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Statement by Sidney M. Wolfe, M.D.
Director, Public Citizen's Health Research Group about
FDA Article in the 5/12/99 Issue of the JAMA:
The Safety of Newly Approved Medicines
(embargoed until 4:30 P.M., 5/11/99)

The Editorial by Dr. Alastair Wood accompanying the FDA article repeatedly calls for seeking more information about the circumstances of the withdrawal of the five drugs highlighted in the FDA article, requesting an "open public attempt to define what happened." Unfortunately, the FDA itself has whitewashed this serious problem by selectively providing only the information in their article which exonerates the agency from blame in the approval or failure to earlier withdraw these five drugs.

**Fenfluramine and dexfenfluramine**: The FDA focuses entirely on the valvular heart disease which ultimately caused the agency to take these drugs off the market. There was no mention of hundreds of cases of oft-fatal primary pulmonary hypertension caused by these drugs, known prior to the 1996 approval of Redux (dexfenfluramine), which many doctors on FDA's advisory committee were so concerned about that they initially voted against approval. There was also opposition within the FDA to the approval of Redux.

**Terfenadine (Seldane):** At least two years before this drug was taken off the market, the FDA was aware of a large number of cases of fatal or near-fatal heart arrhythmias caused by its use in combination with other drugs. But, as Dr. Wood points out, the agency waited until the manufacturer could gain approval of a less-toxic metabolite of the drug so as to minimize its marketing losses although this delay prolonged the risks of death to those using the drug after it should have been taken off the market.

**Mibefradil (Posicor)**: Early results of a study of this drug for treatment of heart failure--known to the FDA before approval--had shown an increased number of sudden cardiac deaths in people using the drug, prompting one of the three members of FDA's advisory committee who opposed the approval to state, prior to approval, that "aren't we obligated to provide some assurance the ECG [electrocardiogram] changes we've seen are not ultimately lethal?" He advocated waiting for approval until the end of the trial, whose later results helped to propel the drug off the market, only after 600,000 people were subjected to its dangers.

**Bromfenac (Duract) :** The amount of liver toxicity known to the FDA before approval caused a cancellation of planned use of this drug for treating arthritis and the FDA doctor in charge of the drug recommended a box warning about liver damage when the drug came on the market. He was overruled.

None of these drugs were breakthrough drugs and the serious safety concerns should have prevented their approval in the cases of Redux, Posicor, and Duract and a much earlier market withdrawal for Seldane. FDA's conclusion that there is no problem associated with these drug safety withdrawals should not be taken seriously because to do so will continue to jeopardize the safety of American patients.