyo. A series of drug-related deaths that followed the prescription of drugs for non-approved applications has renewed calls for a review of the way Japan regulates drug safety. Critics say the government needs to establish an effective system for monitoring adverse drug reaction, and to put more resources into its drug approval process.

The calls for reform follow the release of a report from the Ministry of Health and Welfare (MHW) revealing that four premature babies died and three others were in a critical condition after they had been prescribed mefenamic acid for the treatment of arterial malformations.

In a separate incident, at least one patient died after being prescribed Danazole, an approved treatment for certain causes of infertility in women, for the treatment of idiopathic thrombosis (IDP). Danazole is recognized as an effective non-steroidal treatment for IDP. But critics claim that no effective watch was kept on its side-effects, as the MHW had not given official approval for this application under its 'Hokenteikyo' price-setting mechanism. Under this system,

the government sets a price for the drug and allows it to be paid for by the national health insurance scheme, which it administers.

A spokesman for the ministry's pharmaceutical affairs bureau denies that the safety aspects of approved and non-approved drugs are treated differently, and adds that it is common for drugs to be used without official sanction. Danazole, for example, has been used for treating thrombic conditions at a number of national and university hospitals since at least 1983.

But critics such as Masanori Fukushima, of Aichi Cancer Center in Nagoya, west of Tokyo, claim that official approval is being withheld from effective treatments because of under-staffing and other inadequacies in the drug approval process.

According to Fukushima, the MHW has only 20 full-time staff with a background in pharmacy dealing with drug applications, and no medical doctors; by contrast, the Center for Drug Evaluation and Research of the US Food and Drug Administration (FDA) has roughly 1,400 full-time staff, including 131 MDs.

As evidence of the Japanese system's failings, Fukushima points to the recent Sorivudine scandal, in which 15 people died within two weeks of the drug's approval (see *Nature* 369, 697; 1994) after they took it in combination with uracil-based anti-cancer drugs. Although the ministry blamed Nippon Shoji, the Osaka-based company that marketed the drug, Fukushima maintains that the MHW should have issued more explicit warnings of the danger.

There is also a long list of new drugs developed outside Japan that the MHW has so far failed to approve, including Taxol, a potent drug for treating ovarian cancer that was approved by the FDA in 1992, and Methotrexate, used in the treatment of small-cell lung cancer.

Fukushima claims that a fundamental problem in Japan's system of drug testing is the "lack of people in universities, in companies and in the MHW itself who possess the necessary training to oversee the clinical trial process". As long as this shortage remains, he claims, these deficiencies will persist.

Stephen Barker

Safety dispute ignites over plans for UK nuclear sell-off

London. The controversy over plans to privatize Britain's nuclear industry intensified last week as opposing groups clashed before a parliamentary committee about whether the future private owners of nuclear power stations would be able to maintain acceptable levels of safety.

The Electricity Supply Trade Union Council (ESTUC), which represents many electricity workers concerned that they may lose their jobs under any privatization scheme, told a House of Commons select committee that privatization would compromise safety standards as companies sought increased profitability.

But a spokesman for the Health and Safety Executive (HSE) disagreed, telling the Trade and Industry committee that privatization may improve safety standards, as it will be in the industry's self-interest to generate and maintain public support.

The government has promised to privatize the most modern parts of Britain's £3-billion nuclear industry, including the country's seven modern advanced gas-cooled reactors, as well as its pressurized water reactor, Sizewell B in Suffolk.

Trade unions point to an accident in July 1993 at a nuclear power station at Wylfa, North Wales, as an example of the type of safety lapse they are concerned about.

The station's owner, Nuclear Electric, was fined £250,000 earlier this year. At the time, there were suggestions that a "commercially intense environment" leading up to privatization had contributed to the nine-

hour delay in shutting down the reactor after a crane fell into the reactor core.

But Chris Willby, deputy chief inspector of the HSE's Nuclear Installations Inspectorate, reassured the committee that lapses would not recur. "A lot has been learned since Wylfa," he said. "We must remember that it was two years ago."

Similar confidence was expressed by Jenny Bacon, director general of the HSE. She maintained that existing safety procedures would remain firmly in place, regardless of the ownership and structure of the nuclear industry. Bacon was confident that privatization, rather than being detrimental to safety, was likely to bring improvements.

ESTUC officials also fear erosion of the

existing 'safety culture' within the industry because of low morale among staff, particularly those now working for Magnox Electric, the new publicly owned company that will retain the older Magnox reactors. These reactors will not be privatized as their total decommissioning costs of £8.5 billion exceed the revenue they could possibly generate during their lifetime.

Whereas Bacon told the committee that staff who were assigned to Magnox Electric had expressed optimism about their future careers in a company that still has 30 to 40 years to run, Tony Cooper, secretary of ESTUC, said that staff optimism stemmed from relief that the Magnox reactors were not being privatized. Such high morale, he added "can't last in a declining company".

There was also concern about the future of nuclear power research under privatization. The unions believe that short-term priorities may tempt the new owners of nuclear power to reduce long-term research spending, with serious consequences. "The research in the nuclear industry is concerned with safety and back-up. If the industry suffered as the coal-burning industry has, I think that would be a disaster," said Cooper.

But the HSE countered with the claim that research was stronger than ever. "Though we have powers to fund research if it is not met by industry, it is increasingly running research itself. We are seeing results two to three years before we would otherwise have done," said Willby.

Ayala Ochert