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Heart arrhythmias from allergy drug

The Food and Drug Administration (FDA) last week asked the manufacturer of the popular prescription allergy drug terfenadine — sold under the trade name Seldane — to warn physicians that the drug can cause potentially fatal abnormal heart rhythms in some patients.

Terfenadine's manufacturer, Marion Merrell Dow, Inc., of Kansas City, Mo., responded by sending 600,000 mailgrams to health care professionals, informing them of "rare cases of serious cardiovascular adverse events" following use of the drug, especially in patients also taking the antifungal drug ketoconazole or the antibiotic erythromycin.

Since terfenadine was approved in the United States in 1985, the FDA has recorded 64 serious cardiac events — including cardiac arrest and various types of life-threatening arrhythmias — among the 200 million patients who have taken the drug. Four patients who experienced the adverse events died.

A Marion Merrell Dow spokesman said that most of the events are attributable either to drug interactions with ketoconazole or erythromycin, or to preexisting liver damage that allowed terfenadine to build up to toxic levels in patients' bloodstreams. He said the company has changed terfenadine's label to advise against its use by such patients. He added that Marion Merrell Dow has deferred a decision on whether to apply for approval to sell an over-the-counter preparation of terfenadine, pending further tests of the drug's safety.

Renewed flap over AIDS test patent

The Pasteur Institute of Paris has requested millions of dollars in past and future royalties from the U.S. government on sales of the patented AIDS blood test developed by U.S. and French scientists, according to an American attorney representing the French research center.

The request was made on the grounds that U.S. negotiators misled the French over the timing and sequence of the scientific discoveries that led up to the test's roughly simultaneous development by U.S. National Institutes of Health researcher Robert C. Gallo and Pasteur Institute scientist Luc Montagnier. Those negotiations ended with a 1987 agreement to share the royalties on the AIDS test patent, which have so far totaled roughly \$50 million.

The Pasteur Institute's U.S. attorney, Michael Epstein of the New York City law firm Weil, Gotshal & Manges, says his client has not received a response from the U.S. Department of Health and Human Services (HHS) regarding a January request for all of the royalties from sales of the test. He says the Pasteur Institute is "actively considering" filing suit against HHS to resolve the issue.

The French are demanding all of the royalties from the test on the basis of a public admission by Gallo that his laboratory isolated the virus upon which the test is based from samples that had been inadvertently contaminated by a virus in a separate sample sent to him by Montagnier. Gallo admitted the mix-up last summer in a letter published in *NATURE*. Montagnier has subsequently conceded that he and his colleagues did not know of the existence of that virus and that they based their blood test on another, slightly different virus.

Gallo's attorney, Joseph Onek of the Washington, D.C., law firm Crowell & Moring, contends that the source of the virus used in either the U.S. or the French blood test is irrelevant to the issue of the AIDS test patent. What's important, he says, is who first performed the tricky feat of using proteins from an AIDS virus to detect AIDS antibodies in the blood of infected individuals.

"Nothing has been learned that gives [the French] any justification for changing the settlement," says Onek. "If they want to go to court, let them . . . they don't have a case."

Modeling a shower's toxic threat

Studies have documented the presence in drinking water of many potentially toxic volatile organic chemicals (VOCs) — from chloroform and pesticides to carbon tetrachloride. Such findings have spurred investigations into the inhalation hazards these compounds may pose when released into the air during baths and showers. However, because shower and tub equipment, as well as other design features, differed widely in these experiments, air releases for a single VOC could vary up to 10-fold from one studied system to another, observes John C. Little of Lawrence Berkeley (Calif.) Laboratory.

A general model incorporating known factors such as a chemical's volatility, water temperature, and the flow rates of water and air would help gauge the relative impacts of other shower variables. Little developed such a model, described in the July *ENVIRONMENTAL SCIENCE AND TECHNOLOGY*, by applying a classic engineering theory to data from five shower studies that others conducted. The trick to modeling a shower's turbulent air-water interface, he explains, is to treat the material on either side of that interface as a stagnant thin film.

The most volatile chemical studied in the experiments was a Freon known as CFC-11. Little's worst-case analyses indicate that people showering for 10 minutes in water containing this VOC would inhale 50 percent more of the potential toxicant than they would ingest by drinking two liters of that water. Indeed, his analyses indicate, under the same shower conditions, exposures to CFC-11 would be three times higher than those to the lowest-volatility VOCs studied — the pesticide 1,2-dibromo-3-chloropropane, a suspected carcinogen.

The more volatile chemicals also take longer to saturate indoor air. "I don't want to sound alarmist," Little says, "but this could have serious implications for institutional shower facilities, like health clubs," that are in use all day and don't provide a lot of ventilation. While air concentrations of the low-volatility compounds peak in enclosed spaces in about three hours, Little's model indicates that concentrations of very volatile compounds can keep growing for up to 16 hours.

By confirming that water turbulence represents one of the biggest factors affecting a VOC's release, Little says, the model suggests that ways to minimize a shower head's creation of turbulent mists may offer a fertile field for study.

The new model makes possible "much better predictions of VOC-inhalation exposures from showers" for chemicals and conditions not yet studied, Little says. At a minimum, that should help drinking-water regulators, he adds, since it makes no sense to regulate contaminants solely on ingestion risks if daily showers can present comparable or greater dangers.

Insects mine lake contaminants

Many winged insects spend their early life at the bottom of a lake, feeding in or near sediment. As they mature and fly away — often to become dinner for birds, amphibians, or bats — they can transport back into the food chain pollutants formerly locked away in sediment, a new study shows.

Canadian researchers deposited tetrachlorodibenzofuran (TCDF) — a dioxin-like chemical — into 5-meter-diameter tubes anchored in shallow lake water. TCDF levels in mature bugs leaving the tubes over succeeding weeks were compared to those of insects from tubes with no added TCDF. The data indicate that insects from even a relatively unproductive northern lake can remove "a small [about 1 percent] but biologically significant portion" from sediments each year, report Wayne L. Fairchild and his co-workers at the Freshwater Institute in Winnipeg, Manitoba. Moreover, they write in the June *ENVIRONMENTAL TOXICOLOGY AND CHEMISTRY*, these totals don't count the contribution of insects too big for effective trapping, such as mayflies and dragonflies.