DRUG PROMOTION

OTA study reports on drug labelling in developing countries

WHILE appropriate drug prescribing information - "labelling" - is the norm in the United States, it is not always so in developing countries, reports a major new study from the US Government Office of Technology Assessment (OTA). In *Drug Labelling in Developing Countries**, OTA examines labelling by US-based multinational pharmaceutical companies for the drugs they sell in developing countries. Four countries - Brazil, Kenya, Panama, and Thailand - were chosen for the report.

Of the 241 drugs sampled,"*two-thirds failed to provide the labelling information a physician needs to use the drugs safely and effectively*". On a scale from zero (no problems) to three (most serious problems), half were rated two or three. Reliance on this labelling information alone could lead to serious or life-threatening medical problems, or, at best, ineffective treatment, the study reports.

Here are some examples of what OTA found:

- A combination drug including a corticosteroid, an antihistamine, and an antipsychotic was recommended for relief of itching. It had no warnings about the serious side effects of steroids, including suppression of the adrenal gland, or about the side effects of antipsychotics, including the risk of tardive dyskinesia, a sometimes irreversible movement disorder, and the risk of neuroleptic malignant syndrome, a potentially fatal side effect.
- A synthetic version of the male hormone testosterone was recommended for treating women for frigidity and benign breast conditions, to suppress production of breast milk, and to relieve menopausal symptoms. The company provided inadequate evidence that the drug is effective for these indications, and the labelling failed to warn about serious side effects of this potentially dangerous drug.
- A drug for relief of pain and inflammation was recommended for a number of minor ailments, such as headache, without mentioning potent side effects of this drug, including the complete shut down of the body's production of white blood cells - a fatal complication and the reason the drug is no longer on the US market.
- One indication for a magnesium-containing antacid was to add it regularly to infant formula to "prevent milk from souring and forming curds in the stomach", to aid digestion, and to prevent constipation in healthy babies. The company provided no evidence to support these uses, and the labelling did not warn of the danger of magnesium overdose in infants.

Current status

Consumer activists first raised the issue of inadequate drug labelling in developing countries in the late 1970s, and they still play a key role in highlighting problems and pushing for improvements, the report states. Because the governments of developing countries lack the resources necessary to review and evaluate proposed drug labelling, solutions have been sought largely outside these governments.

Under the Federal Food, Drug, and Cosmetic Act (FDCA), the US Food and Drug Administration (FDA) has no authority to require specific labelling for products sold in other countries. The OTA says that the reach of the US Government is limited further because the bulk of products sold by US-based multinational corporations in developing countries is manufactured not in the United States, but in third countries. Although legislative remedies are possible, they would require a controversial exercise of extraterritorial power.

"*International mechanisms available to tackle the issue include codes of conduct, which are voluntary binding agreements among countries, or less authoritative agreements, such as guidelines. Multinational treaties also are possible, but politically difficult*", the study concludes.

In the absence of stronger measures, the World Health Organization (WHO) has developed two strategies - the Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce and the Ethical Criteria for Medicinal Drug Promotion - that encourage countries to require better prescribing information.

And the pharmaceutical industry has itself adopted the International Federation of Pharmaceutical Manufacturers Association's Code of Pharmaceutical Marketing Practices. "*While these programmes and others under the auspices of national governments (including the United States, through the Agency for International Development) are important, they do not constitute complete or substantial solutions*", the study concludes.

Options to consider

OTA has identified the following options to improve drug labelling in developing countries:

Option 1:

"Require that all pharmaceuticals sold in developing countries by US multinational corporations and their controlled subsidiaries be accompanied by the FDA-approved label or a translation in the appropriate language".

Limiting this requirement to developing countries whose governments have agreed to it would mitigate objections by the international legal community over possibly unwarranted extraterritorial reach of US law.

Option 2:

"Endorse a voluntary international code of conduct for pharmaceutical labelling and press for adoption of the draft United Nations Code of Conduct for Transnational Corporations".

A WHO code of conduct for pharmaceutical labelling was debated by the World Health Assembly through the early 1980s. By 1983, it was off WHO's agenda, in part because the United States opposed codes of conduct to control specific industries. Given the findings of this OTA study and other recent work, it might be time to reconsider this position, says the report. It specifies that an international code of conduct would apply to all pharmaceutical manufacturers, multinationals as well as domestic companies.

The United States could press for adoption of the UN Code of Conduct for Transnational Corporations, a code that would apply to the whole range of consumer products, and which has existed in draft for many years.

Option 3:

"Endorse strengthening and expanding WHO's "Ethical Criteria for Medicinal Drug Promotion" to set standards for pharmaceutical labelling".

The Ethical Criteria are considered "guidelines", a nonbinding, weaker form of policy than a code of conduct. These could be strengthened with US support, says OTA. The United States could also help developing countries to incorporate the Ethical Criteria into their national laws, which would make them enforceable.

Option 4:

"Continue to support and expand direct assistance to developing countries for projects to improve pharmaceutical regulation, and provide additional information on pharmaceuticals to regulatory authorities".

US assistance to improve the legal and technical drug regulatory infrastructure in developing countries, currently at a minimal level, could be expanded by the FDA and USAID, and through support of WHO programmes.

Option 5:

"Mandate ongoing surveys of pharmaceutical labelling in developing countries".

Progress in improving labelling in developing countries could be monitored by periodic surveys. No provision for criminal or civil penalties would be attached to this option, avoiding possible objections of the international community to extraterritorial application of US laws. ❑

**Drug Labelling in Developing Countries, US Congress, Office of Technology Assessment, OTA-H-464, Washington, D.C., USA. Available from the US Government Printing Office, Superintendent of Documents, Mail Stop SSOP, Washington D.C. 20402-9328, USA: price US$ 11.00.*

Japanese drug manufacturers adopt new marketing code

THE potential damage to the pharmaceutical industry if any company were to put short-term profit before social considerations was the main motivation for the new promotion code for prescription pharmaceuticals in Japan, according to the Japan Pharmaceutical Manufacturers' Association (JPMA).

The code, which came into effect on April 1st, replaces one introduced in 1976 outlining minimum ethical requirements. Various guidelines and codes of practice were added between 1979 and 1984, covering sales representative training, provision of materials and samples, along with a fair competition code which restricted certain financial incentives. Industry awareness, however, remained relatively low. Companies were not well prepared to formulate in-house guidelines, and the transparency of promotional practices in general still needed to be improved, according to the chairman of the JPMA's marketing committee, Yasuhisa Yamada.

Writing in the latest edition of *JPMA Update*, Mr Yamada (who is an executive vice-president of Takeda) says that the new code takes into account the WHO Ethical Criteria and the IFPMA marketing code. It calls on companies to formulate individual plans for in-house implementation based on their awareness of ethical standards, and notes that companies must bear all responsibility for their promotional activities.

The main sections of the code cover standards for salesforce activities, production/use of promotional materials and advertisements (labelling is covered by the Pharmaceutical Affairs Law), post-marketing surveillance, supply of samples, conduct of seminars and study meetings, provision of gifts and financial inducements, and the code's relation to the fair competition code restricting financial inducements. Mr Yamada notes that certain financial inducements have caused problems in Japan.

The JPMA has set up a committee to oversee implementation of the code. Sanctions for violations range from warnings to expulsion from the JPMA - names of violating companies may also be published.

The Association has also established an ethics committee (comprising JPMA board members) to determine measures to be taken in the case of other corporate transgressions. This committee will decide on cases where expulsion from membership is being considered for serious violations of the promotion code.

Source: Scrip, 3 August 1993.