Contact: Arthur Holden
Chairman, iSAEC, Ltd

8770 W. Bryn Mawr Ave., Suite 1300
Chicago, Illinois
Phone: 1-773-867-8595

INTERNATIONAL SERIOUS ADVERSE EVENTS CONSORTIUM (iSAEC) ANNOUNCES COMPLETION OF ITS PROGRAM TO STANDARDIZE SAE PHENOTYPE DEFINITIONS

Nonprofit consortium unites industry, academia and government in the development of phenotype definitions for major drug related Serious Adverse Events (SAE)

Chicago (July 7, 2015) – The International Serious Adverse Events Consortium (iSAEC) announced today the completion of its program to accurately define the phenotypes of four major drug induced serious adverse events (SAEs). The four SAE phenotypes of focus in this innovative collaborative effort were Drug Induced Skin Injury (DISI), Drug Induced Liver Injury (DILI), Drug Induced Renal Injury (DIRI) and Drug Induced Torsades de Pointes (DITdP). To date, these definitions have been used to recruit 5,000 well characterized SAE cases, which have underpinned the iSAEC's research into the genetics of SAEs. The iSAEC is a nonprofit research corporation, launched in the fall of 2007, now in its second phase of research, comprised and funded by ten leading pharmaceutical companies and the Wellcome Trust. The iSAEC program to accurately define SAE phenotypes was also supported by financial contributions from the U.S. Food and Drug Administration (FDA) and the Wellcome Trust (London).

Patients respond differently to medicines, and all medicines can have adverse effects in a small number of people. The SAEC's work is based on the hypothesis that many of these differences may have a significant genetic contribution. Its research studies have/are exploring the impact genetics can have on how individuals respond to specific medicines/classes of medicines. There are a large number of drugs that can cause heart, kidney, liver, or skin injury in a small subset of patients. Although the exact mechanisms behind such rare and unpredictable serious adverse reactions are unknown, the iSAEC's research suggests genetic variation, mainly in the area of the genome that regulates immune function contribution, plays an important role.

The objective of this project was to produce standard phenotypic definitions for four (4) major drug induced SAEs, which could then be adopted and used widely by the clinical/scientific/biomedical research communities to better standardize research into the genetic base of SAEs. These definitions were drafted by international clinical experts, reviewed and refined at a consensus conference hosted by the Wellcome Trust, and published as follows:

- **Overview Article** – "The Phenotype Standardization Project: Improving Pharmacogenetic Studies of Serious Adverse Drug Reactions". M Pirmohamed, GP Aithal, E Behr, A Daly et al., Clin Pharmacol Ther., 9(6):784-58, 2011.
- **DISI Article** – "Phenotype Standardization for Immune-Mediated Drug-Induced Skin Injury", M Pirmohamed, PS Friedmann, M Molokhia, YK Loke et al.,Clin Pharmacol Ther., 89(6):896-901, 2011.
- **DILI Article** – "Case Definition and Phenotype Standardization in Drug-Induced Liver Injury", GP Aithal, PB Watkins, RJ Andrade, D Larrey et al., Clin Pharmacol Ther., 89(6):806-15, 2011.

- **DITdP Article** – “Phenotype Standardization for Drug-Induced Torsades de Pointes”, Elijah R. Behr, Dan Roden et al, European Heart Journal, 10.1093/eurheart/ehs172, 22 May 2012.
- **DIRI Article** -- “Defining drug induced renal injury and the different phenotypes of drug induced renal injury”. Ravindra L Mehta, Stewart L. Goldstein, Linda Awdishu, et al. Kidney International, online publication, April 2015.

The effort was chaired by Prof Munir Pirmohamed, MB ChB (Hons), PhD, FRCP, FRCP(E) who is the NHS Chair of Pharmacogenetics and Director, MRC Centre for Drug Safety Science at the University of Liverpool (England).

iSAEC data and more information of this program can be accessed via the iSAEC’s (www.saeconsortium.org) website. Qualified researchers, who enter into a data use agreement, can obtain free access to these data for exclusive use in biomedical research.

iSAEC Membership and Collaborators
The iSAEC’s participants include representatives from the pharmaceutical industry, the scientific community, and government.

- Pharmaceutical industry members are closely involved in all aspects of the Consortium’s research, providing ongoing consultation on the development and structure of the Consortium’s scientific models, and contributing cohort data and underwriting costs of SAE research/operations. The iSAEC’s 10 Phase 2 funding members include: Abbott, Amgen, AstraZeneca, Daiichi Sankyo, GlaxoSmithKline, Merck, Novartis, Pfizer, Takeda and the Wellcome Trust.
- iSAEC provides researchers with open access to its data through a controlled-access database. Twelve months after genotyping studies are complete, data is released without any patent or intellectual property constraints, allowing for further use and study by interested researchers.
- The FDA is providing consultation on the conduct of iSAEC studies and data release.

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About the iSAEC
The International Serious Adverse Event Consortium (iSAEC) is a 501(c) organization* dedicated to identifying and validating DNA-variants useful in predicting the risk of drug-related serious adverse events. The Consortium brings together the pharmaceutical industry, regulatory authorities and academic centers to address clinical and scientific issues associated with drug-related serious adverse events. iSAEC partners are providing financial support, in-kind donations, and participation in data collection to the this research. The iSAEC is the only privately-funded partnership currently dedicated to studying SAE genomics.