

SAFE-T Consortium Safer And Faster Evidence-based Translation

H. FIRAT*, B. MOLAC, A. GARAMI, 35 rue du Fort, 68330 Huingue/France

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]).



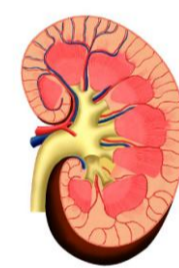
IMI-JU's objective is to support projects that address the main causes of delay, or "bottlenecks", in the pharmaceutical research and development process.

Background

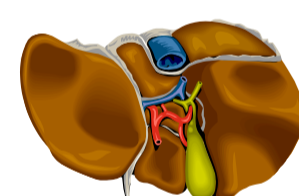
A lack of specific and sensitive mechanistic safety markers and their respective assays for human samples is regularly delaying drug development programs. This is especially the case when a histopathological signal is seen in preclinical toxicology studies which cannot be adequately monitored in humans.

3 target organs critical for drug-induced injury with non-appropriate clinical monitoring :

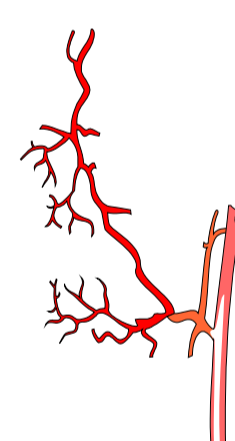
Kidney: Current standards (Serum Creatinine, BUN) are only increased when 50-60% of the kidney function is lost.



Liver: Current standards (AST, ALT, Bilirubin) are not specific and do not predict who will recover and who will develop fulminant liver disease.



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



SMEs (4):

- Firalis SAS (Hüseyin Firat, initiator of the SAFE-T proposal for SMEs and academic partners)
- Argutus Medical Limited - formerly Biotrin Intl (Joe Keenan)
- EDI GmbH (Thomas Joos)
- Interface Europe (Landry Cochard)

Academic (5)

- Barcelona Cardiovascular Research Center (Lina Badimon)
- Charité Hospital (Ulf Neumann)
- APHP, GHPS (Thiery Poynard, Patrice Cacoub)
- Natural and Medical Sciences Institute (Nicole Schneiderhan-Marra)
- Tel-Aviv (Souraski) Medical Center (Nadir Arber)

EFPIA members Pharma (11)

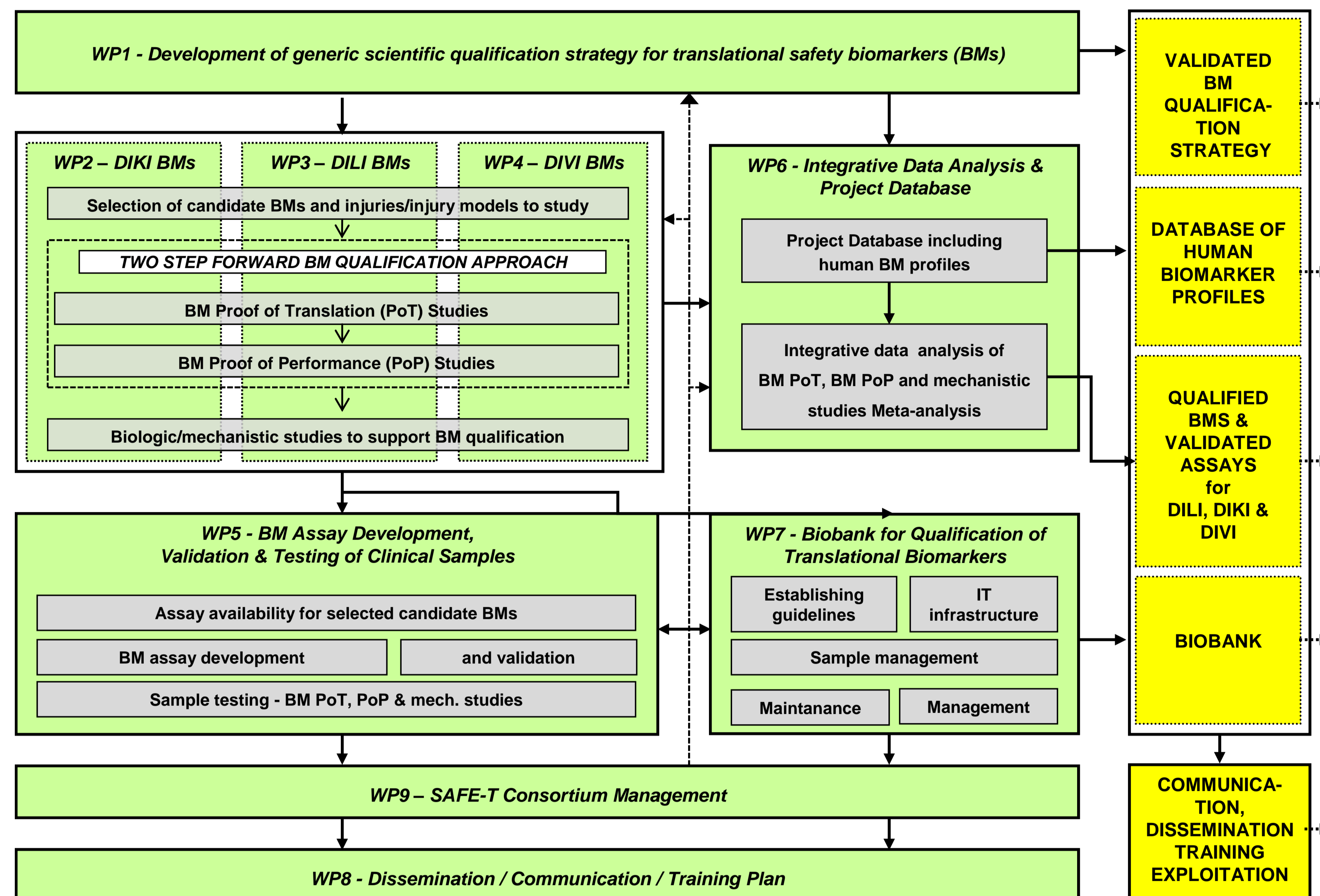
- Novartis (Frank Dieterle)
- Almirall (Neus Prats)
- Amgen (Lauren Brown)
- Pfizer (Denise Robinson-Gravatt)
- Hoffmann La Roche (Lucette Doessegger)
- AstraZeneca (ina.schuppe-koistinen)
- Bayer Schering Pharma AG (Thomas Krahn)
- Boehringer Ingelheim (Arno Kalkuhl)
- Eli Lilly (Karin Briner)
- GlaxoSmithKline (John Haselden)
- Sanofi Aventis (Isabelle Clavier)

External Advisors

- European Medicines Agency, FDA (proposed)
- Above names are the Steering Committee members

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



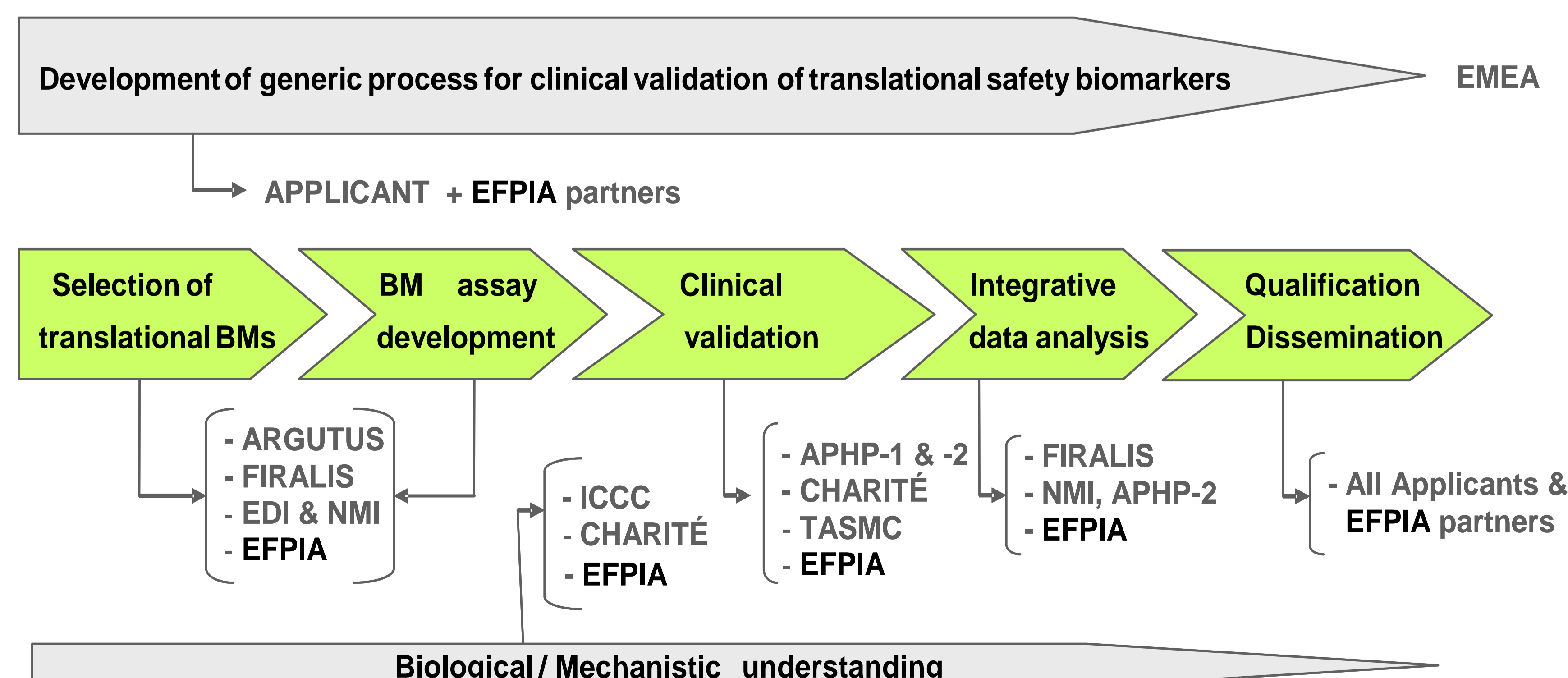
The SAFE-T Consortium will establish a scientific biomarker qualification strategy and apply it in clinical BM studies for the translation, performance testing and eventual regulatory qualification of safety BMs for drug-induced kidney, liver and vascular injury (DIKI, DILI and DIVI).

- 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 DIKI, 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 upcoming 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



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.

For more information about SAFE-T, please contact

Dr. Frank Dieterle, Coordinator of SAFE-T, (frank.dieterle@novartis.com) or
Dr. Ina Schuppe Koistinen, Scientific Coordinator of SAFE-T (ina.schuppe-koistinen@astrazeneca.com) or
*Prof. Hüseyin Firat, initiator of the SAFE-T proposal for SMEs and academic partners (hueseyin.firat@firalis.com)