Innovative Medicines Initiative

Innovative Medicines Initiative

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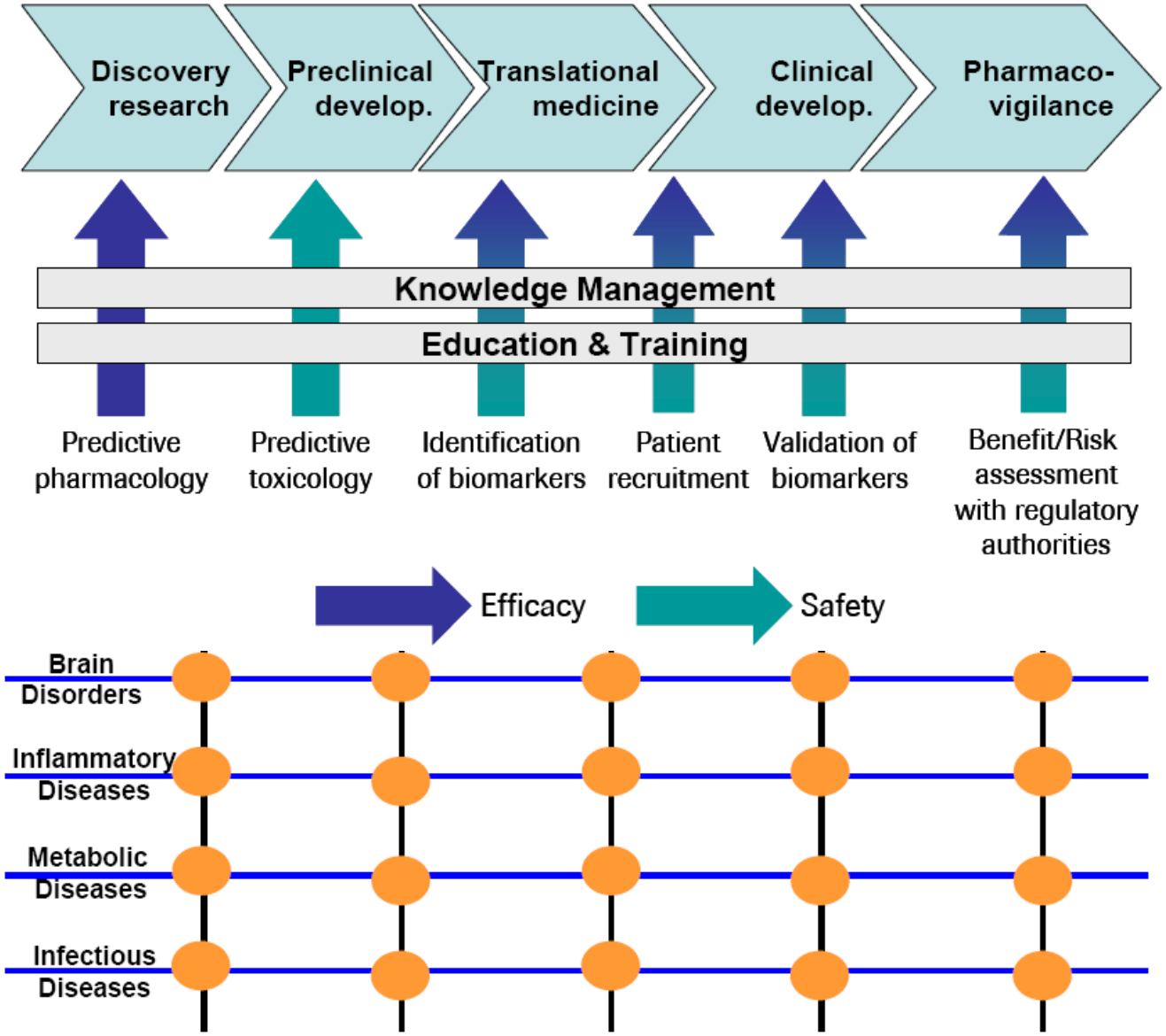
Agenda

- Innovative Medicines Initiative
- Collaborative projects require ...
- Some strategies for Knowledge Management

Innovative Medicines Initiative: the Largest PPP in Life Sciences R&D

The Original Matrix of the Scientific Research Agenda



Key Concepts

- Open Collaboration

- Pre-competitive research

Governance


IMI Joint Undertaking (IMI JU)
Governing Board
efpia
Executive Director (+ staff)
Scientific Committee
Stakeholder Forum
IMI States Representatives Group

IMI Executive Office as a Neutral Third-Party

- To implement programmes and activities in the common interest of all stakeholders
- To monitor the combined use of public funds and industry investment
- To guarantee fair and reasonable conditions for optimal knowledge exploitation and dissemination

Intellectual Property Policy: Guiding Principles

- Aligned with IMI objectives, i.e.
  - to promote knowledge creation
  - to facilitate disclosure and exploitation
  - to achieve fair allocation of rights
  - to reward innovation
  - to achieve a broad participation of private and public entities
- Provides flexibility for participants

nature REVIEWS DRUG DISCOVERY

COMMENT

May 2011, 10: 321-322

Reflections on the Innovative Medicines Initiative

Michel Goldman

The pharmaceutical industry is developing new collaborative models for drug development. This article discusses the experience so far of the Innovative Medicines Initiative, which is currently the largest public–private partnership that is dedicated to pharmaceutical innovation, highlighting lessons learned for the success of precompetitive consortia.

Public–private partnerships (PPPs) are increasingly being established to reinvigorate research and development (R&D) of innovative medicines. In parallel with the creation of US-based PPPs, the Innovative Medicines Initiative (IMI) was set up to enhance the competitiveness of the pharmaceutical sector in Europe for the benefit of both patients and scientists. To this end, the European Federation of Pharmaceutical Industries and Associations (EFPIA) was invited by the European Commission (EC) to develop a series of recommendations to address major bottlenecks in the drug development process. Following the establishment of a research agenda in consultation with various stakeholders, the IMI was launched in 2008 topics were developed, primarily by 23 EFPIA-affiliated companies, with input from the IMI Scientific Committee and from a States Representatives Group. Second, following a call for proposals, consortia that were eligible to receive public funding from the EC competed through the submission of expressions of interest, and the best-ranked consortium, selected by independent experts, was invited to join EFPIA-affiliated companies in the next stage. Third, they formed the final consortium, which developed a full project proposal that was submitted for peer review.

The resulting 23 consortia involve 221 R&D teams from EFPIA-affiliated companies, 298 academic institutions, 47 SMEs, 11 patients' organizations and 7 regula-

Box S2 | Intellectual property in the Innovative Medicines Initiative

Objectives and principles

The Intellectual Property (IP) policy for the Innovative Medicines Initiative (IMI) aims to promote and reward knowledge creation, disclosure and exploitation, and to reward innovation through a fair allocation of rights. In view of the diversity of the projects supported by the IMI and the complexity of IP management in public–private partnerships, the IMI favours a 'case-by-case' approach. Accordingly, the overall IP policy has been designed to allow appropriate flexibility to suit the specific situation of each consortium. In order to facilitate IP negotiations, a guidance note has been produced in which key stakeholders were represented, and the IMI Executive Office acts as a neutral third party to assist consortia in solving difficult or conflicting IP issues.

Major provisions

Each participant remains the exclusive owner of the information and IP rights that they hold before becoming partner of an IMI project. Information and IP rights that are necessary for the completion of the project are identified and defined as 'Background'. This Background information is accessible on a royalty-free basis to other consortium participants to the extent necessary for undertaking the project. The results that are generated during the project as part of its objectives are defined as 'Foreground'. Consortium participants who generated Foreground results are the owners of the corresponding information and IP rights. When several participants contribute to Foreground, joint ownership will apply, unless otherwise agreed.

To the extent necessary for completion of the project, consortium participants will enjoy access to Foreground information that belongs to other partners, under the same conditions as for the Background information. Participants might request access rights to Foreground information for other purposes. In this case, the financial terms governing corresponding agreements will depend on their foreseen use by the requesting parties. Indeed, a distinction is made between direct commercial exploitation, for which usual negotiation practice will apply, and 'Research Use', for which a non-exclusive licence that is provided under appropriate conditions forms a basis for negotiation. The definition of Research Use in the IMI is quite broad as it includes all activities relating to developing the ability to commercialize drug or related product, as well as activities relating to obtaining regulatory approvals.

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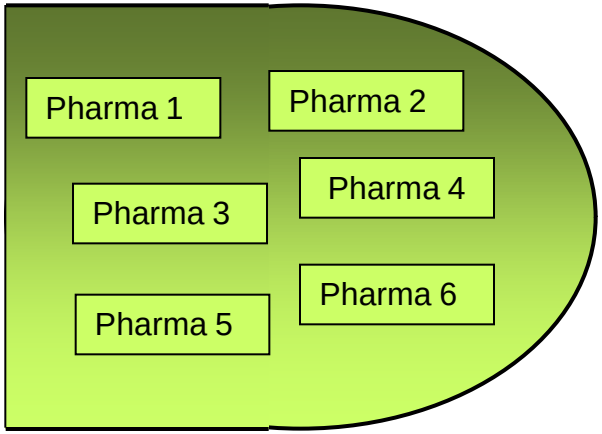
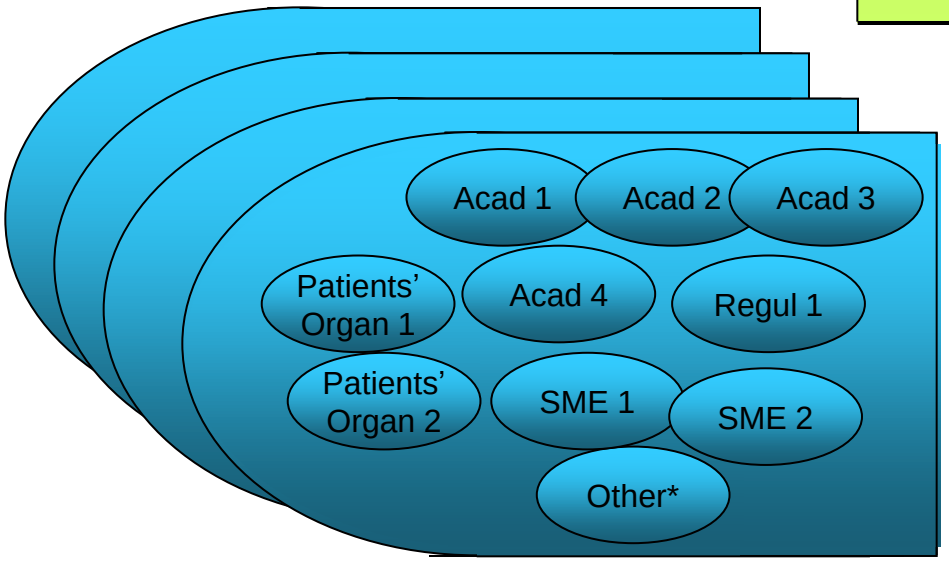
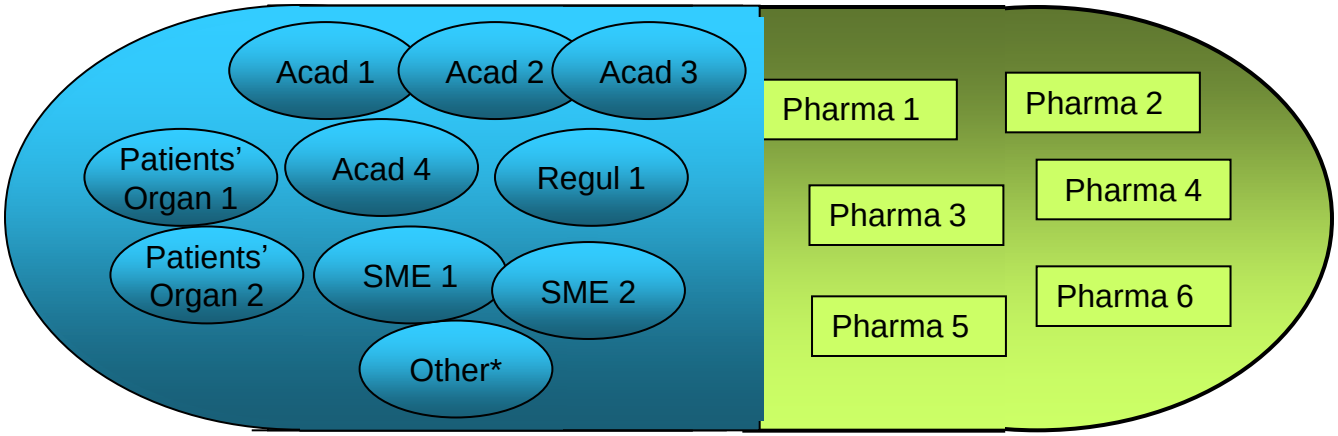
Building a IMI Consortium



Step 1:
A set of EFPIA companies define a topic on which they commit to collaborate



Step 2:
Consortia eligible for EU funding compete through expressions of interest which are ranked by independent experts



Step 3:
The top-ranked EU-fundable consortium join the EFPIA companies to form the final consortium which dev s the full proposal, subject t peer-review before final a

Calls 1&2: Consolidated Figures

	Call 1	Call 2	Total
Projects	15	8	23
EFPIA Companies	21	21	23
EFPIA teams	160	65	225
Academic teams	195	103	298
SME teams	24	23	47
Patients' organisat.	9	2	11
Total Budget (M€)	281	172	453

SMEs in 1st Call Projects

25 Companies: 14.6 M €

AEROCRINE	U-BioPred
ALZPROTECT	PharmaCOG
ARGUTUS MEDICAL	Safe-T
BIOCOMPUTING PLATFORMS	Summit
BIOSCIENCE CONSULTING	U-BioPred
CHEMOTARGETS	E-Tox
CHOICE PHARMA	Proactive
CXR BIOSCIENCES	Marcar
EDI GMBH	Safe_T
ENDOCELLS SARL	Imidia
EXONHIT THERAPEUTICS SA	PharmaCOG
FIRALIS S.A.S.	Safe-T

GABO:MI*	Newmeds
INNOVATIVE CONCEPTS	PharmaCOG
INNOVATIVE HEALTH DIAGNOSTICS	PharmaCOG
INTE:LIGAND SOFTWARE	E-Tox
INTERFACE EUROPE*	Safe-T
ISLENSK ERFDAGREINING	Newmeds
LASER LA Santé	Protect
LEAD MOLECULAR DESIGN	E-Tox
MOLECULAR NETWORKS GMBH	E-Tox
NEUROSCIENCE TECHNOLOGIES	Europain
OUTCOME EUROPE	Protect
QUALISSIMA	PharmaCOG
SYNAIRGEN RESEARCH	U-BioPred

Patients' Organizations in1st Call Projects

- Int. Alliances of Patients' Organizations
- Alzheimer's Europe
- Eur. Genetic Alliances' Netw.
- Genetic Interest Group
- European AIDS Treatment Group
- European Lung Foundation
- Int. Primary Care Resp. Group
- British Lung Foundation
- Asthma UK
- Lega Italiano Anti-Fumo
- Dutch Asthma Foundation

Regulators in 1st Call Projects

- European Medicines Agency (EMA)
- MHRA (UK)
- DKMA (DK)
- AEMPS (SP)
- SwissMedic (CH)
- AFSSAPS (FR)

Key Deliverables of Non-Competitive Research

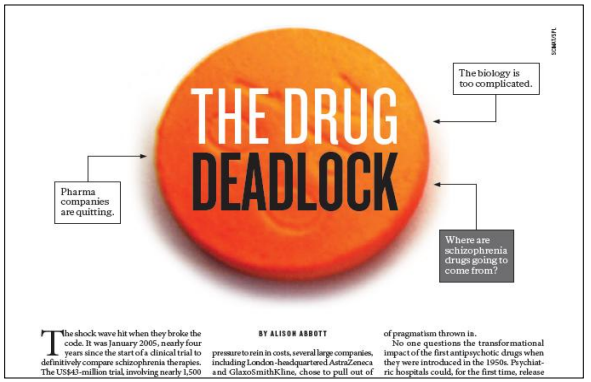
- Establishment of common databases
- New tools for identification of drug targets
- Standardization and harmonization of models and assays for drug efficacy and safety (*biomarkers*)
- Patient reported outcomes
- Classification of diseases

NEWMEDS

Develops biomarkers and tools and models to allow better targeted treatments for schizophrenia and depression

19 Partners

- 9 EFPIA companies
- 7 Public organisations
- 3 SMEs



Nature, 11 November 2010

First achievements

- ✓ Has assembled the largest known repository of antipsychotic clinical trial data.
- ✓ The database contains information on 23 401 patients from 67 industry sponsored studies.
- ✓ Bringing together data from public projects and 3 companies on the genetics and clinical response in 1800 well characterized patients with depression.

eTOX

Builds a large searchable database containing drug toxicity-related data extracted from relevant pharmaceutical pre-clinical legacy reports

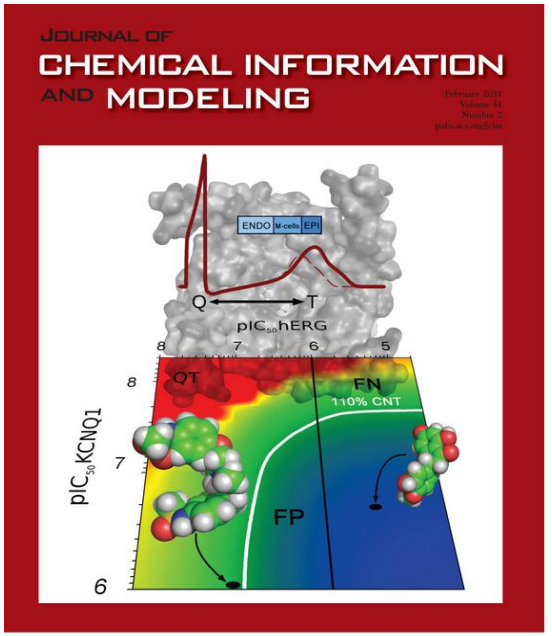
Develops innovative methodological strategies and novel software tools to better predict in silico the toxicological profiles of new molecular entities in early stages of the drug development pipeline, using its database background

25 Partners

- 13 EFPIA companies
- 8 Public organisations
- 4 SMEs

First achievements

✓ An innovative multi-scale modelling strategy for the prediction of cardiotoxicity has been developed, successfully tested and published



J. Chem. Inf. Model. 2011; 51:483-92

EUROPAIN

Deciphers chronic pain mechanisms in order to improve the development of pharmacological treatments against pain thereby reducing the burden of illness of large groups of the population

20 Partners

- 7 EFPIA Pharma Companies
- 12 Academic Institutions
- 1 SME

First achievements

✓ Database based on a standardized Quantitative Sensory Testing (QUAST)
✓ Novel imaging technique based on magnetic resonance imaging (MRI) to visualise brain changes patients with low-back pain

SAFE-T

Addresses the current lack of sensitive and specific clinical tests to diagnose and monitor drug-induced injury to the kidney, liver and vascular tissues in man, which is a major hurdle in drug development

20 Partners

- 11 EFPIA Pharma Companies
- 5 Academic Institutions
- 4 SMEs

A generic operational strategy to qualify translational safety biomarkers

Katja Matheis[1], David Laurie[2], Christiane Andriamandroso[3], Nadir Arber[4], Lina Badimon[5], Xavier Benain[6], Kaïdre Bendjama[7], Isabelle Clavier[6], Peter Colman[8], Hüseyin Firat[7], Jens Goepfert[9], Steve Hall[8], Thomas Joos[10], Sarah Kraus[4], Axel Kretschmer[11], Michael Merz[2], Teresa Padro[5], Hannes Planatscher[9], Annamaria Rossi[8], Nicole Schneiderhan-Marra[9], Ina Schuppe-Koistinen[12], Peter Thomann[7], Jean-Marc Vidal[13] and Béatrice Molac[7]

[1] Boehringer-Ingelheim Pharma GmbH & Co. KG, Biberach, Germany
[2] Novartis Pharma AG, Basel, Switzerland
[3] Interface Europe, Brussels, Belgium
[4] Tel-Aviv (Souraski) Medical Center, Tel-Aviv, Israel
[5] Barcelona Cardiovascular Research Center (ICCC-CISC), Barcelona, Spain
[6] Sanofi-Aventis, Paris, France
[7] Firalis SAS, 35 rue du Fort, 68330 Huningue, France
[8] Pfizer Ltd, Sandwich, UK
[9] Natural and Medical Sciences Institute, Reutlingen, Germany
[10] Experimental & Diagnostic Immunology GmbH, Reutlingen, Germany
[11] Bayer Schering Pharma AG, Leverkusen, Germany
[12] AstraZeneca R&D, Södertälje, Sweden
[13] EMA, London, UK

Drug Discov Today, in press

First achievements

- ✓ 153 potential biomarker candidates for drug-induced injury of the kidney, liver and vascular system have been evaluated and are currently undergoing clinical evaluation.
- ✓ The strategy adopted has been agreed with the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA).

MARCAR

Developing biomarkers that will allow the prediction of unwanted non-genotoxic carcinogen (NGC) effects of drugs at a very early stage of their development

12 Partners

- 5 EFPIA Pharma Companies
- 6 Academic Institutions
- 1 SME

First achievements

OPEN ACCESS Freely available online

PLoS one

Phenobarbital Mediates an Epigenetic Switch at the Constitutive Androstane Receptor (CAR) Target Gene *Cyp2b10* in the Liver of B6C3F1 Mice

Harri Lempiäinen[1☯], Arne Müller[1☯], Sarah Brasa[1], Soon-Siong Teo[1], Tim-Christoph Roloff[2], Laurent Morawiec[1], Natasa Zamurovic[1], Axel Vicart[1], Enrico Funhoff[1], Philippe Couttet[1], Dirk Schübeler[2], Olivier Grenet[1], Jennifer Marlowe[1], Jonathan Moggs[1], Rémi Terranova[1*]

1 Investigative Toxicology, Preclinical Safety, Translational Sciences, Novartis Institutes for Biomedical Research, Basel, Switzerland, 2 Friedrich Miescher Institute for Biomedical Research, Basel, Switzerland

PlosOne 24;6:e18216, 2011

U-BIOPRED

By comparing data from several hundreds of people, the team will characterise different kinds of severe asthma, paving the way towards a **new classification of asthma** *and personalised treatments for patients*

19 Partners

- 8 EFPIA companies
- 7 Academic Institutions
- 3 Patients' organizations

First achievements

✓ Consensus statement on the definition of severe refractory asthma

Diagnosis and definition of severe refractory asthma: an international consensus statement from the Innovative Medicine Initiative (IMI)

Elisabeth H Bel,[1] Ana Sousa,[2] Louise Fleming,[3] Andrew Bush,[4] K Fan Chung,[5] Jennifer Versnel,[6] Ariane H Wagener,[1] Scott S Wagers,[7] Peter J Sterk,[1] Chris H Compton,[8] on behalf of the members of the Unbiased Biomarkers for the Prediction of Respiratory Disease Outcome (U-BIOPRED) Consortium, Consensus Generation[9]

ABSTRACT

Patients with severe refractory asthma pose a major healthcare problem. Over the last decade it has become increasingly clear that, for the development of new targeted therapies, there is an urgent need for further characterisation and classification of these patients. The

DIAGNOSIS AND DEFINITION OF SEVERE ASTHMA OVER THE LAST 15 YEARS

Various documents proposing different clinical definitions of 'severe asthma' in adults and children have been published over the last 15 years by international task forces, workshops, networks and

Thorax, in press

Patient reported outcomes (1)

PROTECT Consortium

To strengthen the monitoring of the benefit-risk of medicines by developing modern methods of data collection directly from consumers in several European Union countries, including using web-based screens And computerised telephone interviews.

29 Partners

- 6 Regulatory bodies (coordinator: EMA°
- 11 EFPIA Pharma Companies
- 10 Academic Institutions
- 1 SME

PROTECT has launched a prospective study of pregnant women who agree to provide information about medication use, lifestyle factors and risks for congenital malformation

Patient reported outcomes (2)

PROACTIVE Consortium

Develop, validate and use patient reported outcome (PRO) tools investigating dimensions of physical activity that are judged by patients living with chronic obstructive pulmonary disease (COPD)

19 Partners

- 8 EFPIA companies
- 7 Academic Institutions
- 3 Patients' organizations

IMI Education & Training Programmes

- ✓ First course in Nov 2010 on drug discovery development
- ✓ Certificate and Master courses in pharmacovigilance and pharmacoepidemiology in Sept 2011
- ✓ EU syllabus on pharmaceutical medicine
- ✓ Database on over 700 master courses, 110 professional development courses, 380 learning tools

2nd Call Projects

Acronym	*Coordinator*	*Managing Entity*	*Budget (M€)*
PREDECT	Servier	University of Helsinki	17.7
ONCOTRACK	Bayer Schering	Max-Planck Institute	30.7
QUIC-CONCEPT	AstraZeneca	EORTC	17.1
RAPP-ID	Johnson&Johnson	University of Antwerp	14.4
BTCURE	UCB	Karolinska Institute	38.2
DDMoRe	Pfizer	Uppsala University	21.2
OpenPhacts	Pfizer	University of Vienna	16.4
EHR4CR	AstraZeneca	European Institute for Health Records	16.0

Projects under Finalization

- Early prediction of drug-induced liver injury
- Risk minimization of antibodies to biopharmaceuticals
- Immunosafety of vaccines
- Translational research on autism spectrum disorders
- Personalized medicine in type II diabetes
- New strategies to treat tuberculosis
- Patient awareness on pharmaceutical innovation

Towards New Business Models for “Big Pharmas”:

- Patents Expiration and Fights
- Generics and « Biosimilars »
- Unpredicted late stage failures
- Increased regulatory rules
- Fragmented knowledge

The Path to Innovative Medicines

nature medicine

Mechanism matters

The path of drug development is fraught with hurdles. Gaining a clear understanding of how a drug works before it enters clinical trials is the intelligent route to drug discovery and could increase the likelihood for drug success.

Drug development is a risky business. According to the US Food and Drug Administration (FDA), only eight percent of drugs that enter clinical trials are eventually approved. For a drug to gain FDA approval, it must be safe and show some efficacy. Because the FDA does not require any understanding of the mechanism by which a drug acts, it could be tempting to move into clinical trials without this knowledge. However, this may set the stage for failure. An investigational

It is true that we use many highly prescribed drugs without a clear idea of how they work—which targets they hit, what processes they alter and which of these actions are required for therapeutic efficacy. For instance, lithium, used to treat bipolar disorder, modulates many molecular targets, but which—or how many—of these are required for its beneficial effects is uncertain. Nevertheless, understanding a drug's mechanism could guide drug development and help to prevent late-stage failures such as Dimebon's.

Rare Diseases as Surrogates in Drug Development

Disease	Surrogate for	Molecular targets	Drugs
Familial hypercholesterolemia	Common forms of hypercholesterolemia	HMG CoA PCSK9	Statins
Cryopyrin-associated periodic syndromes	Rheumatoid arthritis	IL-1β	Rilonacept Canakinumab
Idiopathic Hypereosinophilia	Allergic asthma	IL-5	Mepolizumab
Castleman Disease	Rheumatoid arthritis	IL-6	Tocilizumab
Tuberous sclerosis	Various cancers	mTor	Temsirolimus

NEWS & ANALYSIS

Antisense progress p401

NIH drug database launched p403

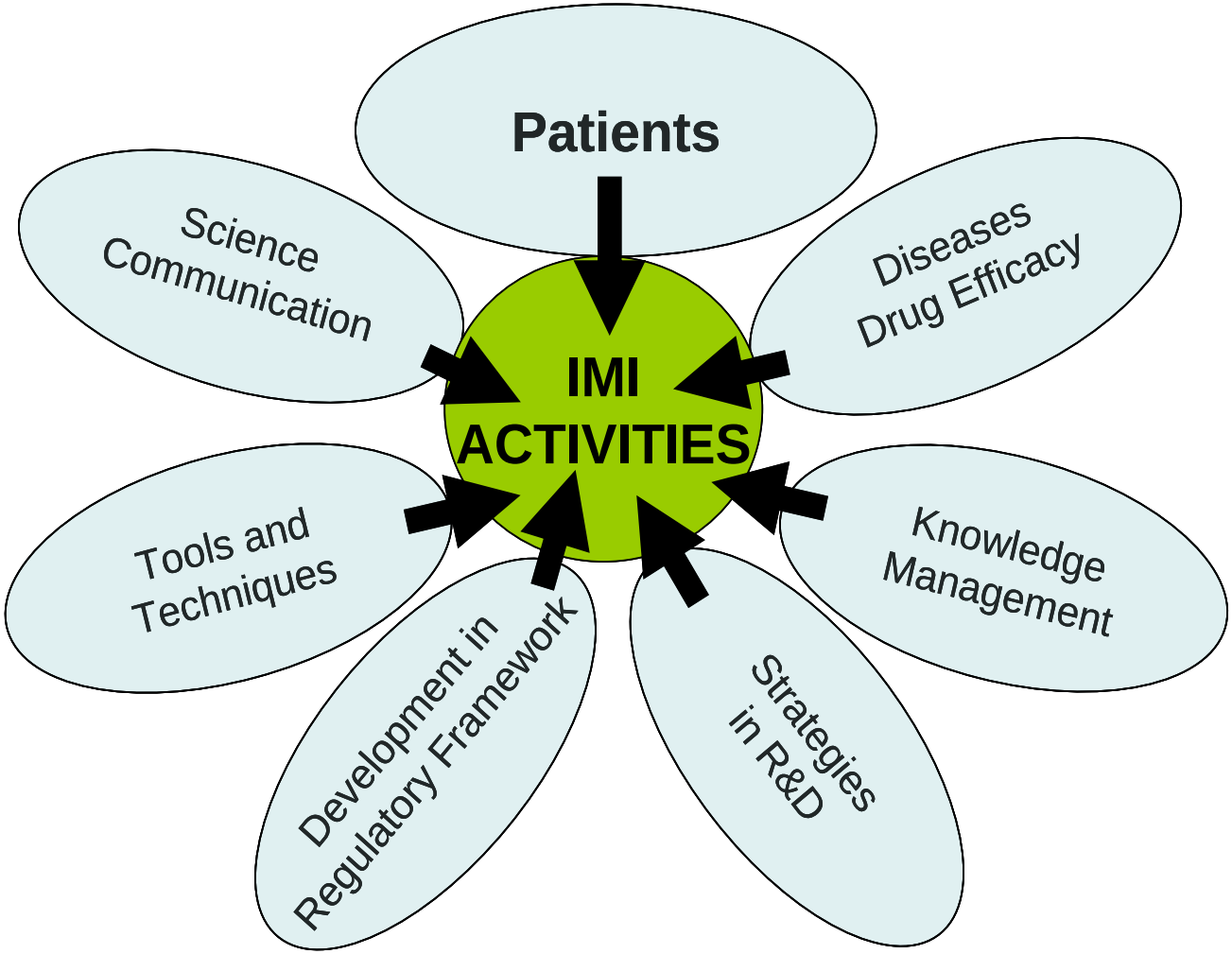
EFPIA Director General discusses his agenda

Could pharma open its drug freezers?

The NIH wants industry to contribute old, new and experimental drugs to a systematic, collaborative approach to drug rescue and repurposing.

Nature Reviews Drug Discovery **10,** 399-400

The Revised Agenda: Key Areas



Call 4 Topics (1)

Cluster A: Medical Information System

- A European medical information framework (EMIF) of patient-level data to support a wide range of medical research
  - Information Framework / Knowledge Management Service Layer.
  - Metabolic complications of obesity.
  - Protective and precipitating markers for the development of Alzheimer's disease (AD) and other dementias.

- eTriks: European translational information and knowledge management services

Call 4 Topics (2)

Cluster B: Chemistry, Manufacturing and Control

- Delivery and targeting mechanisms for biological macromolecules
- In vivo predictive biopharmaceuticals tools for oral drug delivery
- Sustainable chemistry – Delivering medicines for the 21st century

Cluster C: Technology and Molecular Disease Understanding

- Human induced pluripotent stem (hiPS) cells for drug discovery and safety assessment
- Understanding and optimising binding kinetics in drug discovery

<u>Indicative financial contribution from IMI JU:</u>

Up to 105 M€

Major Challenges Ahead

- « Consortium fatigue »
- Frontiers of pre-competitive research
- Management of intellectual property
- Definition of Key Performance Indicators
- Incentives/rewards for collaboration
- Alignment with Regulators' Priorities

Agenda

- Innovative Medicines Initiative
- Collaborative projects require ...
- Some strategies for Knowledge Management

Collaborative projects require an infostructure: OBVIOUS

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Collaborative Projects Require Governance

A lot of data is generated or consolidated, GOVERNANCE, is needed to address:

1. the need for metadata
2. description of the quality of data
3. ensure standards to ensure syntactic and semantic interoperability

- ESFRI set up +/- 10 large BMS Research Infrastructures
- eIRG Data Management Task Force recomendations for the data intensive sciences
- Detailed subcriteria - checklist

Agenda

- Innovative Medicines Initiative
- Collaborative projects require ...
- Some Strategies for Knowledge Management

Background

- IMI KM workgroup
- EFPIA KM affinity group
- 23 ongoing projects incl 4 KM projects

KM projects

Ongoing projects:

- eTOX
- OpenPHACTS
- DDMoRE
- EHR4CR

Open Call (deadline 18 October):

- EMIF
- eTRIKS

Ongoing projects KM

- eTOX:
- DDMoRe: Drug Disease Model Resources
- OpenPhacts:
- EHR4CR: Electronic Health Records for Clinical Research

Call 4 Topics KM

Cluster A: Medical Information System

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- eTriks: European translational information and knowledge management services

IMI KM workgroup

The primary goal of the KM workgroup is to collect and share information on the KM component of the IMI projects and give guidance to the project coordinators and their KM WP leaders where possible.

KM pertains to e-collaboration, document management, data management and biobanking (see SRA)

KM operational definition (draft)

Success will mean:

- Solutions are identified for interoperability issues between project e-collab spaces and data repositories.
- KM platforms are shared across projects and a Data Vault (notary-like) is identified for retrieving project data and ensuring sustainability.
- Metadata is available and quality of data are documented

So far in 2011

- Monthly KM workgroup meeting
- Summary e-collaboration platforms used, e-collaboration platform to be tested with a single project
- Data Standards:
  - MOU CDISC-IMI
  - Membership for the IMI beneficiaries for the duration of the projects
  - Overview course CDISC for the projects
- Open LinkedIn group IMI started