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Physician-Scientist Urges Improved Drug Regulation to Ensure Heart Safety of Non-Heart Drugs

Recommendations by NewYork-Presbyterian/Weill Cornell's Dr. Jeffrey Borer Emphasize Need for Better Attention to Cardiovascular Effects, Beginning With Early Studies and Continuing Past Drug Approval

NEW YORK (Dec. 28, 2007) -- Current regulatory policies should be strengthened to ensure acceptable cardiovascular safety of drugs developed primarily for non-cardiovascular medical problems, according to a recent presentation made by Dr. Jeffrey Borer, an authority in cardiovascular medicine and surgery at NewYork-Presbyterian Hospital/Weill Cornell Medical Center in New York City.

His recommendations include earlier testing of all drugs' cardiovascular effects and giving regulatory bodies the authority to mandate continuing evaluation of drug effects, even after approval for marketing.

"The importance of evaluating the cardiovascular safety of new drugs has been highlighted by recent examples of drugs -- anti-arthritis drugs and others -- that were withdrawn from the market when unacceptable cardiovascular risks were discovered after regulatory approval," says Dr. Borer. "It is clear that drugs intended for non-cardiovascular problems must be more fully scrutinized than in the past in order to allow doctors and patients to be assured that risks are well defined and that they do not outweigh the benefits provided by the drugs for the individual patient. The primary strategy to achieve this goal is increasing formal observations in both pre- and postapproval studies."

Specific recommendations include:

- Cardiovascular safety assessment should be incorporated in drug development beginning with animal studies of drug effects on cardiac physiology/pharmacology, even if the drug is not intended for cardiovascular problems. Similarly, evaluation of cardiovascular effects should begin in the earliest phases of drug testing in patients. The definitions of adverse cardiovascular events like heart attacks and strokes should be standardized for all observers before the drug is administered to any patient. (Currently, for drugs not intended for heart problems, cardiovascular effects often are assessed only minimally, generally in later phases of drug development. And, the definition of adverse events is left up to each observer individually, limiting the strength of conclusions about cardiovascular safety.)

- Regulatory bodies should be given the authority to mandate continuing evaluation of drug effects, even after approval for marketing. This will allow updates in drug labeling to increase the precision with which doctors and patients can know the relation of benefit and risk, enabling the best decisions about selection of treatment strategies.

• Regulatory bodies should be empowered to withdraw approval if mandated postmarketing studies are not performed. Currently, the FDA, for example, does not have such authority.

• If the drug is likely to be used by people who have relatively high cardiovascular risk (as,
for example, might be the case with a drug for arthritis), at least one study of the drug's beneficial effects should be carried out among such patients, not only in low risk people as is now commonly the case.

• Analysis plans should be designed to incorporate all data collected during development, including results of so-called observational studies (which do not employ randomization to eliminate study bias, and which do not employ "control" groups for comparison) in order to increase statistical power to find problems if they exist. Currently, this kind of analysis plan is not usually employed.

Dr. Borer's presentation was made at the recent annual meeting of the European Society of Cardiology in Vienna, and was drawn in part from his article in the Aug. 2007 issue of the *European Heart Journal*. This paper summarizes the conclusions of a group of co-authors -- including cardiologists, biostatisticians, FDA and EMEA (European Medicines Agency Home) regulators and representatives from the NIH and the pharmaceutical industry -- who had met previously at a Cardiovascular Clinical Trialists roundtable in Paris to consider these issues. Jeffrey S. Borer has been an FDA advisor since 1977 and served three terms as Chair of the FDA's Cardio-Renal Drugs Advisory Committee between 1982 and 2004. He is director of the Howard Gilman Institute for Valvular Heart Diseases at NewYork-Presbyterian/Weill Cornell and the Gladys and Roland Harriman Professor of Cardiovascular Medicine and professor of cardiovascular medicine in cardiothoracic surgery at Weill Cornell Medical College.The Howard Gilman Institute for Valvular Heart Diseases at NewYork-Presbyterian/Weill Cornell helps cardiologists, cardiothoracic surgeons and other physicians take advantage of the most current concepts in the evaluation and treatment of heart valve diseases and provides state-of-the-art patient care. The Institute's co-directors, Dr. Jeffrey S. Borer and Dr. O. Wayne Isom, are leaders in their fields and direct a team of clinical cardiologists, surgeons and research scientists who are at the cutting-edge of this emerging public health concern. For more information, visit www.gilmanheartvalve.org.

NewYork-Presbyterian Hospital/Weill Cornell Medical Center
NewYork-Presbyterian Hospital/Weill Cornell Medical Center, located in New York City, is one of the leading academic medical centers in the world, comprising the teaching hospital NewYork-Presbyterian and Weill Cornell Medical College, the medical school of Cornell University. NewYork-Presbyterian/Weill Cornell provides state-of-the-art inpatient, ambulatory and preventive care in all areas of medicine, and is committed to excellence in patient care, education, research and community service. Weill Cornell physician-scientists have been responsible for many medical advances -- from the development of the Pap test for cervical cancer to the synthesis of penicillin, the first successful embryo-biopsy pregnancy and birth in the U.S., the first clinical trial for gene therapy for Parkinson's disease, the first indication of bone marrow's critical role in tumor growth, and, most recently, the world's first successful use of deep brain stimulation to treat a minimally-conscious brain-injured patient. NewYork-Presbyterian, which is ranked sixth on the U.S.News & World Report list of top hospitals, also comprises NewYork-Presbyterian Hospital/Columbia University Medical Center, Morgan Stanley Children's Hospital of NewYork-Presbyterian, NewYork-Presbyterian Hospital/Westchester Division and NewYork-Presbyterian Hospital/The Allen Pavilion. Weill Cornell Medical College is the first U.S. medical college to offer a medical degree overseas and maintains a strong global presence in Austria, Brazil, Haiti, Tanzania, Turkey and Qatar. For more information, visit www.nyp.org and www.med.cornell.edu.
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