FDA NEWS RELEASE

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FDA and International Consortium Report New Data on Drug-Induced Liver Injury

The U.S. Food and Drug Administration and the International Serious Adverse Event Consortium (SAEC) today announced important strides in the understanding of the genetic basis for drug-induced liver injury.

The consortium has identified a genetic link associated with liver injury in some people who receive the antibiotic Flucloxacillin. The drug is widely used in Europe and Australia but is not available in the United States.

Drug-induced liver injury or DILI occurs in a small subset of patients. It is often associated with a drug of unpredictable liver toxicity, and may be the cause of acute liver failure in some patients. Although the exact mechanism of DILI is unknown, research suggests that a person's genes contribute to their likelihood of developing the injury.

"These findings provide the research community with novel genomic data on DILI events and make an important contribution to the science of drug safety," said Janet Woodcock, M.D., director of the FDA's Center for Drug Evaluation and Research. "By making these data available, the research community will have better tools to evaluate predictive biomarkers for adverse events such as DILI. This type of collaborative research will eventually reduce a patient's likelihood of experiencing serious, and sometimes life-threatening, adverse drug events."

SAEC researchers found that the *HLA-B*5701* genotype was associated with Flucloxacillin-related liver injury after analyzing DNA samples and DILI genomic data. *HLA-B* is one of a number of highly variable genes responsible for immune function on chromosome 6. In addition to *HLA-B*5701*, variations on chromosome 3 were also found to influence risk for DILI. These findings provide new insights into the mechanism of DILI and have the potential to help identify individuals who may have an increased risk for this serious event.

"We are pleased to be able to provide these invaluable data to the research community to both improve the productivity of drug development and to begin the critical process of developing validated biomarkers to forecast patients who may be at risk for DILI," said Arthur Holden, founder and chairman of the SAEC.

The consortium and its academic collaborators are publishing these results in the July issue of the journal Nature Genetics.

The SAEC is a nonprofit partnership of 10 international pharmaceutical companies, the Wellcome Trust, and academic institutions focused on research relating to the genetics of drug-induced serious adverse events. The SAEC collects well-characterized information on the DNA of individuals who have experienced drug-related liver toxicity from the databases of its

participating partners and compares this information to a control group. All personal information has already been de-identified to protect patient privacy. Additional important genetic findings are expected to emerge from these efforts over the next 12 to 24 months.

For more information on the International Serious Adverse Event Consortium and data access see www.saeconsortium.org.

For information on the FDA's Critical Path Initiative see http://www.fda.gov/oc/initiatives/criticalpath/

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