Associated Press
Safety of American Drugs Questioned
By JEFF DONN

BOSTON - In a sharp pivot, many medical authorities are questioning the fundamental safety guarantees for American drugs, threatening to dull the national appetite that has demanded and devoured pharmaceuticals at a faster clip for nearly a generation.

In a challenge unthinkable even two months ago, Dr. Catherine DeAngelis, editor of the Journal of the American Medical Association, now compares the drug safety system to a dangerous building:

"This building is on very shaky ground. Would I condemn it? No, but I would tell people, 'You go in at your own risk.'"

In recent months, troubling news about several high-profile drugs has sapped confidence in the system for flushing out dangerous medicines and assuring the supply of safe ones. Worries abound over the safety of antidepressants, the recall of blockbuster pain reliever Vioxx, and a winter with rationed flu vaccine.

Such intense outcries over safety have rarely been heard since the 1960s, when the European thalidomide scandal of deformed babies motivated this country to fashion a more protective federal Food and Drug Administration

Since the late 1980s, Americans have mostly been begging for faster approval of presumed lifesaving drugs for such diseases as AIDS and cancer. Lately, they are wondering if medicines - now pumped out by a $200 billion annual industrial powerhouse - are arriving too fast and doing too much harm. Are medicines safe? They ask.

Interviewed in recent days by The Associated Press, experts within and outside government respond with some jarring answers: No drug is ever fully safe, any more than a drive down the highway. The safety net isn't designed to catch rare side effects until drugs reach the market. By then, regulators are often powerless to spot mistakes quickly and reluctant to jump on them, according to many drug authorities.

Dr. Jerry Avorn, a Harvard Medical School expert who wrote a book on the drug industry, says recent revelations about the FDA suggest "a culture of denial" about dangerous side effects, especially once a drug is on the market. Some authorities contend that FDA's post-marketing safety monitors need more independence from the unit that evaluates drugs for approval.

Dr. Steven Galson, acting director of FDA's drug operation, says the agency forces companies to overcome "a high hurdle" to demonstrate drug safety. However, he also says that "the group that approves new drugs does invest a lot of time and energy, and it is a verylegitimate question to ask if they can (properly) look at new information that comes up."

Some policy specialists think the safety system ruptured in recent years, allowing far too many of the 100,000 annual drug deaths estimated in one study. Others say many flaws are old. Some weaknesses may reflect much heavier drug use than in the past and the slow evolution of the safety apparatus. Nearly everyone believes repair is possible, but few predict quick sweeping action.

"The system itself is completely broken," says Dr. David Graham, senior safety scientist at FDA who has begun speaking outside the agency's chain of command. "The system is incapable of preventing another Vioxx." He says the agency approves drugs if it can't prove them unsafe, instead of forcing makers to demonstrate safety - a point challenged by his superior, Galson. Graham has put forth his own list of five marketed drugs to re-evaluate. Dr. Sidney Wolfe,

director of the nonprofit Public Citizen Health Research Group, says there are better, safer alternatives to more than 180 drugs.

Yet only 16 drugs have been pulled from the market since 1997, mostly voluntarily - if under FDA pressure. Some FDA defenders say a new antidepressant warning and Merck's withdrawal of Vioxx prove the system is working.

Many analysts trace purported safety failings to 1992, when Congress adopted industry-paid user fees to pay for faster FDA reviews. Waits for standard drug approval have typically been cut by more than half, to under one year, government data show.

However, critics say the funding makes the industry, not the public, the agency's master. Also, many members of influential FDA advisory panels have ties to drug companies.

"The industry has now captured the agency that is supposed to be regulating it," claims Dr. Marcia Angell, a former editor of the New England Journal of Medicine who wrote a recent book on the drug industry.

The corporate influence has seeped into doctor's offices too, where drug salesmen make routine house calls. Doctors often prescribe drugs for conditions beyond their demonstrated usefulness, often to satisfy patients who may have seen an ad depicting a treated illness as a prance through a flower bed.

Yet relatively few new drugs are dramatic or one-of-a-kind additions to the national medicine cabinet. Last year, less than a third of 72 new drugs had novel active ingredients, and the FDA viewed only a quarter as "significant improvements." Makers must show only that their drug works better than a dummy treatment, not better than a competing drug.

Drug testing usually involves just a few thousand patients, with few elderly or having special conditions. "When a new drug is marketed, there will usually be safety problems as yet unknown," says Dr. Brian Strom, a drug risk specialist at the University of Pennsylvania.

The FDA's Galson says it is legitimate to ask if more or better testing is needed. "Everybody knows that the system we have now is not adequate to pick up all adverse events that will occur once a drug gets out into the population. The question is, are we willing to pay for more trials?" he says. He adds that, above all, the FDA must do more to expose its data and decision-making to doctors and patients.

Tony Plohoros, a spokesman for Vioxx maker Merck, cautioned against requiring more safety data for drug approval, potentially delaying patient access to important new medicines.

Many experts think safety especially suffers later, when rare harmful effects pop up only with mass consumption. Doctors are merely encouraged to report them, and the FDA forces the industry to carry out relatively few studies of drugs on the market, critics say.

Many critics argue that an independent body should take over this monitoring role with heftier public funding, stronger authority to shoo bad drugs and a firewall against industry pressure.

"If a plane crashes off the coast of New York, we don't leave the investigation to the controllers that were controlling the plane and the airline that was flying it," says Dr. Alastair Wood, a Vanderbilt University pharmacologist and FDA drug safety adviser.

Despite such complaints, most critics readily acknowledge that thousands of Americans survive or lead better lives thanks to effective drugs. "Medicines that receive FDA approval are among the safest in the world," Acting Commissioner Lester Crawford declared recently. The agency has

commissioned the independent nonprofit Institute of Medicine to study drug safety and recommend improvements.

Drug makers say their profits drive innovation. Jeff Trewhitt, a spokesman for the Pharmaceutical Research and Manufacturers of America, says the latest problems cropped up in just a handful of more than 10,000 treatments.

"In the vast majority of cases, these medications are doing what they are supposed to do," he says.