IMI: Where we are today

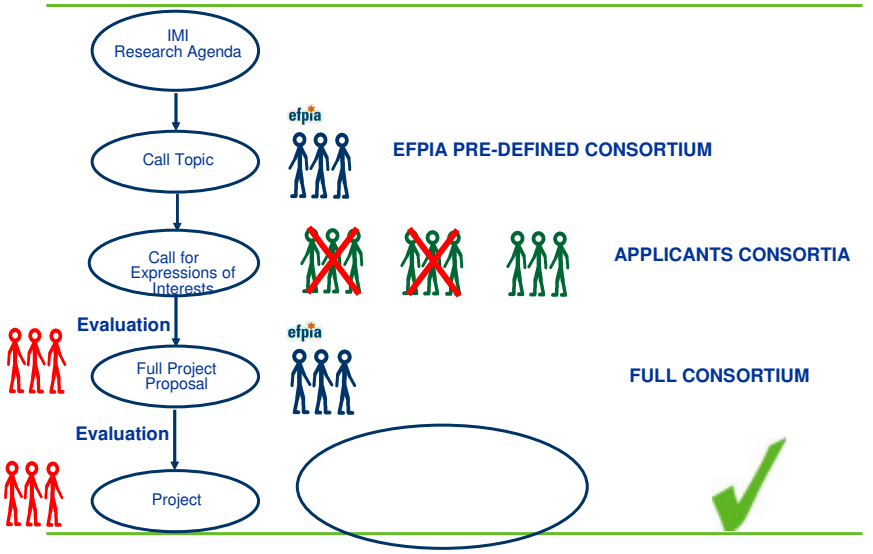
1st Call launched April 30, 2008.
Projects started from mid 2009 - early 2010 (15 projects).
Total Project Budget 280 Mio €.

2nd Call launched November 27, 2009.
Projects are currently in final negotiation phase (8 projects).
Total Project Budget 180 Mio €.

3rd Call launched October 20, 2010 (7 projects).
Total estimated Project Budget in the range of 140 - 200 Mio €.

Decision on 2-3 further calls (2011 – 2013) to be taken.
Total remaining Project Budget in the range of 1.3 – 1.4 Billion €.

IMI Call Process



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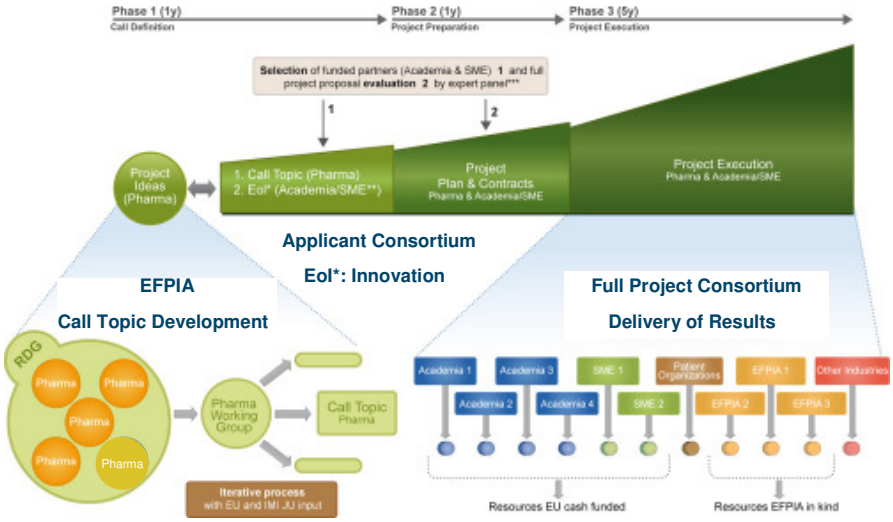
Wien, Mittwoch, 3. November 2010

IMI JU: Driving from idea to delivery of results



* EoI: Expression of Interest ** SME: Small and Medium Enterprise (e.g. Biotech) *** selected by IMI JU

IMI: Achievements first examples

SAFE-T (project start: June 15, 2009):

DILI Biomarker qualification process agreed with FDA and EMA

First clinical trial completed and 21,504 frozen specimens (blood and urine) delivered to Biobank

e-TOX (project start: January 1, 2010):

First Report on Data Classification: final draft available

Predictive system requirements: review process ongoing

First version of the common ontology available

IMIDIA (project start: February 1, 2010):

First imaging Biomarker to enter in-vivo evaluation

Bio-repository (human islet) for Biomarker discovery/validation established at 4 clinical sites

First standardized human ß-cell lines under evaluation

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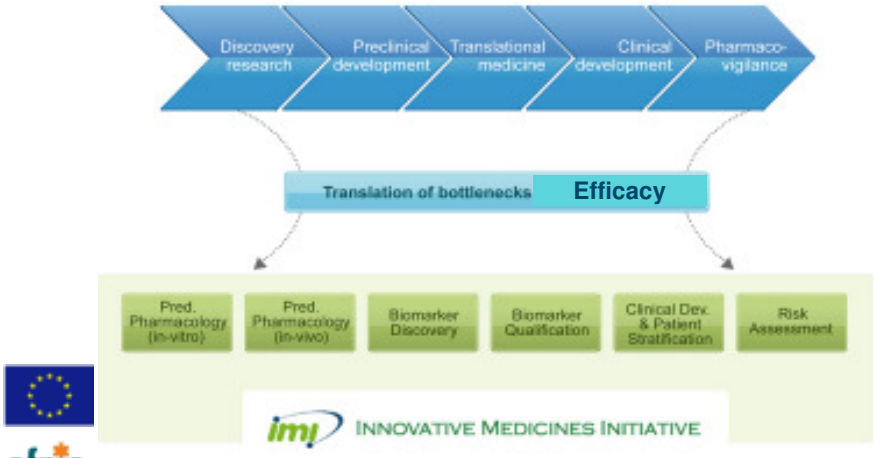
IMI Efficacy Pillar



Innovative Medicines Initiative

Personalized Therapy in Diabetes

EFPIA Coordinator: Hartmut Ruetten (Sanofi-Aventis)

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Wien, Mittwoch, 3. November 2010

Personalized medicine in Diabetes

Disease

- Complex heterogeneous disorder
- Multiple genetic and environmental factors
- A ‚silent' disease
- No quantitative determinants for individual, patient-specific progression
- Diagnosis often comes late

Treatment

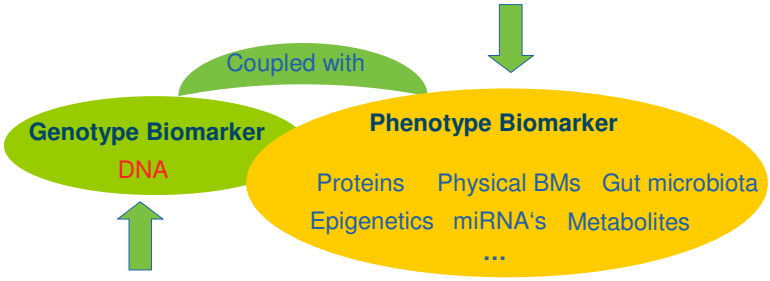
- Treatment guidelines with few phenotypic selection criteria
- Trial and error approach to find effective drug(s) for individual
- 9 classes of drugs available
- Challenge to position new drug classes in treatment scheme

Introduce personalized approaches

- Better treatments for individual patients
- More effective drug development and easier market access

Personalized Medicine:
Genetic + phenotypic + environm. traits

….and here is the opportunity



So far, we only handled this…

Objectives

- **Develop stratification and response tools for drug development**

- **Personalized therapeutic strategies in well-defined sub-populations**

- **PART 1:**
  - Disease hypothesis based on data from well phenotyped patients.
  - Harmonisation of data mining across academia and industry
  - Standardisation of protocols for basic (e.g. Hb1Ac, FPG, OGTT, etc.) and deep/specific (e.g. MRI, PET, clamp, etc.) phenotyping.
- **PART 2:**
  - Prospective clinical trials to qualify new disease hypothesis

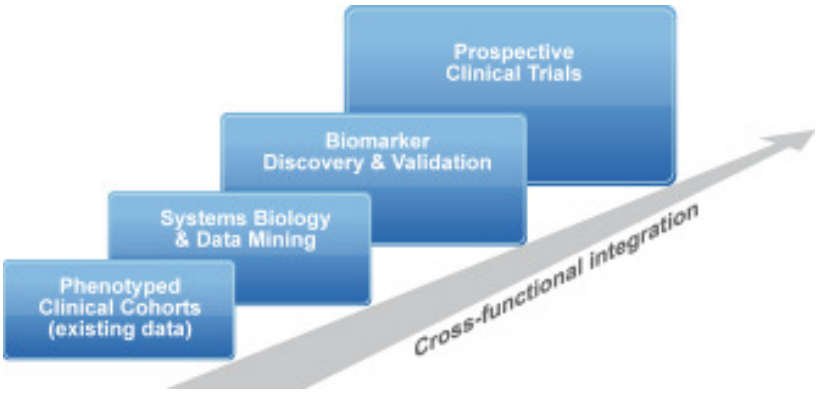
Deliverables (Part 1)

- **Patient samples and data: generation of a high quality European data bank to generate relevant phenotypical data sets**
- **Systems Biology Platform: Integrating clinical data, biological data, genomics, metabonomics and other relevant data**
- **Data Mining: Application and development of novel data mining tools and algorithms to generate stratification and response biomarker candidates**
- **Development of Biomarker Assays**

Deliverables (Part 2)

- **Prospective Clinical Trials: Validation of biomarker candidates in prospective clinical trials (potential scenarios depending on the Biomarker Candidate types to be tested; follow-up of 5-7 years):**
- **Assessment of the response (or lack of response) to established therapies (targeting extensively characterized mechanisms, for instance incretin pathway) in well defined sub-populations.**

Translation of bottlenecks into IMI Projects: Personalized Therapy in Diabetes



Expected contributions of the applicants

Pre-clinical and clinical expertise and ability for inter-disciplinary and intersectorial work

- build a large high quality EU database from phenotyped patients
- develop a diabetes specific systems biology platform.
- indentify, evaluate and qualify biomarker candidates
- perform phenotyping, genetic and metabolic assays.
- develop and validate new biomarker tools and corresponding predictive biomarker assays
- have experience in conducting (small and/or large land mark) clinical trials.
- provide and develop novel clinical trial design concepts (adaptive clinical trial designs).

Expected (in kind) contributions of EFPIA members

- **Overall**
  - Project Management
  - Statistical Analysis
- **PART1:**
  - Database Establishment + Retrospective Hypotheses Testing (samples and data from clinical trials, which may also come from outside EU/FP7)
  - Phenotypic data generation
  - Systems Biology Platform (expertise and know how)
  - Data Mining (expertise and tools)
  - Biomarker Assay Development (expertise and application support.)
- **PART2:**
  - Design of prospective clinical trial(s): resources and expertise for trial design,
  - Execution of prospective clinical trial(s) and interpretation of results: resources and expertise to conduct multi-centre clinical trials (monitoring, data management, etc.)

** different innovative project designs are welcome, if properly justified.*

Suggested architecture* of the project

- **Overall**
  - **WP1: Project Management**
    - Focus: management, project management and support.
  - **WP10: Statistical Analysis**
    - Focus: Evaluation of novel statistical and clinical trial design concepts and methods for the clinical evaluation of biomarker tools.
- **Part 1**
  - **WP2: Database Establishment + Retrospective Hypotheses Testing**
    - Focus: Merging of existing data from small/individual cohorts into a large, high quality European data bank for data mining
  - **WP3: Phenotype Data Generation:**
    - Focus: To consolidate / generate a broad data set for individual patients (in line with corresponding legal and ethical guidelines) using highly disease relevant technologies (for example clamp, MRI, PET, etc.).Project Management
  - **WP4: Systems biology**
    - Focus: Systems biology platform to be established by integrating clinical data, biological data, genomics, metabonomics and other relevant data.
  - **WP5: Data mining**
    - Focus: Application and development of novel data mining tools and algorithms to generate stratification and response biomarker candidates (i) describing patients at risk of diabetes and at risk for disease progression, (ii) to derive a personalized treatment strategy and (iii) potentially identify new drug development targets.

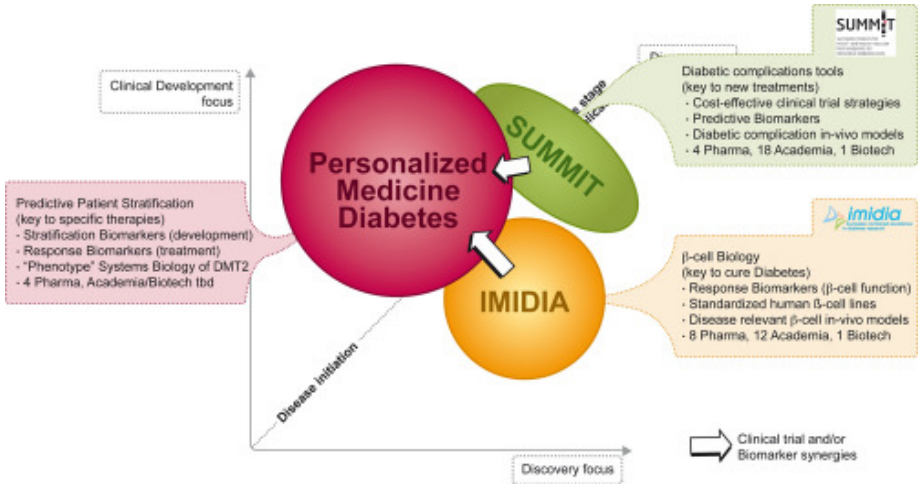
Suggested architecture of the project

- **Part 1 (continued)**
  - **WP6: Biomarker assay development**
    - Focus: : “Industrialized” confirmation and qualification of new or already known biomarkers for personalized therapy in well defined sub-populations (Part 1: application in retrospective trials; Part 2: support exploring novel clinical design strategies, e.g. adaptive clinical trial designs). Quantification of patient metabolism and target variability.
- **Part 2**
  - **WP7: Design of prospective clinical trial(s)**
    - Focus: Design of prospective clinical trials for Validation of biomarker candidates. Potential scenarios depending on the Biomarker Candidate types to be tested (follow-up of 5-7 years; example 1: deep phenotyping, e.g. PET, MRI, clamp in ~ 500 patients; example 2: basic phenotyping in ~ 3000 patients). Assessment of the response (or lack of response) to established therapies (targeting extensively characterized mechanisms, for instance incretin pathway) in well defined sub-populations.
  - **WP8/9: Execution of prospective clinical trial(s) and interpretation of results**
    - Focus: Execution of trials (examples see WP7)

Expected impact on the R&D process

- Better definition of patient subpopulations based on biomarker for early proof of concept studies.
- Enabling to design specific clinical studies for early proof of efficacy and safety for new treatment modalities. Cost reduction in clinical development.
- Common basis across academia and industry for patient stratification.
- The systems biology description of early type II diabetes will increase the understanding of the pathophysiology of the disease (provided by a single data repository).
- Potential delivery of new drug targets
- Potential translation of new biomarker(s) from preclinical animal models to proof of concept in patients.

IMI Diabetes Platform - Complementarities



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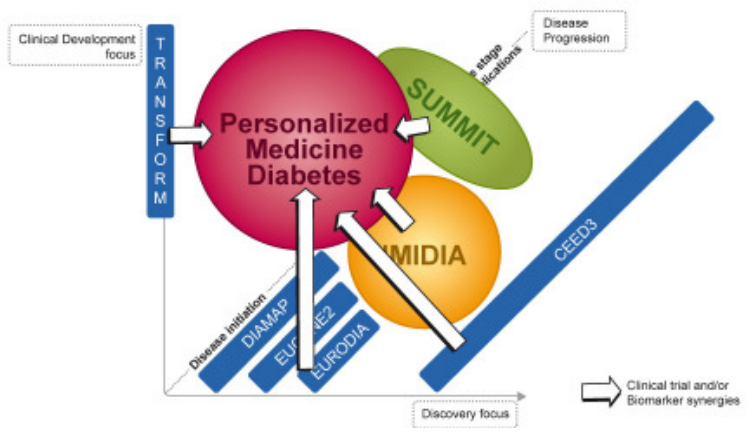
IMI Diabetes Platform – Gateway to additional synergies



Improving the preclinical models and tools for tuberculosis medicines research

EFPIA Coordinator: Martin Pan (GSK)

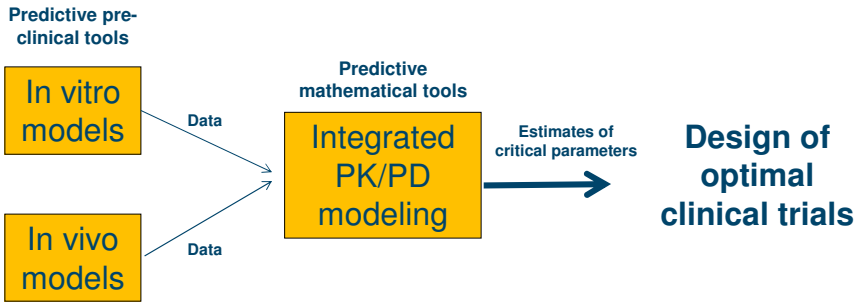
FFG Veranstaltung zur Innovative Medicines Initiative (IMI): Startklar für die 3. Ausschreibung, Wien, Mittwoch, 3. November 2010

Tuberculosis: Major global health threat

- Poverty-related disease, public health emergency, global dimension of the problem
- Duration & cost of drug development
- Scientific challenge
- No single organisation can be successful: joint collaborative public and private efforts are critical

Objectives

- To define an integrated set of pre-clinical in vitro and in vivo models that provide critical data to design optimized clinical studies in TB patients



Deliverables

- Optimized, standardized and validated drug discovery models
- Mathematical models predictive of efficacious exposures in humans

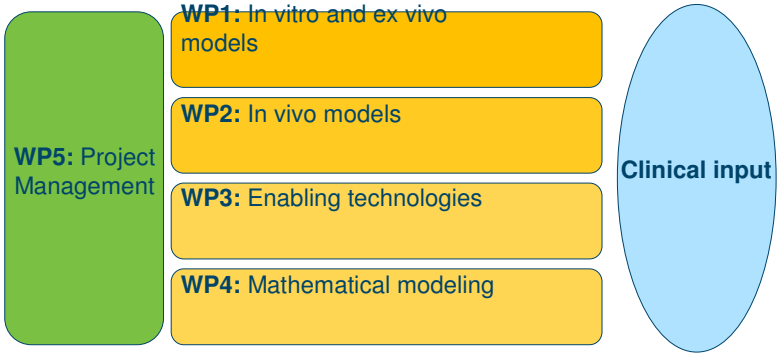
Expected contributions of the applicants

- Microbiology of TB. Cellular Biology and Immunology related with TB
- In vitro / in vivo / in silico models
- Enabling technologies (e.g. imaging, biomarkers)
- Pharmacokinetic/pharmacodynamic (PK/PD) modeling and simulation

Expected (in kind) contributions of EFPIA members

- In vitro models (e.g. whole blood assay, intracellular)
- in vivo models (e.g. Zebrafish model)
- Imaging technologies
- Microbiology expertise
- PK/PD modelling & simulation
- Chemical library and compounds
- OpenLab space
- Predictive biomarkers expertise
- Project Management

Suggested architecture of the project



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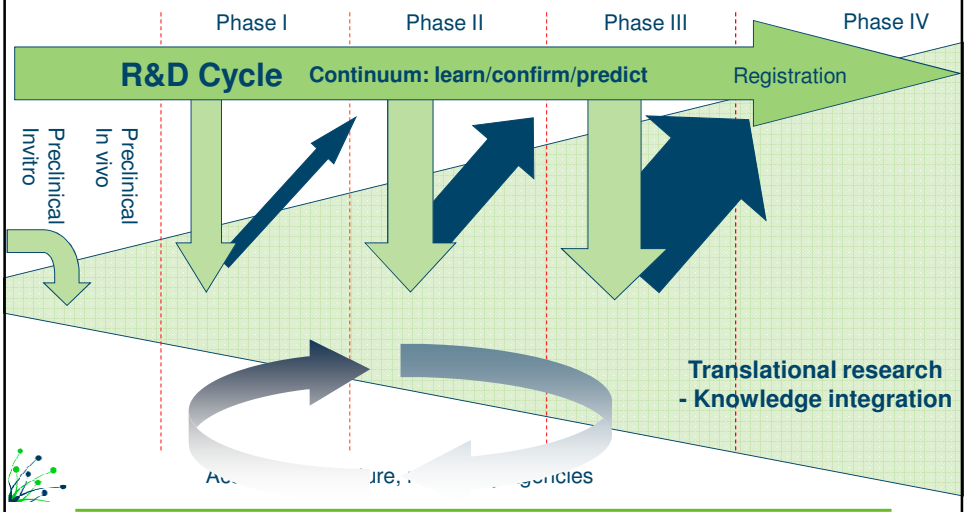
Expected impact on the R&D process



Innovative Medicines Initiative

Translational endpoints in Autism

EFPIA Coordinator: Will Spooren (Roche)

ASD - Family of heterogeneous neuro-developmental disorders

- Autism spectrum disorders (ASD): characterized by deficits in (a) social interaction, (b) communication, and (c) unusual repetitive behaviours
- 1% of all children, increasing prevalence
- no medication available to change core symptoms
- lack of evidence based therapy
- new promising findings
  - Core deficit in synaptic function in many of the genetic forms of ASD
  - Using animal models of monogenetic diseases leading to ASD, key behavioural and neuroanatomical phenotypes have shown to be responsive to drug intervention:
    - mGlu5 receptor antagonists for Fragile X
    - Sirolimus for Tuberous Sclerosis
    - Statins for neurofibromatosis Type 1
    - Insulin-like Growth Factor-1 (IGF-1) for RETT syndrome.

Objectives

Create a European wide strategy for ASD treatment

- Set new standards in Research and Clinical Development to aid the drug discovery process.
- Develop and validate translational approaches for the advancement of novel therapies to treat ASD.
- Identify, standardize and develop expert clinical sites across Europe
- Evidence based treatment of ASD patients
  - Diagnosis, clinical assessment, outcome measures

Deliverables

Establishment of an integrated approach to enable drug discovery and development in ASD

- Development of cellular/animal models with a close link to the neurobiology of ASD (translation from animals to patients).
- Validation of biomarkers to predict pharmaco-dynamic responses to drug (allow patient stratification and support regulatory submissions).
- Integrated clinical and preclinical research approach for ASD
- Promotion of an educational awareness program

Expected contributions of the applicants

Scientific/pre-clinical/clinical expertise in ASD and ability for interdisciplinary and intersectorial work

- Innovative project design and science
- Clinical trial expertise
- Regulatory expertise
- Data management and integration expertise
- Involvement of Patient organisations
- Educational program to create awareness
- Professional Project management

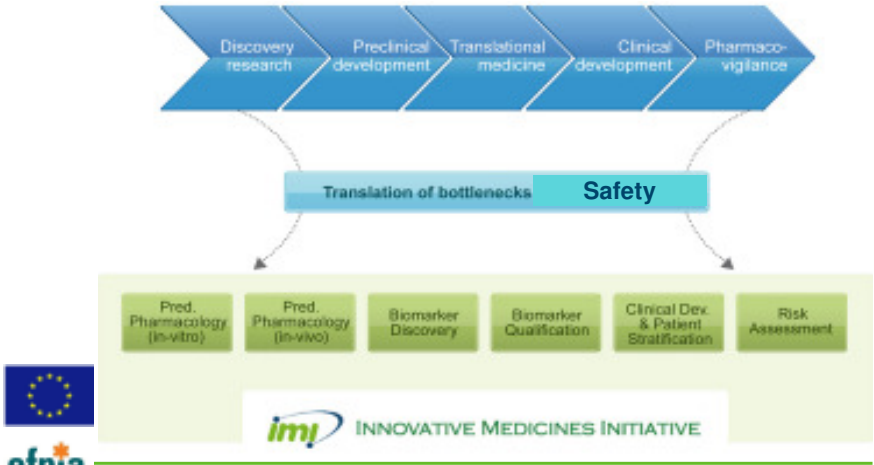
Expected (in kind) contributions of EFPIA members

- In vitro technologies expertise and experiments
- Neuro-anatomical and electrophysiological expertise and experiments
- Behavioural models and generation of transgenic animals
- Supplies of pharmacological tools
- Biofluid biomarker development and experiments
- Translational behavioural procedures and experiments
- Clinical and neuropsychological expertise and experiments
- Imaging and electrophysiological expertise and experiments
- Experience, expertise and data from relevant clinical trials
- Clinical trials supplies and logistics
- Regulatory approach

Expected impact on the R&D process

- Identification of reliable and predictable assays
  - Cellular
  - Animal
  - Translational
- Standardization in research and clinical praxis
- Alignment of the field including regulatory praxis
- Well designed and controlled clinical studies

IMI Safety Pillar



Improved early prediction of Drug Induced Liver Injury (DILI) in man

EFPIA Coordinator: Gerry Kenna (Astra Zeneca)

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Wien, Mittwoch, 3. November 2010

DILI: leading cause of drug withdrawal and candidate attrition

- Most common pattern of DILI observed in man is idiosyncratic.
- Numerous scientific advances with potential to provide useful new predictive approaches.
- Effective evaluation of these approaches needed ("best practice" guidelines)
  - Academic groups have been limited by lack of access to compounds
  - Pharmaceutical companies have been hampered by the complexity of the science

Objectives

1. ***Identify and validate an improved panel of in vitro "best practice assays" for predicting DILI in the human population***
2. Explore and understand the relationship between *in vitro* assay signals and DILI *in vivo*
3. Develop and validate novel predictive Systems Modelling approaches
4. Enhance shared understanding (academia, pharma, regulatory) of the value and limitations of new and existing approaches for DILI hazard identification and risk assessment

Deliverables

- A panel of improved and/or novel *in vitro* assays which enhance prediction of DILI in man
- Novel *in vivo* preclinical models that improve DILI hazard identification and risk assessment
- Industrial and regulatory acceptance of the new approaches
- Understanding the most appropriate use of new preclinical approaches for replacement, refinement and reduction of animals usage
- New data and knowledge, resulting in best practice guidance and computational DILI systems models

Expected contributions of the applicants

Evaluate and build predictive in vitro and in vivo assays and models

Multi-disciplinary approach:

- close collaboration with pharma incl. SME technology service providers (e.g. for cell supply, mathematical modelling).
- Engagement with regulatory bodies since (regulatory acceptance is a long term goal).

Expected (in kind) contributions of EFPIA members

- Provision of legacy data that aids in selection of the most promising assays and models for evaluation.
- Supply of reference hepatotoxic compounds plus non-hepatotoxic compounds.
- Support to experimental design and data analysis (informatics, statistics, computational modelling).
- Complex instrumentation and technology (e.g. robotics, high content biology, omic profiling).
- Design and execution of live phase evaluation of promising new *in v*ivo models.

Expected impact on the R&D process

Develop safer drugs more effectively

- Select compounds that have reduced likelihood to cause DILI
- Reduce the incidence of compound attrition and project delay caused by DILI

Innovative Medicines Initiative

Immunogenicity: Assessing the Clinical Relevance and Risk Minimization of Antibodies to Biopharmaceuticals

EFPIA Coordinator: Kathleen Beach (GSK)

The clinical relevance of anti-drug antibodies (ADAs) is poorly understood

- At present it is impossible to fully predict the immunogenicity of biopharmaceuticals due to:
  - complexity of the immunological mechanisms
  - wide diversity of biopharmaceuticals
  - concentrating on single products or dedicated predictive tools
- Opportunity through PPP
  - compare all relevant predictive tools
  - pool data in order to gain the statistical power to identify the factors relevant for immunogenicity
  - share scientific expertise on immunogenicity

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Objectives

- Investigate the clinical relevance of biopharmaceutical-associated immunogenicity
- Evaluate the predictive value of existing tools and develop new ex-vivo methods
- Investigate the immunological mechanisms that drive the development of anti-drug antibodies
- Provide data-driven feed-back to regulators and healthcare professionals

Deliverables

- Improved understanding of clinical relevance of ADAs
- Evaluation of different technologies used to detect ADAs
- Establishment of database to house patient and drug characteristics, exposures, safety and efficacy outcomes, ADA assay results, prediction tool results
- Clearer understanding of the value of prediction tools, correlation to immunogenicity assay data and clinical outcome
- Evaluation of relevance of factors currently used in risk based approach to immunogenicity assessment
- Identification of early activation biomarkers as potential predictors of immunogenicity
- Feedback to the health authorities regarding factors influencing the clinical relevance of immunogenicity
- Educational materials for healthcare providers

Expected contributions of the applicants

- Provide access to patient registries for a selected set of marketed drugs (e.g. TNF-alpha blockers, IFN-beta compounds and clotting factors)
- Provision of prediction tools and application of these tools to a selected set of marketed drugs
- Development of innovative methods and approaches leading to improved predictability of ADA responses and/or ADA characterization
- Establishment and maintenance of the database
- Identification of mechanisms of immunogenicity and its relationship to immune-mediated adverse events
- Intellectual and practical scientific input to address bottlenecks in translation of pre-clinical to clinical data

Expected (in kind) contributions of EFPIA members

- Provision of prediction tools currently used by the EFPIA companies and application of these tools to a selected set of marketed drugs (e.g. TNF-alpha blockers, IFN-beta compounds and clotting factors)
- Scientific input for innovative approaches (assay methodologies, ADA characterization and/or immunogenicity prediction technologies
- Know-how in immunogenicity assay development, validation and data interpretation
- Expertise in analysis of observational data and data management
- Clinical safety expertise

Expected impact on the R&D process

- Investigation of the clinical relevance of immunogenicity will increase patient safety, and optimize drug development
- The evaluation of the predictive value of existing tools and newly developed ex vivo methods will result in improvements of existing and development of innovative predictive tools. These tools might subsequently be used for candidate selection in early drug development
- The investigation of immunological mechanisms that drive the development of anti-drug antibodies may ultimately lead to the identification of patient stratification markers and reduce the risk of immunogenicity

Immunosafety of Vaccines
New Biomarkers associated with adverse events (early inflammation and autoimmune disease)

EFPIA Coordinator: Aldo Tagliabue (Novartis)

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Wien, Mittwoch, 3. November 2010

Vaccines are for all ages.

Harmonization, standardization and optimization of both reporting and grading as well as the prediction of early and late adverse events

Objectives

1. The characterization of early inflammation induced by vaccines currently on the market and the identification and validation of biomarkers of early inflammation and allergic responses
2. The identification and validation of early biomarkers of autoimmunity and their use to help identifying population at risk of developing autoimmunity
3. The analysis of the incidence and epidemiology of autoimmune disease in the general population and the link to genetic background or previous events in the life of patients

Deliverables (1)

1. Innovative biomarkers and assessment methods to accurately describe vaccine induced inflammation
2. Validation of acceptable type/level of inflammation after administration of vaccine
3. Validation of new and reliable in vivo (animal models) or in vitro (cell culture) models predicting early inflammation and potential exacerbations of latent autoimmunity induced by vaccines
4. Harmonization of guidelines to identify and record early clinical symptoms after vaccination

Deliverables (2)

5. Early biomarkers of autoimmunity and allergy “qualified for use” to predict potential risk of revealing chronic disorders at time of vaccination
6. Identification of early biomarkers of potentially at risk individuals which could allow adopting a more personalized vaccination strategy
7. Large databases of samples from recipients of current vaccines, innovative tools and adequate IT/Knowledge management structure allowing to determine the link between occurrence of autoimmune and allergic disorders and new biomarkers/historical events in the general population that will serve as a baseline for future vaccines

Deliverables (3)

7. A better understanding of the frequency of more common autoimmune diseases (namely those claimed to be revealed/exacerbated by vaccines) in the general population
8. New general guidelines approved by Regulatory Authorities to evaluate the immuno-safety of vaccines

Expected contributions of the applicants

New innovative approaches on the way to evaluate the immunosafety of vaccines

•Expertise in vaccinology and in the clinical and preclinical identification and assessment of biomarkers for inflammatory diseases and autoimmunity.

•Experience in conducting pan-European clinical trials, establishing and maintaining biobanks, sample and data management, bioinformatics and mathematical modeling.

•Regulatory authorities (FDA/EMEA) should be closely associated to the project as well as experts in infectiology and cohorts of patients suffering from autoimmune diseases.

Expected (in kind) contributions of EFPIA members 1

- General immunological and toxicological expertise's regarding inflammation
- Know how in statistical analysis (genomic and pre-clinical / clinical study data)
- Know how in bioinformatics
- Know how in sample and data management
- Marketed vaccines
- Animal models or in vitro models to evaluate immunosafety of vaccines
- Harmonize and standardize preclinical tests to evaluate the safety of vaccines
- Bio samples from internal bio banks (sera, cells ….)
- Support and expertise in clinical data management and biostatistics
- Standardize immunoassays to evaluate the safety of vaccines (evaluation of cytokines, inflammatory proteins ……)

Expected impact on the R&D process

Modify the vaccine development process:

•Creating awareness in the industry and academia on the immunosafety of molecules impacting the immune system (e.g., antigens, adjuvants, etc.)

•Establishing a common language on the vaccine immuno-safety problems

•Having an impact on the way to develop and to evaluate new vaccines

•Addressing the problem of immuno-safety of vaccines much earlier than before (before first clinical trials)

Innovative Medicines Initiative

IMI JU 3rd Call for proposals
Education & Training Pillar

FOSTERING PATIENT AWARENESS ON PHARMACEUTICAL INNOVATION

Objectives

Build innovative information programmes for different **stakeholders** involved on:

- the **biomedical research** and the **processes** leading to drug approval
- the multiple facets of **personalized** and **predictive medicine**
- **rational** approach to **drug safety** and **risk benefit assessment** of novel drugs
- the importance of **health technology** and **pharmaco-economics assessment** in modern medicines
- the **design** and **objectives** of **clinical trials**
- the **synergies** between **innovative medicines** and other **strategies** to enhance patient-centred chronic disease management

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Deliverables

- establishment of a multidisciplinary and multilingual network of experts including patient advocacy groups to conceive and implement balanced information programs for patients, carers and other lay audiences interested in health policy

- establishment of an information programme to be available in a minimum of 6 major European languages

- implementation of informational strategies and activities based on novel information and communication technologies, targeting large audiences across Europe

- establishment of methods to assess and monitor the understanding and perception of pharmaceutical research linked to the development of new medicines

Applicant Consortium is expected to:

- gather the **multidisciplinary expertise** necessary to **conceive** and **implement** the **informational activities** together with patient organizations representative of major disease areas across the European Union

- **address all areas** making key contribution on the defined deliverables in synergy with the EFPIA consortium

EFPIA participants* will contribute by:

- developing and implementing informational activities together with the other consortium partners

- participating in the overall organisation and governance of the project

- supporting translation activities

contacts

All questions should go through the IMI Executive office

infodesk@imi.europa.eu

www.imi.europa.eu