# IMI Scientific Priorities 2010

**Disclaimer:**
Please note that the Scientific Priorities set forth hereunder should not, in any case, be regarded as the topics for the 3rd Call of the IMI JU.

**Summary of Scientific Priorities**

| Priority | Title | Pillar | Scientific Area |
|---|---|---|---|
| **A** | Assessment of drug induced toxicity in relevant organs - surrogates for early drug failure | Safety | General Safety |
| **B** | Immunological Safety of Biopharmaceuticals | Safety | Immunology |
| **C** | Assessment inflammatory disease | Efficacy | Inflammatory Diseases |
| **D** | Improve the scientific and pre-clinical infrastructure for Tuberculosis medicine | Efficacy | Infectious Diseases |
| **E** | Enhancing translation in neurological disease | Efficacy | CNS |
| **F** | Development of personalized medicine approaches in diabetes | Efficacy | Metabolic Diseases |
| **G** | Fostering a broader understanding of pharmaceutical R&D in the broader public | Education & Training | |

## Safety Pillar: General Safety

## Scientific Priority A :
**Assessment of drug induced toxicity in relevant organs - surrogates for early drug failure**

**Problem statement**
Assessment of drug induced toxicity in relevant organs like liver, cardiovascular system, testes still suffers from a lack of sensitive and highly predictive test systems. Adverse events in these organs represent an increased risk for the patient and often cause delays, termination in development, or lead to regulatory actions on drugs when on the market. There is a strong need for new markers, tools and assays to detect drug induced injuries in various organs early in research and development and to enhance human risk assessment.

**Benefits from Private-Public Partnerships (PPP)**
Combination of long-lasting knowledge in performance and evaluation of *in vitro* assays, *in vivo* experiments and clinical studies (EFPIA companies) together with knowledge about specific methods for mechanistic investigations and data mining (Academia and SMEs).

**Objectives/deliverables**
- Knowledge Management: Share, pool and explore the growing but fragmented body of knowledge on drug induced toxicity and genetic variation on drug response
- Improve mechanistic understanding of organ specific drug injuries
- Identification of novel biomarkers, tools and assays with a high sensitivity and predictivity to aid preclinical to clinical translation from the mechanisms explored
- Introduction of a common set of validation principles to defining the utility of each model in pharmaceutical risk assessment, based on guide-lines recommended by ECVAM to the European Commission
- Qualification of candidate biomarkers, corresponding assays and diagnostic methods in close interaction with Regulatory Authorities

**Examples of potential complementarity/synergies with other EU initiatives**
The FP7 projects “PSIP”, “EU-ADR”, and “preDICT”; The IMI 1st Call projects MARCAR and SAFE-T

## Safety Pillar: Immunology
## Scientific Priority B :
## Immunological Safety of Biopharmaceuticals

**Problem statement**

Evaluation of the immunological safety of biopharmaceuticals, such as monoclonal antibodies, vaccines, interferons and thrombolytic agents, is of concern for the pharmaceutical industry and regulatory health authorities. A wide variety of clinically significant biopharmaceuticals-induced immunotoxic effects have been described, some of which could not be predicted despite the use of state-of-the-art toxicity studies and clinical trials. These effects include immunosuppression, severe inflammation, anaphylactic reactions and autoimmune disorders. Whether acute or delayed, there is currently no harmonization in the way investigators characterize or report these adverse events, notably the systemic symptoms (e.g. pain, myalgia, arthralgia, headache). This often leads to a lack of understanding between the level of immunogencity and the clinical relevance to patients. Further complicating matters, there is currently no possibility to stratify patients according to susceptibility to develop immunogenicity. Also no guidelines to support immunogenicity analysis in a clinical setting with respect to risk/benefit analysis are in place.

**Benefits from Private-Public Partnerships (PPP)**

Harmonization of the reporting and the grading of early adverse immune reaction of biopharmaceuticals and their standardization will only be possible by sharing practices between companies involved in the manufacture and clinical development of biopharmaceuticals and engaging regulatory authorities to develop guidelines.

**Objectives/deliverables**

- Define the key proteins of immunogenicity of biopharmaceuticals.
- Develop consistent assays with appropriate specificity to support common immunogenicity testing
- Understand the clinical relevance of immunogenicity
- Address genomic variations of the immune system
- Minimize the immunogenicity risk of a compound, before it is administered to man
- Investigate the predictive value of pre-clinical tools
- Develop predictive,animal models
- Develop immunogenicity tests, neutralising antibodies, binding antibodies
- Develop guidelines to support the use of routine immunogenicity testing which take into account the clinical relevance of the specific antibody response
- Regulatory aspects, Patent and IPR issues will be addressed.
- Application of Knowledge Management Techniques for consistent information gathering and evaluation.

**Examples of potential complementarity/synergies with other EU initiatives**

The FP6 projects “ImmunoGRid” and “COMPUVAC”

## Efficacy Pillar: Inflammatory Diseases
## Scientific Priority C :
## Assessment of inflammatory diseases

**Problem statement**

Inflammatory diseases affect many people in the developed world and represent the greatest collective burden of suffering and economic cost in the developed world. New drug development in this field have been hampered by a lack of validated / accepted measurements that can be used as intermediates in intervention studies to target disease manifestation and identify more homogeneous subgroups of patients. In addition, certain pre-clinical models lack key structural features of the human disease. Moreover, many medications give only symptomatic relief, rather than treating the underlying medical condition, increasing the need to identify new treatment approaches and/or safer, more efficacious pharmacological therapeutics. Also, acute inflammatory responses are commonly discussed to be the primary cause of diseases like acute respiratory stress syndrome or multi-organ failure in sepsis and trauma. Despite continuous improvements in intensive care medicine the mortality for these diseases still remain high indicating a high medical need for therapy in both acute and chronic inflammatory diseases.

**Benefits from Private-Public Partnerships (PPP)**

A harmonized approach involving government, academic institutions, hospitals, and pharmaceutical companies is necessary to facilitate the identification and validation/ qualification of biomarkers and/or clinical intermediates to overcome limitations in pre-existing data-sets and effectively combine knowledge and expertise in this field to gain the necessary critical mass to address unmet medical need in this area.

**Objectives / Deliverables**

- Identification / validation of new models (including new or modified animal models) representing key mechanisms in disease pathology
- Validation / qualification of candidate biomarkers (molecular and/or imaging) for diagnosis, prognosis and efficacy
- Better define the characteristics of known and novel disease phenotypes
- Identify/confirm predictors to support patient stratification
- Better characterize systemic disease / poly-comorbidity

**Examples of potential complementarity/synergies with other EU initiatives**

The IMI 1st Call project PROACTIVE; ongoing FP7 projects in the area of lung disease

## Efficacy Pillar: Infectious Diseases
## Scientific Priority D :
## Improve the scientific and pre-clinical models and tools for Tuberculosis medicines research

**Problem statement**

The current therapies for TB are more than 40 years old. As a result, a large amount of the scientific and clinical infrastructure required to effectively deliver new medicines to TB patients requires improvement. In order to enhance the efficiency of the drug discovery process for TB and accelerate effective medicines to patients there is a need to

- Develop new *in vitro* and *in vitro* models that better reflect the complexity of TB to support progression of molecules with novel mechanisms of action
- Develop tools to support mode of action studies
- Develop biomarkers to support rapid pre-clinical screening and support early hint of efficacy studies and support dose ranging studies clinically
- Consolidate the number of initiatives to larger more coordinated efforts

**Benefits from Private-Public Partnerships (PPP)**

There are a number of different Public and Private Initiatives for TB Drug Discovery already existing in Europe, however many of these efforts are fragmented and very much focussed on the development of new chemical entities much needed in the TB field. Through the partnership of academics, SMEs, patient groups and regulators IMI offers the opportunity to compliment and focus a number of these efforts on further developing the tools required to more efficiently progress drugs with novel mechanisms of action through pre-clinical and clinical development.

**Objectives/deliverables**

- New pre-clinical models ( *in vitro* and *in vitro*) that better represent the complexity of TB which can support compound ranking and mechanism of action studies.
- Novel translatable biomarkers to support pre-clinical PK/PD studies for ranking novel chemical entities and predicting clinical dose ranges
- Novel translatable biomarkers to support novel clinical trial designs, clinical dose ranging and early hint of efficacy (PhaseI/II) studies
- Development of mathematical models to predict drug response and support patient stratification.
- Standardized technology/protocols across Europe aligned with regulatory requirements

**Examples of potential complementarity/synergies with other EU initiatives**

FP 7 projects in the area of tuberculosis

## Efficacy Pillar: CNS
## Scientific Priority E :
## Enhancing translation in neurological disease

**Problem statement**
Development of efficacious novel assets for neurological disorders remains a challenge largely driven by a) the complexity of the diseases, b) the lack of translatable animal models and c) the lack of standardised clinically validated tools for assessing disease progression, drug response and patient stratification.

**Benefits from Private-Public Partnerships (PPP)**
Due to the large unmet medical need, there are a huge number of research groups working on aspects of CNS disorders, however efforts are generally fragmented and often focused around very specific disease populations. In order to make significant advances towards validating tools to a level where they can be used for internal decision making or in regulator submissions, or understanding fundamental biological mechanisms, it is essential to consolidate efforts and share knowledge and expertise from a number of different scientific areas.

**Objectives/Deliverables**
- Identification of relevant animal models, assays and biomarkers resulting in better understanding of pathological processes and standardization of therapies for neurological diseases
- Confirmation of defined translational end-points (e.g. imaging) from animal studies in patients and vice versa
- Establishment of a network of European clinical sites with expertise in the specific disease areas allowing validation of the identified measures.

**Examples of potential complementarity/synergies with other EU initiatives**
FP 7 projects in the area of neurological diseases

## Efficacy Pillar: Metabolic Diseases
## Scientific Priority F :
## Development of personalized medicine approaches in diabetes

**Problem Statement**

Diabetes is a disease with increasing tendency in Europe and all around the world. The current treatment is far away from an individualized approach; all patients are treated with a very limited number of compounds. Different treatments depend only on the stage of the disease but not on the individual patient. Many external disease initiating- or disease- modifying factors are already described but the information about the internal, patient-specific reasons for different susceptibilities is limited. It will be of high scientific interest and in the interest of many diabetic patients as well to collect the available data and to increase the general knowledge in this area to be able to develop 'customized' drugs for smaller but better-defined populations of patients.

**Benefits from Private-Public Partnerships (PPP)**

Regrouping within the same project of different but complementary expertise and backgrounds. Improved access to specialised technology and knowledge which, when combined, will accelerate achievement of project goals. Enriched interactions between basic science (both in industry and academia) and clinical research.

**Objectives/Deliverables**

IMI Research projects responding to this scientific priority should generate the following:

- Generate databases and conduct clinical studies to identify genotypes and phenotypes of diabetic patients; establish the necessary knowledge management infrastructure and ensure fit to other projects in this area
- Classical genetics, genomic, transcriptomic, proteomic and metabolomic profiling of diabetic conditions which could identify a) low frequency gene variants with high individual impact, b) generate new molecular targets, c) biomarkers of susceptible sub-populations, disease progression and drug efficacy
- increase understanding of newly developed cell and animal models by comparing molecular profiles with clinical subpopulations

**Examples of potential complementarity/synergies with other EU initiatives**

The FP7 project "TRANSFoRm"; IMI 1st Call projects "IMIDIA" and "SUMMIT"

**Education and Training Pillar**
## Scientific Priority G :
## Fostering a broader understanding of pharmaceutical R&D in the broader public

**Problem Statement**
Understanding of the complex nature of the medicines research and development process and the chances and risks of modern medicine is very limited in the general population. On the other hand, new technologies like genomics or proteomics offer chances for a more targeted therapy, but require the support by well informed citizens / patients. The information and communication technology and infrastructure in Europe allows broad dissemination of information but is not well enough used for healthcare information yet.

**Benefits with Public Private Partnerships**
Consortia of experts from academia, industry and other stakeholders including patient organizations allow the creation of innovative, tailor-made information programs with a higher chance to be accepted by the public and supporting a closer involvement of patients in research and development for new medicines.

**Objectives / Deliverables**
Identify innovative ways to communicate information on medical research and development and new medicines to laymen including e.g., representatives of patient organisations and members of ethics committees.
The information programs or tools will cover the scientific aspects but include also information on ethics, regulatory requirements, assessments of risk and benefit, intellectual property matters, business skills and understanding of the business environment.

**Examples of potential complementarity/synergies with other EU initiatives**
EU initiatives such as the “GPS for health platform”