The Innovative Medicines Initiative (IMI) Qualification of Translational Safety Biomarkers

SAFE-T Consortium
Safer And Faster Evidence-based Translation

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Introduction
The SAFE-T consortium is the first project to start under the EU Innovative Medicines Initiative-Joint Undertaking (IMI-JU), a unique public-private partnership between the European Communities (represented by the European Commission) and the pharmaceutical industry (represented by the European Federation of Pharmaceutical Industries and Associations [EFPIA]).

IMI-JU’s objective is to support projects that address the main causes of delay, or “bottlenecks”, in the pharmaceutical research and development process.

Background
A lack of specific and sensitive mechanistic safety markers and their respective assays for human samples is regularly delaying drug development programs. This is especially the case when a histopathological signal is seen in preclinical toxicology studies which cannot be adequately monitored in humans. 3 target organs critical for drug-induced injury with non-appropriate clinical monitoring:

Kidney: Current standards (Serum Creatinine, BUN) are only increased when 50-60% of the kidney function is lost.
Liver: Current standards (AST, ALT, Bilirubin) are not specific and do not predict who will recover and who will develop fulminating liver disease.

Vascular System: There are currently no biomarkers to monitor drug-induced vascular injury in human.

Objectives
➢ To evaluate the utility of safety biomarkers for monitoring organ safety in humans.
➢ To develop assays and devices for clinical application of safety biomarkers.
➢ To compile enough evidence to qualify safety biomarkers for regulatory decision making in clinical drug development and in translational context in cooperation with the health authorities.
➢ To gain evidence for how safety markers may also be used in the diagnosis of diseases and in clinical practice.

SMEs (4):
➢ Firalis SAS (Hüseyin Firat, initiator of the SAFE-T proposal for SMEs and academic partners)
➢ Argus Medical Limited - formerly Boston Int (Joe Keanan)
➢ EDI GmbH (Thomas Joss)
➢ Interface Europe (Lindy Cochrane)

Academic (5):
➢ Barcelona Cardiovascular Research Center (Lina Badimon)
➢ Charité Hospital (Ulf Neumann)
➢ AHPF, GPHS (Thiery Pognard, Patrice Cacoub)
➢ Natural and Medical Sciences Institute (Nicola Schwanthaler-Munz)
➢ Tel-Aviv (Souraski) Medical Center (Nadir Arber)

EFPIA members Pharma (11):
➢ Novartis (Frank Dieteler)
➢ AstraZeneca (Neus Prats)
➢ Amgen (Lauren Brown)
➢ Pfizer (Deirdre Robinson-Gravatt)
➢ Hoffmann-La Roche (Lucette Dosschevier)
➢ AstraZeneca (ma.schuppe-kolsien)
➢ Bayer Schering Pharma AG (Thomas Krahne)
➢ Boehringer Ingelheim (Arno Kaufhold)
➢ Eli Lilly (Karen Briner)
➢ GlaxoSmithKline (John Hasselstein)
➢ Sanofi Aventis (Isabelle Clarinier)

External Advisors:
➢ European Medicines Agency, FDA (proposed)
➢ Above names are the Steering Committee members

Conclusion:
The SAFE-T consortium will strongly influence the science and the regulatory acceptance of safety biomarkers to support drug development and ultimately to improve patients’ health.

The SAFE-T Consortium will establish a scientific biomarker qualification strategy and apply it in clinical BM studies for the translation, performance testing and eventual regulatory qualification of safety BMs for drug-induced kidney, liver and vascular injury (DILI, DILI & DIVI).

➢ Definition of scientific clinical qualification processes for safety BM qualification in clinics
➢ New clinical BMs compared to current standards and criteria to be met in DILI, DILI & DIVI
➢ Assay development procedures: fit for purpose for exploratory phase, multiplexed and GLP-validated for confirmatory phase
➢ Establishing baseline values and their variability in healthy subjects and various patient populations.
➢ Run protocols to measure the performance of these BMs against current standards in clinical studies and hospital units with expected drug-induced injuries and in patients with relevant diseases (exploratory and confirmatory phase for all 3 organs)
➢ Setting up a common database and biosample repository to be able to build up on any new data set up coming in the future and to investigate further BM candidates
➢ Qualification of appropriate biomarkers for regulatory decision making in clinical contexts together with health authorities.
➢ Gaining mechanistic understanding when needed via pre-clinical studies

SAFE-T Consortium, partners in project
Duration: 5 years, 36 Mio € research budget proposed 18 Mio Pharma in-kind, 14 Mio EC contribution, 4 Mio SME / academic overhead
➢ The most extensive project of the first round of IMI projects
➢ Consortium approved for funding in March 2009
➢ Kickoff meeting in Stockholm on June 15, 2009