Innovative Medicines Initiative

IMI2 JU Annual Work Plan for 2014*

(updating the IMI JU Annual Implementation Plan for 2014)

* approved by the IMI2 JU Governing Board on 7 July 2014

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FOREWORD

The Innovative Medicines Initiative Joint Undertaking (IMI JU) is now established as an efficient public-private partnership (PPP) that fosters high quality collaborative projects bringing together the different stakeholders involved in drug development. By consistently ensuring a fair selection of applicant consortia and facilitating agreements between the different partners, IMI JU has come to be appreciated as an effective neutral platform.

At the same time, the new challenges faced by the pharmaceutical industry and the healthcare sector at large have led IMI JU to revisit its priorities for the future. The current objective is to address the needs common to industry and society by focusing on major public health issues and ensuring a permanent dialogue with regulatory authorities and patient organisations.

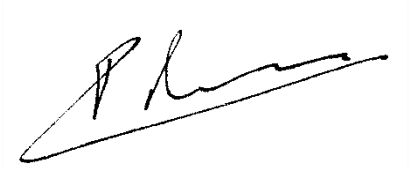
This document, initially adopted by the Governing Board in December 2013, has been updated to reflect IMI2 entry into force and associated requirements and features.

In 2014, IMI JU will continue to manage its portfolio of 46 projects and will carry out the evaluation and kick-off of projects resulting from Calls for proposals launched in the second half of 2013. As running projects are progressing and maturing, specific efforts will be dedicated to document and monitor progress, notably through key performance indicators, and best exploit outputs. In parallel, IMI JU's communication activities will be further expanded by conducting outreach campaigns targeting different audiences. Furthermore, IMI JU will continue to ensure the delivery of high-quality work according to strict ethical standards, administrative and financial processes which will be continuously reviewed and adapted as needed.

IMI JU will also start implementing recommendations arising from the second interim evaluation, and most notably the following:

- A more articulate communication strategy with clear and measurable goals and objectives, addressing both the key stakeholders and a wider audience;
- Expanding the key performance indicators (KPI) framework to better demonstrate IMI impacts and socio-economic benefits;
- Further enhancing the efficiency of the Executive Office.

With an enthusiastic team fully committed to fulfil our ambitious mission, I am confident that 2014 will set the stage for a successful future!



Michel Goldman
Executive Director

1 OBJECTIVES, TRANSITION TO IMI2 JU AND KEY PERFORMANCE INDICATORS

1.1 Strategic Objectives and transition to IMI2 JU

IMI JU was set up by Regulation (EC) No 73/2008 of the Council of 20 December 2007 as one of the instruments of the European Commission's Seventh Framework Programme (FP7) for research, technological development and demonstration activities. The Joint Undertaking was entrusted with the important goal of significantly improving the efficiency, effectiveness and quality of the drug development process needed to bring innovative and safer innovative medicines to patients.

Over the past six years, IMI JU has already effectively facilitated the mobilisation of 46 public-private consortia which are delivering results of high relevance to healthcare challenges. The Joint Undertaking is recognised globally as the leading business model for PPP in healthcare, having consistently and effectively demonstrated the feasibility and added value of large, multi-stakeholder PPPs for research and development in biomedicine. IMI JU has achieved this by building trust and pioneering collaboration among a wide range of participants including the European pharmaceutical industry, academia, patient groups, regulatory and small to medium enterprises (SMEs). It has also served as a unique and neutral platform for leveraging research strengths, allowing access to other partners' expertise and for fostering open innovation across Europe in healthcare research and development.

The success of IMI JU has led to the adoption on 6 May 2014 of Regulation No 557/2014 by the Council of the European Union for the setting up Innovative Medicines Initiative 2 Joint Undertaking (IMI2 JU) with a lifespan of ten years, until 31 December 2024. IMI2 JU for all intents and purposes replaces and succeeds IMI JU, and apart from implementing its own objectives under the EC's Horizon 2020 Framework Programme, it will also continue to achieve the objectives of IMI JU, including the implementation of the remaining actions and providing continued support to the research programme initiated under FP7.

The main policy objectives of both IMI JU and IMI2 JU are broadly set out in the respective Council Regulations, with the combined aims being to:

- develop and implement pre-competitive research and innovation activities of strategic importance to the European Union (EU)'s competitiveness and industrial leadership;
- address specific societal challenges;
- improve European citizens' health and wellbeing;
- pool resources and foster knowledge sharing and collaboration; and
- promote the involvement of SMEs in its activities.

The Strategic Research Agenda is the main reference for the implementation for research priorities of both IMI JU and IMI2 JU. The first annual scientific priorities for IMI2 JU for the remaining part of 2014 are summarised in Section 2. These are based on the new Strategic Research Agenda (SRA) for IMI2 JU which is publically available at http://www.imi.europa.eu/content/imi-2#SRA .

In addition, in the case of IMI2 JU, the Regulation also sets out how, from its establishment in 2014, the Joint Undertaking will gradually seek to contribute towards health research and development.[1] These expected outcomes will be important in the longer term as IMI2 JU implements the programme under the framework of Horizon 2020.

1.1 Annual Objectives, Key Performance Indicators and Related Targets

An updated set of annual objectives of IMI2 JU, for the remaining part of 2014, have been developed for the measurement of performance and progress in 2014, together with the associated KPIs and targets. These take into account:

- The continued implementation of actions related to IMI JU and the establishment of IMI 2 JU in 2014;
- The experience gained so far in developing KPIs, metrics and other qualitative assessment for measuring the results and achievements of IMI JU;
- The longer-term objectives and aspirations of IMI2 JU under Horizon 2020.

The 2014 annual objectives and KPIs, presented in Table 1 overleaf, are linked to the main policy objectives of IMI2 JU (established under Council Regulation 73/2008 of 20 December 2007) and IMI2 JU (replacing and succeeding IMI JU and established through Council Regulation 557/2014 of 6 may 2014) and measure performance on the following key strategic areas of the Joint Undertaking's activities, namely:

1. the coverage of the research **portfolio**, i.e. adequate implementation of the new annual scientific priorities under IMI2 JU,
2. the degree of **progress** of IMI projects in delivering pre-set results and achieving targeted **research performance** under IMI JU,
3. the impact of the IMI programme on the **regulatory framework** as well as **EU competitiveness**,
4. the level of **collaboration** and **SME participation** so far,
5. the level of **involvement of patients groups**, and
6. the overall **efficiency**, **budget execution** and **the level of awareness** of the new Programme Office (formerly known as Executive Office) covering both IMI JU and IMI2 JU.

In addition, the Programme Office will also continue to measure and track, with the assistance of external consultants and service providers, other aspects of the Joint Undertaking's 2014 performance, outputs and impact using different methods for reporting results and outcomes including qualitative assessments, periodic scoreboard and other metrics. These will continue to reflect the evolution and needs of the Joint Undertaking and its stakeholders and the longer term outputs and impact of both the IMI and IMI2 programmes for the ultimate benefit of patients, as well as European competitiveness, economic growth, and advancement of science and innovation.

[1] According to Article 2(b), IMI2 JU will aim to:
i) increase the success rate in clinical trials of priority medicines identified by the World Health Organisation;
ii) where possible, reduce the time to reach clinical proof of concept in medicine development, such as for cancer, immunological, respiratory, neurological and neurodegenerative diseases;
iii) develop new therapies for diseases for which there is a high unmet need, such as Alzheimer's disease and limited market incentives, such as antimicrobial resistance;
iv) develop diagnostic and treatment biomarkers for diseases clearly linked to clinical relevance and approved by regulators;
v) reduce the failure rate of vaccine candidates in phase III clinical trials through new biomarkers for initial efficacy and safety checks; and
vi) improve the current drug development process by providing support for the development of tools, standards and approaches to assess efficacy, safety and quality of regulated health products.

Key Strategic Focus	Annual Objectives 2014	Link to the Council Regulations setting up IMI JU & IMI2 JU		Selected Key Performance Indicator (KPI)	Method	2014 Target
		73/2008 of 20.12.2007[2]	557/2014 of 6.05.2014[3]			
Portfolio	IMI2 JU's new calls for Proposals support the implementation of the research priorities as set out in the Strategic Research Agenda and updated by the Governing Board	• Article 2(a) and 2(b) • Article 1(c) in Statutes of IMI JU	• Article 2(a) • Article 1(b) in Statutes of IMI2 JU	**KPI 1:** Target number of priority areas defined in IMI2 JU's Annual Scientific Priorities for 2014 that are addressed by IMI2 JU call for proposals launched in 2014	Extent of coverage of priority areas for 2014 as defined in Section 2 of the IMI2 JU Annual Work Plan for 2014 (updating the IMI JU Annual Implementation Plan for 2014)	**KPI 1:** ≥4 priority areas from IMI2 JU's Annual Scientific Priorities for 2014
Scientific Output	IMI JU projects effectively deliver and disseminate high quality outputs[4]	• Article 2(a) and 2(b)	• Article 2(a) and 2(b)	**KPI 2:** Target estimated percentage of IMI JU projects that are assessed by the Programme Office as having achieved at least 100% of pre-set deliverables by the last reviewed reporting period by the end of the year	Progress for each project is calculated by the responsible IMI Scientific Officers, on the basis of cumulative achievements reported from the project start date up to the last reviewed reporting period by the end of the year	**KPI 2:** ≥80% of IMI JU projects
				KPI 3: Target estimated average number of IMI publications[5] per €10 million of total IMI JU funding requested by the projects **KPI 4:** Target to measure extent to which IMI JU's estimated average impact factor of journals in which IMI publications[5] have been published is higher than the EU average **KPI 5:** Target to measure extent to which IMI JU's estimated citation impact of IMI publications[5] is higher than the EU average **KPI 6**: Target to measure the extent to which IMI JU's bibliometric results compare with those of other international funding bodies	The main source of information is the independent bibliometric analysis and results as last compiled and reported to the Programme Office by Thomson Reuters, applying internationally recognised standards and criteria Latest available information from SOFIA will be used for the calculation of the estimated requested IMI JU funding by the end of the year under review For the benchmarking with other international funding bodies, the method will be explored with Thomson Reuters and the baseline data for establishing the target will be compiled and analysed in 2014-2015	**KPI 3:** ≥20 publications **KPI 4:** ≥10% higher than EU average **KPI 5:** ≥20% higher than EU average **KPI 6:** Not applicable in 2014

2 OJ L 30 of 4.2.2008

3 OJ L159 of 7.6.2014

4 During 2014, initial baseline data will also be collected and analysed on the number of patents resulting from IMI JU projects, particularly on the first finalised projects.

5 Covering all publications resulting from IMI projects from the start of IMI JU up the end of the year under review.

Key Strategic Focus	Annual Objectives 2014	Link to the Council Regulations setting up IMI JU & IMI2 JU		Selected Key Performance Indicator (KPI)	Method	2014 Target
		73/2008 of 20.12.2007[2]	557/2014 of 6.05.2014[3]			
Impact on regulatory framework and standardization	IMI JU projects translate key scientific discoveries into clinical practice and regulatory framework	• Article 2 • Article 1(e) in Statutes of IMI JU	• Article 2 • Article 1(b) in Statutes of IMI2 JU	**KPI 7:** Target to measure the number of scientific advice and qualified opinions initiated by the IMI projects at the EMA and FDA **KPI 8:** Target to measure the number of regulatory guidelines derived from IMI projects **KPI 9:** Target to measure new standards and best practices derived from IMI projects	The main source of information is the annual periodic reporting, as well as close follows up of the project by the respective Scientific Officers through attendance of the project annual meetings, and other exchanges Each Scientific Officer will report annually during the preparation of the Annual Activity Report If necessary, additional complementary information may also be collected as part of an annual survey of the consortia For KPI 8 and KPI 9, the methodology for capturing information and the baseline data for establishing the targets will be determined in 2014-2015	**KPI 7:** ≥ 5 **KPI 8:** Not applicable in 2014 **KPI 9:** Not applicable in 2014
Business development and sustainability	IMI JU projects increase EU competitiveness and foster innovation	• Article 2	• Article 2	**KPI 10:** Target to measure, on average, the number of patent applications filed and/or awarded to those IMI projects which have been reimbursed at least for the third year of implementation **KPI 11:** Target to measure impact on competitiveness **KPI 12:** Target to measure the number of spin-off companies or foundations created as a result of IMI projects	The main source of information is the annual periodic reporting, as well as close follows up of the project by the respective Scientific Officers through attendance of the project annual meetings, and other exchanges. Each Scientific Officer will report annually during the preparation of the Annual Activity Report If necessary additional complementary information may also be collected as part of an annual survey of the consortia For KPI 11, the methodology for capturing this information from industry and other sources and the baseline data for establishing the target will be determined in 2014-2015	**KPI 10:** ≥2 patent applications per € 10 million of costs accepted and reimbursed by IMI JU. [6] **KPI 11:** Not applicable in 2014 **KPI 12:** 25% of finalised projects

[6] The calculation will be based on the total value of interim and final payments made by IMI by the end of the year under review to projects that have completed at least the third year of implementation and the total amount will be divided by the cumulative number of patents filed and/or awarded to these projects.

Key Strategic Focus	Annual Objectives 2014	Link to the Council Regulations setting up IMI JU & IMI2 JU		Selected Key Performance Indicator (KPI)	Method	2014 Target
		73/2008 of 20.12.2007[2]	557/2014 of 6.05.2014[3]			
SME participation	IMI JU projects promote the participation of SMEs	• Article 2(e)	• Article 2(a) • Article 1(c) in Statutes of IMI2 JU	**KPI 13:** Target percentage of participants in signed Grant Agreements that are SMEs **KPI 14:** Target percentage of overall budget for projects that has been allocated to SMEs	Calculation is based on the latest available data extracted from IMI applications SOFIA and QlikView. Participations in IMI JU projects may count the same organisation multiple times when the same organisation is involved in several project in line with current practice. All participations from the start of IMI JU up the end of the year under review are considered in this calculation	**KPI 13:** ≥20% **KPI 14:** ≥20%
Patient participation	IMI JU projects promote the involvement of patient organisations	• Article 2	• Article 2(a) • Article 1(c) in Statutes of IMI2 JU	**KPI 15:** Target percentage of projects involving patients organisations as consortium partners, members of Advisory Boards, Ethical Advisory Boards or on consultancy basis for topics of relevance **KPI 16**: Target to measure impact for patients	Calculation is based on the latest available data extracted from IMI applications SOFIA and QlikView for the project partners Participations in IMI JU projects may count the same organisation multiple times when the same organisation is involved in several project in line with current practice If necessary, additional complementary information may also be collected as part of an annual survey of the consortia For KPI 16, the methodology for capturing this information and baseline data for establishing the target will be determined with the European Commission in 2014-2015	**KPI 15:** 100% **KPI 16:** Not applicable in 2014
Socio-economic impact	IMI JU projects lead to job creation and increased economic activity	• Article 2	• Article 2	**KPI 17:** Target to measure the estimated number of reported jobs created since the start of IMI JU and that can be considered as directly related to the IMI programme **KPI 18:** Target to measure additional impact on healthcare systems	Total number of jobs created will be reported. The data will be collected directly from the consortia via an annual survey For KPI 18, the methodology for capturing the information and the baseline data for establishing the target will be determined in 2014-2015	**KPI 17:** ≥ 1500 **KPI 18:** Not applicable in 2014

Key Strategic Focus	Annual Objectives 2014	Link to the Council Regulations setting up IMI JU & IMI2 JU		Selected Key Performance Indicator (KPI)	Method	2014 Target
		73/2008 of 20.12.2007[2]	557/2014 of 6.05.2014[3]			
Information, communication and dissemination	The Programme Office raises the awareness of IMI JU and IMI2 JU among all target groups	• Article 1(g) in Statutes of IMI JU	• Article 1(i) in Statutes of IMI2 JU	**KPI 19:** Target number of average monthly visitors to the IMI website **KPI 20:** Target to measure the performance of communication activities	Average number of monthly unique visitors as reported by Google Analytics for the year under review For KPI 20, the methodology for capturing the information and the baseline data for establishing the target will be determined in 2014-2015	**KPI 19:** ≥10 000 **KPI 20:** Not applicable in 2014
Efficiency of the Programme Office	The Programme Office meets the timeframe for Time to Grant (TTG) established by the EU for Horizon 2020	• N/A	• Article 17	**KPI 21:** Target timeframe for TTG of 240 days	Comply with the timeframe set out in the Horizon 2020 Rules for Participation (Article 20.2 in Regulation (EU) No 1290/2013) Average Time to Grant (TTG) for a two stage evaluation is defined as the time between the deadline for the submission of a Full Project Proposal and the signature of the grant agreement. This will be calculated annually for each grant agreement signed during the year under review	**KPI 21:** ≤240 days
	The Programme Office achieves high levels of performance in its annual budget execution	• Article 1(l) in Statutes of IMI2 JU	• Article 1(f) in Statutes of IMI2 JU	**KPI 22:** Annual budget execution target for commitment appropriations of running costs **KPI 23:** Annual budget execution target for commitment appropriations of operational costs **KPI 24:** Annual budget execution target for payment appropriations of operational costs	Extracted from annual figures compiled for IMI JU report on the budgetary and financial management	**KPI 22:** ≥95% **KPI 23:** ≥95% **KPI 24:** ≥95%
	The Programme Office meets the maximum time limits for expenditure operations established by the EU			**KPI 25:** Annual Average Time to Pay (TTP) target for pre-financing payments to beneficiaries **KPI 26:** Annual Average TTP target for interim payments to beneficiaries	Comply with time limits as established in the EU's Financial Regulation (Article 92 in Regulation (EU, EURATOM) No 966/2012)	**KPI 25:** ≤30 days **KPI 26:** ≤90 days

2 SCIENTIFIC PRIORITIES FOR 2014

The Scientific Priorities for 2014 reflect the principles of the Council Regulation on the Innovative Medicines Initiative 2 (IMI2) Joint Undertaking, specifically:

- Research related to the future of medicine should be undertaken in areas where societal, public health and biomedical industry competitiveness goals are aligned and require the pooling of resources and greater collaboration between the public and private sectors, with the involvement of small and medium-sized enterprises (SMEs);
- The scope of the initiative should be expanded to all areas of life science research and innovation.
- The areas should be of public health interest, as identified by the World Health Organisation report on priority medicines for Europe and the World (2013 update: http://www.who.int/medicines/areas/priority_medicines/en/).

The initiative should therefore seek to involve a broader range of partners, including micro, small and medium sized enterprises[7] from different sectors e.g. biomedical imaging, medical information technology, diagnostic and/or animal health industries while ensuring generally a balanced approach in terms of gender matters etc.). Involving the wider community in this way should help to advance the development of new approaches and technologies for the prevention, diagnosis and treatment of diseases with high impact on public health.

The Scientific Research Agenda (SRA) for IMI2 (see http://www.imi.europa.eu/content/imi-2) sets out the framework that underpins the development of specific projects or research programmes to be prioritised for funding.

Twelve key health priorities have been identified on the bases of the WHO Priority Medicines Report, and it is anticipated that throughout the lifetime of IMI2, many of these health priorities will be addressed. The SRA furthermore identifies data and knowledge management as key enabling technologies and education and training and excellence in clinical trial implementation as key implementation strategies.

The SRA places the research objectives of IMI2 under four major research axes:

1. target validation and biomarker research (efficacy and safety);
2. adoption of innovative clinical trial paradigms;
3. innovative disease prevention, interception and treatment solutions;
4. patient-tailored adherence programmes.

The activities generated from the priority areas will be designed considering relevant differentiating enablers for early and effective patient access to innovative prevention and treatment solutions (Medicines Adaptive Pathway to Patients-MAPPs-[8]):

- target validation based on human biology;
- stratified medicine, precision medicine;
- innovation in clinical trials for new drugs and therapeutic modalities;
- data generation and interpretation (knowledge management);
- prevention, disease interception, patient adherence (incl. societal acceptance of vaccines);

[7] See Commission Delegated Regulation (EU) No 622/2014 of 14 February 2014 and in particular Article 1 (micro, small and medium-sized enterprises and other companies with an annual turnover of EUR 500 million or less, the latter not being affiliated entities of companies with an annual turnover of more than 500 million)

[8] Press release: European Medicines Agency launches adaptive licensing pilot project: http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2014/03/news_detail_002046.jsp&mid=WC0b01ac058004d5c1

- patient-centric approach – effect on medical practice and outcomes (health/disease management);
- regulatory framework (including pharmacovigilance);
- reimbursement/patient access.

Using the framework of the SRA, the 2014 Priorities for the design of the first IMI2 Call topics have been selected on the basis of their potential to foster a first set of high impact initiatives, in areas where the maximum number of stakeholders can join forces. In particular five therapeutic areas (including rare forms of diseases) and cross-cutting themes have been identified:

1) metabolic disorders;
2) neurodegeneration;
3) prevention and treatment of immune-mediated disease, and advancement in prophylactic and therapeutic vaccines for infectious & non-infectious diseases;
4) infection control including incentives for reinvestment in antimicrobials, antivirals, and vaccines;
5) translational safety.

In addition to these priority areas, EFPIA and/or other industries active in health care may propose further priorities under one or more of the 12 key health priorities or based on emerging needs which are identified in the Scientific Research Agenda. Topics will be selected based on the level of unmet need, the need for a public-private partnership to make a difference, the extent to which the science is capable of delivering a high impact over the next decade, and the synergies/complementarity with similar initiatives.

To implement these Scientific Priorities, IMI2 will initiate competitive Calls for proposals and any other necessary procedure to evaluate proposals and award funding to projects[9]. Each priority may be implemented via the launch of one or more topics, which might generate one or more multi-stakeholder projects, potentially including (or driven by) other non EFPIA industry partners, or tailor-made projects for specific stakeholder groups. These details will be further elaborated in the course of the maturation of the individual topics.

All proposals must conform to the conditions set out in the H2020 Rules for Participation (http://ec.europa.eu/research/participants/data/ref/h2020/legal_basis/rules_participation/h2020-rules-participation_en.pdf) and the Commission Delegated Regulation with regard to IMI2 (add web link), unless they are supplemented in the call for proposals.

The proposals will be evaluated against the evaluation criteria (including scoring and threshold) and according to the evaluation procedure described in the call text.

For topics including clinical trials/studies/investigations, a specific template for essential information is available under
http://ec.europa.eu/research/participants/portal/doc/call/h2020/h2020-phc-2014-single-stage/1600139-essential_information_for_clinical_studies_en.pdf

Consortia will be requested to disseminate research data based on the basis of open access.

The call topics to be launched are described in Annex III of this work programme. Furthermore it is foreseen to establish Strategic Advisory Groups in the areas of immunology, metabolism, neurodegeneration, translational safety, and data and Knowledge management. The contribution that EFPIA companies make to these groups represents contributions to the operational costs of the IMI2 JU.

[9] Please see Article 1 (f) and (g) of the Statutes, annexed to the IMI2 JU Council Regulation.

2.1 Metabolic disorders

Activities in this priority area should seek progress towards novel diagnostic and treatment paradigms for early onset and progression of diabetes (type 1 and type 2) and its complications, and for early diagnosis and development of novel experimental medicine approaches to safe and efficacious diabetes treatments, considering also health system sustainability of treatment intervention.

Synergies will have to be created with several ongoing EU-wide and global initiatives including ongoing IMI projects such as SUMMIT, IMIDIA and DIRECT. All these efforts are already generating large scale sequencing data, and are performing genome-wide association studies (GWAS), and metabolomic and epigenomic studies in a large number of patients to identify new targets and biomarkers for prediction of disease progression and drug response.

IMI2's activities will build on the progress made through each of these initiatives, continuing to grow the science base required to support a personalised/precision medicine approaches for diabetes.

Activities in this area planned for 2014 will focus for example on one or more of the following:

- Predictive biomarkers, targets and pathways involved in insulin resistance and disease progression in the pre-diabetic stage of the cardio-metabolic continuum should be identified. Of relevance will be early non-glucose-related biomarkers for disease initiation and progression to complications and renal failure, and cardiovascular mechanisms as independent risk factors for type 2 diabetes.

- Tools and methods for the monitoring of key markers of glucose metabolism and diabetes complications using nanotechnologies should be defined.

- Data should be generated to allow a molecular definition of diagnosis criteria, and the determination of the best time point for pharmacological intervention to prevent disease progression to overt diabetes and complications.

- The interactions of immune cells (T-cells) with pancreatic ß-cells should be defined, and the development of early predictive biomarkers for the immunodestruction of ß-cells should be sought. This should lead to a better understanding of common and rarer immune mechanisms in type 1 diabetes and other auto-immune diseases, paving the way towards a molecular taxonomy of type 1 diabetes.

- Reliable and generally accepted outcome parameters and clinical trial designs for immune therapy in type 1 diabetes patients should be established. This might include comparative experimental clinical trials with different immune-modulatory drugs for a tailor-made, immune-modulating therapy of type 1 diabetes, and the definition of the safety and efficacy parameters, regulatory rules and a roadmap for immune-modulating therapy in newly-diagnosed type 1 diabetes patients.

2.2 Neurodegeneration

Given the healthcare burden that neurodegenerative diseases pose, together with the current disinvestment by major pharmaceutical companies, joint and urgent action from public and private sectors is essential.

The focus will be on the early and correct diagnosis of neurodegenerative diseases, the development of more preventative treatment approaches, the development of innovative patient focused endpoints, trial designs, and simulation and analytical approaches to devise new clinical trial paradigms both pre-and post-marketing. This will be critical to assess outcomes (good and bad) in small patient populations, thus balancing the needs for regulation (efficacy/safety) and HTA (Health Assessment Agencies) agencies (effectiveness/safety), as well as the risk and cost for pharmaceutical companies while responding to the urgent patient needs in this area.

A framework for scaling the collection of biomarker and clinical data is already in place, at least for some neurodegenerative conditions, with successful implementation of worldwide efforts such as the Alzheimer's Disease NeuroImaging Initiative (ADNI).These include IMI's EMIF-AD project, the Joint Programme – Neurodegenerative Disease Research (JPND), the Centre of Excellence Network (CoEN) and UK Dementias Platform supported by the UK's Medical Research Council (MRC) and the German Centre for Neurodegenerative diseases (DZNE) and others. Any new activities undertaken in IMI2 will collaborate with such initiatives and data resources available from academia across Europe to ensure synergies are maximised, and efforts are not duplicated.

Furthermore, important learnings should be generated by tackling alternative neurodegenerative and aging-related diseases with a high societal burden such as ophthalmic indications.

Activities in this area foreseen for 2014 will focus among other possible neurodegenerative conditions for example on one or more of the below:

- Age-related macular degeneration (AMD) is a serious neurodegenerative condition and leading cause of progressive blindness in patients of middle age and older. Outcome measures, biomarkers and composite endpoints that may be used in efficacy and safety trials for AMD, should be identified, and validation and regulatory agreement in principle should be sought;
- Health economic models and ways of monitoring therapy for AMD after marketing authorisation is granted should also be developed.

2.3 Prevention and treatment of immune-mediated disease

Autoimmune diseases cover over 100 distinct diseases and syndromes, together affecting approximately 5% of the population of Europe, with two-thirds of the patients being female. The burden of autoimmune disease crosses medical and scientific boundaries, and requires cross-functional collaboration by scientists and physicians with interests in diseases of widely differing organ systems. Activities should seek to identify therapeutic opportunities and design and implement clinical strategies, which will transform the diagnosis and management of autoimmune diseases.

The proposed work will build on the knowledge base and infrastructure present within the EU from ongoing research-based initiatives e.g. Eumusc.net, EMEUNET, EUSTAR, ERS/ELF, ECCO, BILAG, EUVAS and Euro Lupus OMERACT, as well as relevant IMI projects (BTCURE, PRECISESADS), which together have aggregated substantive information on disease phenotypes, biomarkers and other factors associated with disease progression in many autoimmune disorders in order to guide better patient treatments.

For some conditions, like multiple sclerosis (MS), while disease modifying therapies have been available for 20 years, there has been limited progress in evaluating the real world outcomes and impact of treatment. Similarly there is a limited amount of long term data to support the impact of the approved therapeutic approaches in terms of disability and quality of life.
There are efforts at national and international levels to capture real world data, however up to now there have been only limited efforts to improve, expand and link up this data in a way that would enable the use of real world evidence to develop tools to guide health professionals in how and when to use treatments and support their management decisions to optimise outcomes (personalised medicine).

Activities in this area foreseen for 2014 will focus for example on one or more of the below:

- Database efforts across Europe should be further expanded and coordinated leading to a European knowledge platform in MS and its treatment. This should aim to expand and enhance the collection of real world MS data in Europe, explore the use of real world data in innovative regulatory pathways, and develop models for disease risk assessment for better decision making;

- Tools and measures to assist in personalised medicine decision making should be developed and advanced. These should include magnetic resonance imaging (MRI) and other techniques for assessment of brain function, patient reported outcomes (PROs), cognition, adherence, and clinical measures. This will require also developing relevant education in MS with specialist certification courses for healthcare professionals (nurses, neurologists, radiologists, etc.) and pharmaceutical industry professionals.

2.4 Infection control including incentives for reinvestment in antimicrobials, antivirals, and vaccines

Vaccination is one of the most valuable and cost-effective public health measures to prevent and control the spread of viral/bacterial infectious diseases responsible for high mortality and morbidity. It saves at least three million lives every year globally. Changes in society both nationally and internationally have led to the need for research & development on vaccines to address the changing risks and immunological characteristics of the whole lifespan. This requires innovative solutions to understand and measure the maturation of the immune system, and to tackle emerging/unmet medical needs. Research is also needed to better understand drivers underpinning inconsistent utilisation of available immunisation measures, as a rise in the numbers of people hesitating to use vaccines undermines individual and societal public health and exacerbates the challenges of maintaining the financial sustainability of healthcare systems. Furthermore this is a priority area where research to reduce the use of experimental animals is highly relevant.

In the field of vaccines a number of large research infrastructures already exists such as CIMT/CIC (T-cell Immunity), and EU-funded OPTIMALVAC/EMVDA (malaria vaccines) and TRANSVAC (vaccines in general) among others. This provides an excellent opportunity to drive collaboration between these existing initiatives, bringing together industry and public research organisations and maximising synergies. The benefits could be even further enhanced by linking to other European infrastructures such as biobanks and IT infrastructures.

Activities in this area planned for 2014 will focus for example on one or more of the below:

- Alternative approaches to the current animal tests required for lot release testing of established vaccines have been under development in both the public and private sectors for years, and some progress has been made. However, validation of these methods by comparison with the immunisation-challenge potency tests has been very difficult, time consuming and not always successful, for, amongst other reasons, the poor reproducibility of the in vivo tests. Therefore, the development of analytical methods, in vitro models demonstrating functionality of immune responses, and bioinformatics, to generate a set of consistency tests that will allow improved monitoring of vaccine quality during production and final formulation should be sought.

2.5 Translational safety

There is still a critical need for tools and methods that will facilitate the monitoring of safety issues, contributing to the safety of patients beyond the launch of new products. A better understanding of toxicological findings for human risk assessment has to be built for example via a retrospective review of clinical side effects and their relationship to non-clinical safety data. Better preclinical models representing human biology for predicting safety issues, and understanding the molecular causes underlying it, are needed to reduce attrition in the development of novel drugs and enable the development of safety biomarkers for the management of risks in humans.

Activities in the area will build on progress and success from the portfolio of IMI projects on safety, from other relevant European and global initiatives to create synergies (e.g. US Critical Path Institute and NIH driven projects) and from data management initiatives.

Activities in this area planned for 2014 will focus for example on one or more of the below:

- The concordance of toxicity of pharmaceuticals in humans and in animals should be re-assessed. While an extensive arsenal of biomarkers for renal and hepatic safety has been already generated, during clinical studies and particularly during early or adaptive licensing it will be important to monitor early for changes and trends in those biomarkers;

- Identification and/or further validation of known and suggested new safety biomarkers representing different types of molecules, e.g. proteins and enzymes, but also nucleic-acids, might also be sought. One goal will be the characterisation of biomarkers which are easily translatable across preclinical species and human patients. A further goal will be the search for/evaluation of biomarkers for organs other than the liver and kidney, e.g. heart, pancreas, gastro-intestinal tract, brain etc;

- A key component of these activities might be the development of devices to automatically monitor for metabolic changes while being minimally invasive, and the use of contemporary communication technology to aggregate/monitor information in real time. The use of automated biomarkers will also be used in combination with the knowledge management work to understand and optimise real world medicine use more broadly. Points of care for automated safety monitoring will help minimise and provide early detection of drug-drug interactions and unanticipated consequence of treating patients with multiple conditions;

- New platforms should be developed reflecting human organ physiology (e.g. 3D, or organ-on-chip models, single cell-type or co-culture) to predict toxicity and safety during early drug development. In particular, liver, renal and cardiac safety might be studied using induced pluripotent stem (iPS) cells from subjects with a variety of phenotypes to understand better which patient subpopulations are at risk from rare safety issues. These models will be validated based on existing compound libraries and safety databases. Assessment of such new models will include evaluation of the limitations of such models with respect to *in vivo* organ function, which thereby will define their applicability;

- Molecular targets and pathways (through e.g. integrated 'omics' approaches) underlying toxic phenotypes of drugs failed for safety reasons should be identified. One goal will be the development of *in vitro* models representing these pathways which can be employed in early safety testing. This should lead to a reduced and refined use of animals, including the possibility for better prediction of suitable toxicology species;

- Since toxicological phenotypes are the result of both the hazard and the dose, a further activity should include the evaluation and optimisation of existing or new toxicokinetic models with the aim of predicting adaptive and adverse changes based on *in vitro* assay results and modelled exposure data. Of relevance may also be studies of the pharmacokinetic interactions caused by mechanism-based, time-dependent and metabolite- mediated inhibition of drug metabolism and transport as well as relevant pharmacogenetic studies. This will be important to anticipate and study adverse drug interactions, understand variability in the metabolism and disposition of drugs and their metabolites, and guide future revisions of regulatory guidance on drug-drug interaction studies;

- A systematic annotation of observed toxic phenotypes, and the integration of various types of both newly generated and already available data into existing data management structures should be also achieved, with potential consolidation into fewer database formats to allow flexible public and private use.

2.6 Other Priorities derived from the SRA: 1- Psychiatric diseases

More than a quarter of all Europeans are estimated to experience at least one form of mental disorder during their lives. Although several treatments are available, positive response is limited, and for most mental disorders, treatment algorithms are based on trial and error.

Activities are needed for a better understanding of the disease biology and potential biomarkers of psychiatric disorders, which will be the key to increasing rates of diagnosis and treatment success, and to the development of more targeted medicines. Attention should be paid to new techniques for the functional assessment of the human brain.

Activities will build on early successes and progress in ongoing IMI projects (NEWMEDS and EU-AIMS) and will seek synergies with other national, European and global initiatives on mental health.

Activities in this area planned for 2014 will focus for example on one or more of the below:

- A systematic analysis of genetic and environmental factors contributing to different psychiatric disorder categories in a trans-diagnostic way should be considered. This should be the basis for (back)-translational work, taking advantage of new instruments of research and patient characterisation, to allow the establishment of trajectories for the development of psychiatric disorders;

- A taxonomy which better reflects the neurobiological mechanisms of psychiatric disorders and is better suited for developing new and efficacious drugs to treat mental disorders should be developed. This activity will link to ongoing projects on disease taxonomy already implemented by IMI;

- A framework for translation of research on clinically relevant neuropsychiatric endo-phenotypes for regulatory agencies should also be built;

- This might also include the development of surrogate endpoints and markers for efficacy and patient stratification, and for identification of endo-phenotypes of potentially disruptive disorders in ‘at-risk’ patients.

2.7 Other Priorities derived from the SRA: 2- Respiratory diseases

Despite improvements in the way respiratory diseases are managed, they continue to pose a significant burden on patients and healthcare systems. Unlike asthma and other allergic respiratory diseases, chronic obstructive pulmonary disease (COPD) remains a relatively poorly understood disease despite one person dying of COPD every 10 seconds, more than breast and lung cancer combined.

IMI2 activities will have to seek synergy with ongoing initiatives such as The COPD Foundation Biomarker Qualification Consortium, the UK Technology Strategy Board funded ERICA or the Industry-funded ARCADE and ECLIPSE cohort studies, among others. Furthermore the initiatives will build on current relevant activities in IMI (e.g.PROactive).

Activities in this area planned for 2014 will focus for example on one or more of the below:

- A better understanding of what aspects of COPD heterogeneity are relevant for patient-based risk assessment and stratification should be delivered. This should consider an impact on therapeutic strategies and patient management in real life clinical practice. This might include the identification of alterations of pathway regulation associated with poor patient prognosis;

- Rules for subject-specific health risk assessment and patient-oriented stratification with impact on healthcare management (both preventive and therapeutic) should be generated;

- Knowledge acquired by the project should be transferred to clinical practice through well-defined validation strategies and implemented as a fully deployed integrated care scenario;

- The optimisation of the interactions between pharmacological and non-pharmacological interventions in COPD patients might also be relevant;

- The exploration of potential re-orientations of the use of existing drugs for the design of novel therapeutic approaches (i.e. antioxidant therapies) might be also included.

2.8 Other Priorities derived from the SRA: 3 Enabling Technologies and Excellence in Data Management

The increasing volume (terabytes/patient), diversity (clinical, GWAS/RNASeq, eHR, 'omic', cytometry, imaging, pharmacology, pharmacovigilance etc.) and velocity (e.g. real time telemetric monitoring of patients, social media feeds, etc.) of biomedical data create significant opportunities for healthcare R&D. However, common data standards, as well as robust data production and knowledge management (KM) solutions and services will be essential if the full value of these data sets is to be realised in the development of innovative precision medicines.

Furthermore, as healthcare delivery systems change, clinical trials move to more adaptive designs, new monitoring devices become more sophisticated and "live" patient interactions through mobile enabled, social media technology, are implemented, there will be a need to engage with the IT sector. This will be necessary to collaborate on the development of novel enabling technologies and adaptive therapies to facilitate the efficient capture and interrogation of these data sets to ensure effective healthcare practices for patients.
The IMI2 activities will expand upon work from existing IMI projects including EMIF[10], eTRIKS and EHR4CR as well as other FP7 projects in the area of electronic health records, and will require coordination/collaboration with European biomedical research infrastructures through the European Strategy Forum on Research Infrastructures (ESFRI). They will also take into account policies and guidelines for data gathering and sharing from relevant international initiatives such as the International Rare Diseases Research Consortium, International Human Cancer Genome Consortium and the Global Alliance for Chronic Diseases.

Ethical Legal and Social Aspects (ELSA), will have to be carefully considered and developed as part of all research activities in this area.

Activities in this area planned for 2014 will focus for example on one or more of the below:

- Building on EMIF, a comprehensive, large scale, usable and accessible database should be developed that in the long term will link genotype, clinical and phenotype data for any individual (diseased or non-diseased). This will be essential to maximise opportunities to understand disease. This project will include the generation and coordination of a pan-European, controlled access database (data safe haven) for qualified genetic and health record/patient-level phenotype information to provide longevity and accessibility to data for 1-3 pilot disease areas beyond those already tackled by EMIF.

- Real-time identification of behavioural and physiological patterns that culminate in disease relapse is of great importance: early detection and communication of "red flags" to both patients and providers can prompt help-seeking behaviour and deployment of just-in-time interventions that may prevent relapse episodes, effectively altering one's clinical trajectory. This element is particularly critical in the context of patient compliance/adherence and need to develop interventions to reduce the incidence of non-adherence with prescribed medicines. Achieving this objective might involve among others that:

    a) the science of using biosignatures to characterise disease and predict changes in disease state through a series of observational studies is developed and validated;

[10] The European Medical Information Framework (EMIF) programme was established as part of the 4th IMI Call, as an IMI project composed of the EMIF-Platform (the data and technical part) and 2 research topics (in metabolics and Alzheimer's disease).

b) innovation and development of novel biosensors and the associated knowledge management technology is stimulated;

c) the understanding of the regulatory pathways for using remote assessment in healthcare is enhanced;

d) standards for Information exchange that enable seamless integration of sensor, data capture, data management, & analysis technologies are developed;

e) an open source reference platform is created to enable the collection, storage and analysis of remote assessment data.

3 MANAGEMENT OF CALLS AND PROJECTS

3.1 Activities related to Proposals Evaluation and Grant Negotiation

Key activities in 2014 will comprise the evaluation of Expressions of Interest and/or Full Project Proposals submitted for the topics of Calls 9, 10 and 11, launched in Q4 2013. Furthermore, proposals submitted to the third ENSO Call will be evaluated.

The first calls of IMI2 will be launched to implement the 2014 Scientific Priorities. It is expected that at least 2 Calls for proposals will be launched covering at least 4 topics. Details are set out in Annex III.

Besides the launch of competitive Calls for proposals, IMI JU will explore any other necessary procedure to evaluate proposals and award funding to projects.

Timelines for completion of the evaluation process and of negotiation will be kept as lean as possible with the aim of completing signature of the Grant Agreements for Calls 9 projects by Q2 2014, for Call 10 projects by Q3 2014 and for Call 11 projects by Q4 2014.

To maximise efficiency of the calls management, the IMI JU will continuously explore and implement simplification and improvement processes while maintaining the highest standards of the evaluation process.

3.2 Activities to support and monitor on-going projects

46 on-going and currently in preparation projects generated from Calls 1-8 will be running at different stages of their life cycle in 2014. IMI JU will continue to provide support and advice to the consortia, including on amendments to Grant Agreements. In addition, 4 new projects from Calls 9, 1 from Call 10, should start in 2014, as well as 8 projects from Call 11.

An overview of the project support and monitoring activities for 2014 is provided in the table below (status of projects as forecasted for 1st January 2014).

IMI Calls	Number of IMI projects						
	on-going	starting in 2014	1st year	Interim/ scientific reviews	post-interim review phase	final year	submitting annual reports & financial statements
1	15				15	12[11]	15
2	8			2[12]	7	1	8
3	7			7			7
4	7			1[13]			7
5	1						1
6	2						2
7	2		2				2
8	4*		4	1			4*
9		4					
10		1					

[11] Based on a justified demand one project U-BIOPRED has been granted a 1 year extension to finalise the activities.
[12] The project DDMORE will undergo a supplementary scientific review upon request of the interim reviewers.
[13] The project EMIF will undergo a 1st year scientific review.
*Of the 5 topics in Call 8, ND4BB 1C (the "Innovative Trial Design & Clinical Development" subtopic) will become part of the Call 6 COMBACTE project.

IMI Calls	Number of IMI projects						
	on-going	starting in 2014	1st year	Interim/ scientific reviews	post-interim review phase	final year	submitting annual reports & financial statements
11		8					

Figure 1

12 out of 15 of the projects generated from **Call 1** will complete the final year of activities in 2014 and 8 of the mentioned 12will submit their final activity reports.

The 8 projects generated from **Call 2** will enter their fourth year of activities. For one of these projects, OpenPHACTS, a budget neutral 6 months extension of the project period was granted in 2013 and thus 2014 will be the final year of activities, with also submission of the final activity report. Quick-Concept, the latest starting project from Call 2, will undergo an interim review. The project DDMORE will undergo a supplementary scientific review upon request of the interim reviewers.

The 7 projects generated from **Call 3** will enter their third year of activities in 2014, with all of them due for their interim review.

6 out of 7 **Call 4** projects will enter their third year of activities in the Q4 2014.
The Project EMIF from Call 4 will enter its second year of activities and it will be due for its first year scientific review as recommended by the expert panel during the Call 4 Stage 2 evaluation.

The **Call 5** European Lead Factory project and the first two projects part of the New Drugs for Bad Bugs (ND4BB) platform launched in **Call 6** will all enter their second year of activities, while the projects generated from **Calls 7 to 11** will all be in their first year of activities.

A key task will be to continue maximising efficiency, facilitating, optimising, and monitoring the implementation of all these projects and seeking feedback for continuous improvement to IMI JU operations. To this end, further workshops to provide guidance on the financial and administrative aspects of the projects to the EFPIA coordinators, non-EFPIA partners and to beneficiaries will continue in 2014.

Furthermore, **interactions between projects** and sharing of best practices (including on sustainability plans) will be promoted by organising joint and cross-projects meetings and/or using various other channels (e.g. the IMI Group on LinkedIn).

Activities are expected in particular in the following areas:

- Diabetes Research: further collaboration and data sharing will be facilitated by the memorandum of understanding and specific agreements signed in 2013 between SUMMIT, IMIDIA and DIRECT projects;
- Neuroscience: activities will be organized to facilitate links between the Call 1 projects and those generated from later calls (e.g. EMIF-AD and AETIONOMY);
- Knowledge Management (KM): a cross projects meeting between KM projects will be organized. Activities will be developed to foster implementation and development of standards for clinical data (CDISC and CFAST) as well as non-clinical data. Furthermore, 2014 should mark the finalisation of a Code for use of health data in collaborative scientific research projects developed collaboratively across projects, in particular the KM projects;
- Antimicrobial resistance: activities are planned to boost integration of projects under the ND4BB programme. To this effect, dedicated meetings will be organised in 2014 for ND4BB projects and, more widely, for other initiatives active in the fight against antimicrobial resistance.
- Stem Cells and iPS Cells Research and Banking: IMI JU will facilitate in 2014 a networking event with ongoing European funded stem cell initiatives including STEMBANCC from Call 4, EU AIMS Call 3, MIP-DILI Call 3, and EBISC Call 8, for which the ultimate goal is the establishment of a European

Induced Pluripotent Stem Cell Bank. Such event will aim at facilitating the interaction between the different consortia, explore new ways of collaboration and ultimately maximise European added value in health research in this area.

With regard to sustainability plans of IMI projects, IMI JU will also:

- explore any other necessary procedure to evaluate proposals and award funding to on-going projects; and
- launch a tender procedure to make available the necessary legal and financial expertise and support to projects.

3.3 Monitoring and analysis of projects' results

A combination of internal management information systems, external databases, periodic reports on the projects, independent evaluations and, if necessary, commissioned studies and surveys will be used to measure the progress and identify significant achievements of IMI projects.

In order to continuously and effectively monitor IMI projects and the overall program there is a need to develop an online platform that would allow for customisable, real-time analytics on all project outputs beyond publications; such as progress reports, data repositories, Standard Operating Procedures, standards, templates. Due to the high demand for customisation IMI Programme Office will have to resource to external collaboration on this matter to best design such a monitoring tool and explore the feasibility of interlinks with any existing systems.

In 2014 the collaboration with Thomson Reuters will continue to allow the analysis of the IMI project outputs in terms of publications and collaboration among IMI researchers.

Furthermore, IMI JU will explore possible expansions (e.g. through a tender procedure) of the KUL case study carried out in 2013 on IP and business outcomes of six IMI projects, notably by including a macroeconomic perspective.

Exploitation of results

In 2013, a pilot study analysis of project results was undertaken by KU Leuven on a small selection of IMI projects with a focus on IP and business opportunities. The results offered a basis for designing means to optimise the exploitation of IP and value generated in a number of selected IMI projects.

In 2014, the analysis will extend to other areas of focus not necessarily directly linked to IP and commercial exploitation but key to ensure that the impact of IMI projects can be maximised and that the results are sustainable, can be considered in the development of new medicines and maybe taken up in the decision-making process. To that end, IMI launched a tender for an Exploitation of results platform in August 2013. Activities to build the platform started late 2013 and will initially last 9 months. The platform should help maximise the translation of project outputs into standard of care (new practices and processes leading to improved healthcare), by bringing together all key and representative stakeholders, including the clinical community (e.g. clinicians, physicians, nurses, pharmacists), and patients in a discussion forum ('Think tank').

Such a multi-stakeholder Exploitation of Results Forum should be responsible for the following:

- Analysing IMI project outputs;
- Addressing legal, ethical, institutional opportunities and limitations for uptake of such outputs in the current regulatory/legal/institutional framework;
- Defining the uptake route and workable processes and formulate recommendations to be implemented by the relevant stakeholders/organisations to support delivering improved treatment options to society.

Intellectual Property

IMI JU will continue providing information, training and guidance on the handling of IP-related issues from the launch of Calls for proposals to the implementation phases of IMI projects.
To that end, the IMI JU will:

- continue regular communication in order to further improve knowledge and understanding of IMI IP policies to all stakeholders;
- provide SMEs with simple and practical information through the dedicated webpage;
- maintain its IP Helpdesk;
- get feedback from participants and stakeholders on the implementation of the IP policies;
- provide support during the consortium agreement negotiations to ensure compliance with the IMI IP policies and right balance between the participants while maintaining tight timelines;
- participate in Info Day meetings and in events organised at European level on IP management and best practices.

In addition, IMI JU will develop an IP Guidance Note in relation with the IMI2 rules. The purpose of this guidance note is to describe the IMI2 rules concerning Intellectual Property (IP) in contrast to IMI1 policy, to highlight the flexibility provided therein, and by doing so to explore ways to handle IP related issues and pitfalls that participants may encounter during the preparation and completion phases of the grant agreement and the negotiation phase of the consortium agreement.

Finally, IMI JU will explore ways or possibility of closer collaborations with the IPR-Helpdesk managed by the European Commission's Executive Agency for Small and Medium-sized Enterprises (EASME), and with policy guidance provided by the European Commission's Enterprise and Industry Directorate-General.

3.4 Stakeholders' engagement and external collaborations

Patients

Based on the Governing Board's strategy to improve patient involvement at IMI, the IMI JU will invest in improving the patients and lay community understanding of what IMI delivers and how it might impact their lives. This will be achieved through various actions that include the development of a patient-dedicated section on IMI's website, translating outputs from IMI projects into lay language, specific sessions with patients' involvement in IMI stakeholder forum, and the organisation of dedicated patient meetings. This also follows on from the June 2013 pilot patient group meeting, with two Patient Focus Meetings to be held in 2014: one session on diabetes, as requested by the Juvenile Diabetes Research Foundation (JDRF), and the second one around overall challenges facing patients regardless of the disease they are suffering from.

Efforts will also be made to improve the way IMI draws on the patients' expertise by involving patients into defining and executing IMI projects. This has already been implemented in Calls 9-11 by including sections dedicated to patient involvement in call topic texts for relevant projects. In addition, patient input will be sought more systematically in scientific challenge workshops as well as where appropriate in evaluation process. This way patients involvement at all levels will be ensured.

Finally, IMI aims to provide a forum for discussion and interaction between patients and other stakeholders, in particular scientists, to help collaboratively determine the best way to actively involve patients in research. This will be done via workshops where best practices would be exchanged between IMI projects as well as other initiatives.

Regulators

The strengthening of the relations with regulatory agencies including EMA, FDA and PDMA will continue in 2014 to ensure that IMI projects benefit from the Regulators' input. As IMI projects start delivering tangible results, engagement with Regulators is important to facilitate their translation into the regulatory practice, with the aim to enhance the efficiency of the development and the registration of medicinal products. IMI will therefore continue raising awareness of the IMI projects through early liaison with the Regulators in the context of qualification advice/opinions procedures.

In addition, joint meetings and teleconferences will be organised in conjunction with EFPIA and the European Commission to further discuss the impact of the IMI projects in the regulatory environment.
Experiences and lesson learnt will continue to be shared with other initiatives (e.g. C-Path, NIH) to better explore synergies.

Small and Medium Size Enterprises

Based on past activities IMI JU has been successful in encouraging SME participation in IMI Calls. As of the end of September 2013, 15.4% of the successful applicants to IMI were SMEs. Furthermore, SMEs that have successfully applied have been allocated 22.5% of the IMI budget for the projects launched. To build on this success, IMI JU will continue to work with its founding members and other stakeholders to increase support for SMEs and increase SME participation in its projects. IMI JU will achieve this through the provision of targeted support and guidance disseminated through the dedicated helpdesk and IMI website.

The IMI Programme Office will host and attend meetings specifically aimed at involving the SME sector. It will also undertake activities to increase liaison with both individual SMEs and European umbrella organisations that support the SME sector at the regional, national and international level.

To provide further support to SMEs, IMI will increase its efforts in communicating information on sources of funding available within IMI projects but also more widely within European Institutions and bodies, both public and private. It is envisaged that a series of networking events will be held to discuss business funding opportunities for SMEs with life science venture capitalists, representatives from EFPIA investment units and representatives of the European Commission.

CDISC

The collaboration with the Clinical Data Interchange Standards Consortium (CDISC) will continue in 2014 for the benefit of IMI JU beneficiaries, in particular with the training activities by CDISC offered to partners of IMI consortia. In order to further facilitate implementation of data standards, in-depth trainings on CDISC standards (CDASH[14], SDTM[15], ADAM[16], SEND[17]) and any other applicable, as well as a consultancy session will be organized for the projects. The standards developed in the context of IMI projects will continue to be discussed in the context of CDISC standards. The latter will be enhanced with taking part in the Scientific Advisory Committee of the Coalition for Accelerating Standards and Therapies (CFAST), a joint partnership between CDISC and Critical Path Institute created to accelerate clinical research and medical product development by developing and maintaining data standards, tools, and methods for conducting research in therapeutic areas that are important to public health.

C-PATH Institute

The fruitful collaboration of 2013 with C-Path Institute will continue in 2014, notably with a second joint IMI & C-Path meeting scheduled in Q4 of 2014. The objective remains to foster synergy in areas of common interest such as modeling and simulation, and to maintain collaborations between specific projects and research areas as follows:

[14] Clinical Data Acquisition Standards Harmonization
[15] Study Data Tabulation Model
[16] Analysis Data Model
[17] Standard for Exchange of Nonclinical Data

- SAFE-T and PSTC for pre-clinical safety;
- IMI Portfolio of Alzheimer's Projects and CAMD;
- PreDICT-TB and CPTR for tuberculosis research.

IMI and C-Path Institute will work together for synergies and alignment and will seek to avoid duplication of efforts in these programmes. Collaboration will also focus on the data standard space with a view to ensure consistent remapping of respective data sets to enable leveraging the data on both sides.

Furthermore, collaboration in the area of anti-microbial resistance will start in 2014.

FNIH Biomarker Consortium

Collaboration will be enhanced, in particular between EU-AIMS project and FNIH Biomarkers Consortium's Autism Initiative to align initiatives in particular for biobanking and clinical research aspects.

4 COMMUNICATION AND EVENTS

4.1 Communication objectives

The IMI Communication and External Relations Strategy for 2014 will focus on the following objectives:

- Promote the launch of IMI2 and raise awareness levels and perception of IMI among all target groups;
- Attract the best researchers from relevant target groups to apply for funding under the first IMI2 Calls;
- Increase engagement of patients and SMEs in IMI's activities.

4.2 Key audiences

- Academic researchers – convince them of the excellence and applicability of research coming out of IMI projects and encourage them to apply for funding;
- Industry (both pharmaceutical and other, e.g. biomedical imaging, medical information technology, diagnostics, animal health) – convince them that IMI is a forum that allows them to share risks and move forwards, especially in the most challenging disease areas;
- Small and medium-sized enterprises (SMEs) – convince them that IMI provides opportunities to not only receive funding, but to work with networks of the leading experts in their area;
- Patient groups – engage them in IMI's activities, and inform them that IMI is speeding up the development of better, safer drugs;
- Regulatory authorities and payers – further engage them in IMI's activities, so that the novel tools developed by IMI projects can be formally validated as rapidly as possible;
- Policy makers and opinion leaders – convince them that a public-private partnership is an essential component of the health research and innovation landscape, delivering results that would not be possible through other programmes;
- General public – inform them that IMI is speeding up the development of better, safer medicines including for diseases that affect a large proportion of the population.

4.3 Key messages

Top level messages

- IMI is evolving, with an even stronger focus on the needs of patients and society
- IMI delivers breakthroughs that are having an impact on drug research and development and, ultimately, patients' lives
- In terms of both budget and scope, IMI is the world's biggest public-private partnership in the life sciences
- IMI accelerates the development of, and patient access to, new treatments, especially in areas where treatments are lacking / where the impact of a disease on society is particularly high
- By acting as a neutral broker, IMI facilitates collaboration and enables joint investments to tackle challenges that are too big for any one company, organisation or country to tackle alone

Messages for potential applicants on IMI2

- EUR3.276 billion budget for period 2014-2024 makes IMI the world's largest public-private partnership (PPP) in life sciences
- IMI now has simpler funding and reporting rules (funding rates and reporting rules aligned with Horizon 2020, protection for beneficiaries under H2020 Guarantee Fund)
- Funding for all non-profit organisations (not just research-based organisations)
- Funding for mid-sized companies (i.e. annual turnover of up to €500 million)

- Companies from other industries (e.g. biomedical imaging, medical information technology, diagnostic industries, animal health industries) can contribute in-kind (so contributions matched by IMI funding)
- Stronger focus on needs of patient and society
- Increased emphasis on improving patient access to innovative medicines (in addition to medicines development)

Messages for the pharmaceutical industry

- IMI is an attractive instrument to implement collaborative programmes involving industrial and non-industrial partners
- IMI provides incentives for innovation in particularly challenging / high risk areas
- IMI delivers tools and instruments to improve pharmaceutical R&D and speed up patient access to new treatments
- IMI shapes a new image of the pharmaceutical industry
- IMI trains a new generation of industrial scientists and regulators as well as current professionals

Messages for other industries

- IMI welcomes the participation of companies from a broad range of healthcare-related sectors
- IMI is an attractive instrument to implement collaborative programmes involving industrial and non-industrial partners

Messages for academic researchers

- IMI now has simpler funding and reporting rules
- IMI offers unique opportunities to translate breakthrough discoveries into clinically useful tools and products through open innovation networks
- IMI projects are generating scientifically excellent results
- IMI is creating new training schemes designed to address specific unmet needs identified by affected individuals/carers
- IMI has a flexible intellectual property (IP) policy that brings many benefits

Messages for SMEs and mid-sized companies

- IMI now has simpler funding and reporting rules
- IMI supports small and medium-sized enterprises and mid-sized companies engaged in drug development and innovation
- IMI has a flexible intellectual property (IP) policy that brings many benefits

Messages for patients and their families and carers

- IMI projects are focused on patients' needs and interests
- Patients are encouraged to participating in IMI's activities, e.g. by participating in IMI projects and committees

Messages for policymakers

- IMI implements EU policies
- IMI contributes to improving European citizens' quality of life
- IMI creates/maintains jobs and contributes to the competitiveness of the pharmaceutical sector in Europe
- IMI has a flexible intellectual property (IP) policy that brings many benefits
- IMI projects are generating scientifically excellent results

Messages for regulators and payers

- IMI is developing tools to facilitate (innovative) drug approval by regulatory authorities and payers
- Through IMI, regulators and payers can have direct contact with collaborative consortia as opposed to individual research groups or institutes

Messages for general public

- IMI is developing new treatments for diseases where there is a high, unmet societal need
- IMI is contributing to improved medicine and vaccine safety
- IMI creates/maintains jobs and contributes to the competitiveness of the pharmaceutical sector in Europe

4.4 IMI2 launch activities

Activities related to the launch of IMI2 are:

- Update of communication strategy, including key messages and corporate identity
- Draft new texts / slides / infographics explaining IMI: general text, governance, rules & procedures, especially 'what's new'
- Update relevant web pages
- Develop new promotional materials (leaflets, posters)
- Contribute to JTI-2 launch event on 9 July (including with press release)
- Organise webinars to present new rules and procedures and topics of first Call (July)
- Organise a launch dinner to raise awareness of the launch of IMI2 among key stakeholders such as policymakers (September)
- Organise Info Day to present new rules and procedures and topics of first and second Call, and to facilitate networking (September)
- Support STATES REPRESENTATIVES GROUP members and NATIONAL CONTACT POINTSs in organisation of national events.

4.5 Increasing the engagement of patients and SMEs in IMI's activities

Patients and carers have an important role to play in research. Throughout 2013, the IMI made significant efforts to reach out to patients and explore ways of boosting their involvement in IMI projects. This initiative was warmly welcomed by patients and projects alike, and will continue in 2014, with further events and materials dedicated to patients. IMI has a dedicated scientific officer working on outreach to patient groups, and the communications team works closely with her to develop messages and materials relevant to the patient community.

IMI has made great strides in its efforts to reach out to SMEs, and they now receive 18.4% of IMI's budget and account for 15% of all recipients of IMI funding (for the projects under the first eight Calls for proposal). Under IMI2, in line with Horizon 2020, IMI will be expected to ensure 20% of its budget goes to SMEs. IMI has a scientific officer dedicated to relations with SMEs, and this has helped to cement IMI's relations with SME umbrella organisations. In liaison with the scientific team, the Communications Team will continue to develop messages and materials relevant to the SME community, including SME 'success stories'.

4.6 IMI's Corporate Identity

The launch of IMI2 provides an opportunity to refresh the IMI corporate identity, including the visual elements. A new visual identity will also help to reinforce the message that IMI's activities have a renewed focus. To this end, a mission, vision and values have been drafted and our graphic designer will draw on these to develop a revised visual identity that will encompass the logo, other design elements, colours, images, and templates. The draft mission, vision and values are as follows. These will be finalised in collaboration with EFPIA and the European Commission.

Mission
The Innovative Medicines Initiative (IMI) is a partnership between the European Union and the European pharmaceutical industry. IMI facilitates collaboration in research to advance the development of, and accelerate patient access to, innovative medicines for the health and wellbeing of all, especially in areas of unmet medical need.

Vision
Improved health for all thanks to a vibrant, competitive medicines development community in Europe.

Values
Integrity - We always act with integrity and are transparent in our dealings with our projects, stakeholders and society. We take our role as a neutral facilitator seriously, and endeavour to treat all stakeholders and project partners fairly.

Adaptability - While maintaining a focus on the needs of patients, we ensure our work is in line with the latest developments in the fast-moving world of medicines research and development, and where possible adapt our way of working to take account of IMI's evolution.

Collaboration - Collaboration is key to IMI's success. Our projects work because they involve collaboration between experts from different sectors and different countries. Among our staff and committees, we value diversity and our strong team spirit. We also seek out collaboration with like-minded organisations around the world.

Efficiency - Our funding comes from the public purse and the pharmaceutical industry, and we work hard to manage these funds as efficiently as possible.

Passion - We are passionate about our work and ensuring the results of our projects benefit patients and society.

4.7 Communication channels

IMI will continue to develop the following channels in support of its communication goals:

- Events (both IMI and external)
- Website
- Newsletter
- Social media (LinkedIn, Twitter)
- Multipliers (IMI founding members, members of advisory bodies (States Representatives Group, Scientific Committee, IMI Programme Office and staff, , , National Contact Points, relevant umbrella groups / associations, IMI projects, organisations partnered by IMI, e.g. through a Memorandum of Understanding)
- Media (general and specialist, mainly in Europe but also international)
- Direct mailings
- Publications
- Direct contacts with opinion leaders

4.8 Media outreach

In recent years, IMI has enjoyed increased positive visibility in key general and specialist media. In 2014, IMI will work to ensure this trend continues by maintaining links with key journalists, issuing regular press releases, organising press interviews, and inviting media to IMI events. IMI will also maintain close contacts with its projects to ensure a steady flow of success stories that can be used to illustrate IMI's key messages when communicating with the media.

In addition, IMI will continue to work with a public relations agency, Media Consulta, to further develop its work in this important area. Specifically, Media Consulta will provide support in the following areas:

- General communications advice
- Media monitoring
- Assistance keeping media database up to date
- Handling logistics of media attendance at IMI events (invitations, travel, follow-up, etc.)

The Executive Office will also remain alert to issues that could damage IMI's reputation, and respond accordingly, for example by preparing briefings or sets of questions and answers. In order to strengthen IMI's in-house capabilities in this area, IMI will organise, through Media Consulta, a one-day crisis communications course for all senior management, the communication team, and a member of the legal team. IMI will also organise general media training for staff members who would benefit from this.

4.9 Key events planned in 2014

Event	Date - Place	Target audience	Objective
IMI Investing in Excellence - SME networking event	18 February Brussels, Belgium	SMEs, venture capitalists, policymakers, industry	Spotlight IMI SMEs, promote involvement of SMEs in IMI
DIA EuroMeeting	25-27 March Vienna, Austria	Researchers, industry	Raise awareness of IMI
IMI-JDRF Diabetes Patient Focus Meeting	20 May Brussels, Belgium	Patients, researchers, research-funding organisations	Gain patient input on research needs for diabetes
IMI Stakeholder Forum	21 May Brussels, Belgium	Policy makers, researchers, patients	Raise awareness of IMI
Launch of renewed JTIs	9 July Brussels, Belgium	Policy makers, press, other key stakeholders	Raise awareness of IMI & promote 1st Call
Webinars on IMI2 – Call 1 topics	July / September Online	Potential applicants	Encourage experts to apply for funding
Webinars on IMI2 rules & procedures	July / September Online	Potential applicants	Encourage experts to apply for funding
National IMI2 Info Days (organised by States Representatives Group)	Summer / Autumn	Potential applicants	Encourage experts to apply for funding
IMI2 launch dinner	September Brussels, Belgium	Policymakers, opinion leaders, patient groups,	Raise awareness of the launch of IMI2

Event	Date - Place	Target audience	Objective
		other stakeholders	
IMI2 Info Day	September Brussels, Belgium	Potential applicants	Encourage experts to apply for funding
Webinars on IMI2 – Call 2 topics (tbc)	Autumn Online	Potential applicants	Encourage experts to apply for funding
Webinars on IMI2 rules & procedures (tbc)	Autumn Online	Potential applicants	Encourage experts to apply for funding
Workshop on adaptive clinical trials	Autumn tbc	Patients, researchers, industry	Engage patients in debate on alternative trial designs
IMI – C-Path joint event	3 December Washington DC, US	Policymakers, opinion leaders, researchers, industry, patient groups	Promote debate on PPPs
Italian presidency event (tbc)	2nd half of year Italy	Policy makers, researchers, patients	Raise awareness of IMI

Figure 2

4.10 Resources

IMI2 Office

The IMI Communications Team comprises three people and takes the lead in setting IMI's Communication Strategy and overseeing its implementation. The Communications Team also supports the many other groups of people who communicate on IMI. Other IMI staff contribute to IMI's communication activities in a variety of ways.

- Providing news from the projects for use in communications
- Providing expertise on important issues
- Promoting IMI via presentations and scientific articles
- Identifying speakers for IMI events
- Maintaining personal links with opinion leaders and key stakeholder representatives
- Providing technical support (e.g. the IT team liaises with the contractors responsible for the technical side of the website and newsletter content management systems)
- Providing administrative support (e.g. at events)

In addition, two Scientific Officers lead IMI's outreach work for two important stakeholder groups, namely SMEs and patients – the Communications Team supports them in this work, for example by organising events and developing materials. The Executive Director also plays an important role in these activities.

IMI2 Stakeholders

EFPIA and the European Commission regularly promote IMI through their own communication channels.

Members of IMI's States Representatives Group, Scientific Committee, and Governing Board all act as IMI ambassadors, presenting and representing IMI in a variety of situations. In addition, the Governing Board provides regular feedback on IMI's communication plans and activities.

Other stakeholders

National Contact Points, relevant umbrella groups such as scientific societies and patient organisations help to promote IMI.

4.11 Analysing the impact of IMI communication activities

IMI will continue to monitor the impact of its communication activities as follows:

Website – number of visits, visitors, and page views per month
Social media – number of Twitter followers, number of members in IMI LinkedIn group
Press coverage – number, geographical spread and tonality of articles
Events – feedback from participants (gathered via online survey)

In addition to this, in 2014 IMI will carry out a survey of key stakeholders across Europe to gather a broad view of awareness levels and perception of IMI. This will be carried by YouGov via IMI's contract with Media Consulta. The results of this survey will help IMI to further refine its key messages and activities.

5 MANAGEMENT OF THE EXECUTIVE OFFICE

Building on 2013 achievements, a key strategic action for 2014 will be to further consolidate IMI2 JU's Programme Office as a strong and creative organisation, notably in preparation for the transition to IMI2.

5.1 Support to Governance bodies

The IMI2 JU will continue to provide support in 2014 to its Governing Board, the Scientific Committee, the States Representatives Group and the Stakeholders' Forum and their working groups.

The Governing Board gathers representatives of IMI2 JU founding members. It has the responsibility for overseeing the operations of the IMI2 JU and the implementation of its activities. It will meet at least twice in 2014, in addition to monthly teleconferences between the Chair, Vice-Chair and IMI office senior management. The first IMI2 Governing Board is due to meet on 2 July 2014.

The Scientific Committee is an advisory body to the Governing Board. It will meet at least twice in 2014 with a partially renewed membership. The composition will be reviewed on the basis of criteria set out in IMI2 Regulation.

The IMI States Representatives Group will be consulted on the Call texts and will receive the evaluation outputs. At least two meetings of the States Representatives Group are foreseen for 2014.

In addition, as part of the new governance features of IMI2, Strategic Advisory Groups to the Governing Board (called Strategic Governing Groups) will be established in different thematic areas with the primary aim to make the process of topic development and gathering industry commitment more transparent, effective and strategic. Relevant areas identified are:

- Immunology;
- Diabetes and metabolic disorders;
- Neurodegeneration;
- Translational safety;
- Data and Knowledge management.

Continuous attention will be given to enhance communication with these bodies and seek and feedback on any significant IMI activities and developments, including on the future of IMI. In addition, these bodies will be increasingly called upon advising on how best to exploit IMI projects outputs, enhance cross-projects' collaboration as well as explore synergies with similar or complementary activities at national level.

The collaborative platforms for supporting the Governing Board, the Scientific Committee and the States Representatives Group will be maintained and updated both from a content and operations point of view.

In addition, communication on IMI achievements will continue to be available through QlikView, a specific tool that generates statistics and data.

5.2 Budget and Finance

Draft Budget Plan 2014

The draft annual budget plan for 2014 approved by the Governing Board in December 2013 has been increased by the amount covering needs of IMI2.

Commitment appropriations (in EUR)	
Running costs	8,880,000
*Operational costs	213,533,700

Figure 3

*Excluding amounts carried over from 2013

Payment appropriations (in EUR)	
Running costs	8,880,000
*Operational costs	161,187,993

Figure 4

*Excluding amounts carried over from 2013

	Budget for **running costs** (in EUR)
Title 1 – costs related to IMI staff	
Salaries, missions, training and recruitment costs	4,855,000
Title 2 – running costs of the IMI JU office	
Office equipment, IT and telecommunications, external communication and events, audit, formal meetings and expenditure in connection with research activities (experts, workshops, meetings and events targeting the IMI projects).	4,025,000

Figure 5

The budget forecast for **running costs** in 2014 is increased by EUR 980,000 compared to the draft that covered only IMI1 to cover needs of IMI2 in terms of additional staff, office space and furniture, IT costs and costs of evaluations of projects launched under IMI2.

As regards **operational expenditure**, whilst payment appropriation is only increased by EUR 733,257 representing the amount carried over from 2013 based on the Decision of the Governing Board in January 2014, the commitment appropriation is being increased by EUR 213,533,700 which will be used for Calls for proposals launched under IMI2. In addition to this, EUR 880,903 representing the amount carried over from 2013 was entered in the budget increasing commitment appropriation available for 2014. The bank interest is not budgeted at this stage. The amount of bank interest yielded in 2014 will be entered in the budget 2015.

Preliminary Draft Budget 2015

The preliminary annual budget plan for 2015, together with the staff establishment plan, is set out in Annex II.

In a nutshell, the driving elements are the following:

- A total of EUR 185,741,743 in payment appropriations is planned to cover payments of cost claims of Calls 1 to 10 launched under IMI1 and pre-financing of first calls launched under IMI2.
- EUR 217,593,567 is foreseen in commitment appropriations for Calls for proposal launched under IMI2.

Total appropriations for running costs are foreseen at EUR 8,881,400. The increase is related to the needs of IMI2.

Financial Management

During 2014, the finance team will continue with its day to day activities of initiation, verification and payments of invoices and cost claims, creation of commitments, recovery orders, and analysis of periodic reports and negotiations of financial and administrative parts of projects. These activities will be conducted in a timely manner that will be monitored through corporate KPIs, in particular payment times and budget execution.

Best practice and highest quality standards will be ensured through the availability of a Manual of Financial Procedures that is under regular revision. In addition, knowledge dissemination will be further developed through the development of further guidance and the tenure of several financial workshops, in particular targeting beneficiaries, with the aim to reduce errors in financial reporting.

5.3 Human Resources

Together with well-defined workflows and processes, human resources management is at the heart of IMI's Programme Office organisational efficiency, namely through:

- Adequate recruitments and staff performance assessment;
- A balanced workload allocation and clear teams coordination;
- Learning and development opportunities;
- A clear organisational culture and open communication;
- Inter-JU cooperation.

2014 Staffing level

In 2014, 9 work contracts have been extended until 31 December 2017, the end of the organisation's life under IMI1 legal framework. The renewal of a work contract is based on both the business need and the staff member performance appraisal.

Since 2012, IMI has reached the authorised ceiling of 36 staff members, of which 29 temporary agents and 7 contract agents. The total headcount remained identical in 2013 despite a growing workload. In 2014, IMI2 will grow up to 41 staff members, with 5 authorised additional staff (4 Temporary Agents, and 1 Contract Agent) under IMI2. Of these additional posts, 2 have been earmarked for priority recruitment in the fields of science and communication with a view to rapidly address additional activities and workload linked to IMI2 set up. Further details are available in sections 3 and 4.10.

As stated in the amended EU budget for 2014 and in the legislative Financial Statement annexed to the European Commission draft proposal setting up IMI2, the IMI Programme Office should keep on growing until it reaches a total of 49 staff members in 2017. This extension will call in 2015 for an adaptation of the organisation chart.

Learning and professional development opportunities for better efficiency and staff retention

The IMI JU's organisational efficiency is also the result of a rational learning and development policy. This policy relies on internal as well as external trainings in order to keep staff members up-to-date mainly on:

- IT skills on tools such as Word, Excel, MS Project or ABAC, the European Commission's financial IT tool, and on any IT tool developed by IMI;
- Scientific knowledge (Drug Development cycle, Medicines regulations or more specific topics linked to research area);
- Legal context: IP recent case law, financial regulations, audit rules, staff regulations, etc.;
- Communication: communication strategy, social media, public speaking, languages, etc.

All training actions are oriented towards greater flexibility and reactivity of staff (ability to back-up an absent colleague, good understanding of the work context, etc.).

IMI is faced with an inherent risk of high turnover which can be explained by short term contracts offered by a time-limited organisation. This risk points to the importance of stabilising IMI's workforce, which is critical in view of the increase in workload foreseen in 2014. The problem of staff retention is critical for an organisation of this size and remains a key challenge for HR in 2014. This requires maintaining a stimulating and motivating work environment.

A new staff regulation in 2014 but still the same internal culture and open internal communication

In 2014, one of IMI's HR objectives will be to implement the new Staff Regulation of the EU's civil service which entered into force on 1 January 2014. Changes include an increase of working time to 40 hours weekly and a reduction of some leave entitlements. The Governing Board will accordingly adopt IMI's implementing rules in line with the EU new Staff Regulations.

IMI JU will ensure a smooth transition for staff. It will first have to identify:

- Implementing rules from the European Commission to be adopted by analogy by IMI's Governing Board;
- Implementing rules to be redrafted before adoption by IMI's Governing Board in order to take into account the specificities of a Joint Undertaking. Most of the time, the size of the Executive Office explains the need to adapt the text.

If, 9 months after the European Commission has issued an Implementing rule, no action is taken from IMI's side (adoption by analogy, redrafting or opt-out), this Implementing Rule will automatically apply to IMI. In order to be able to implement a rule quicker, and in order to benefit from the input from its Staff Committee, IMI JU will limit this adoption by default to texts that:

- only brings small and/or technical changes;
- cannot be amended (e.g. rules on pensions etc.);
- don't require to be quickly implemented.

Since its autonomy IMI's Office has developed its own identity and work culture. This work culture is based on an open internal communication, ensuring that all staff members do share the same understanding of IMI's overall objectives and priorities. A consistent service-oriented culture has progressively arisen among staff members while maintaining compliance with the EU legal and regulatory framework and the highest ethical as well as integrity principles and rules.

Further efficiency and savings through inter-JU cooperation

In 2013, IMI continued to explore and encourage all flexible arrangements, including close collaboration with other Joint Undertakings, and mechanisms of pooling expertise for specific time-bound tasks. In 2014, IMI will be willing to go further notably through common calls for tender, common recruitment procedures (setting-up of common reserve lists for administrative positions), common approach on implementing rules, etc.

5.4 Information and Communication Technology

IMI ICT strategic objective is to deliver value to the business and to be a key enabler of new business initiatives with the goal of supporting and shaping the present and future of IMI. ICT applications and infrastructure aim at making all IMI processes simpler and more efficient.

The following table sets out an overview of ICT developments and activities planned in 2014.

IMI Core Business	
SOFIA (Submission OF Information Application)	– Electronic Signature (Q2) – Monitoring system for EFPIA In-Kind Contribution cap (Q1) – Ex-post Audit (Q2) – Interim Reviews (Q3) – Enhancements for Experts management (Q3)
ICT Internal Support	
DORA (Document Repository Application)	– Process flow for invoices approval (Q3)
ISA (Information System for Absences)	– Adapt for new staff regulations (Q1)
eMA (electronic Missions Application)	– New platform for managing the missions requests and expenses claims (Q2)
IMI Intranet	– Maintenance (continuous improvements)
ICT Tenders	
File, email and Print Servers plus support services	– Current FWC finishing in Q4 2014. New joint tender.
sTesta	– Current EC FWC renewed till next year. For 2014 a different supplier already selected by the European Commission.
Internet	– Current FWC finishing in Q4 2014. New joint tender.
Software development	– Current FWC finishing in Q4 2014. New tender.
Other IMI Business tools	
Support to Governance Bodies (Governing Board, Scientific Committee, States Representatives Group)	– Maintenance (continuous improvements)
PST (Partner Search Tool)	
Events Registration Tool (IMI and JTIs platforms)	
IMI website	

Figure 6

Support to IMI Core Business

The management of current IMI Calls and Projects plus related processes is done electronically via an integrated IT System: SOFIA (Submission of Information Application) and QlikView - a statistics and KPI monitoring module, with a variety of tailor-made dashboards, enabling the analysis of scientific and financial data in SOFIA.

Due to the increased workload derived also from the Calls launched in 2013 it is of vital importance to achieve completeness of SOFIA. Therefore 2014 developments will be as follow:

- Electronic Signature (Q2)

The financial statements and adjustments are already submitted to IMI electronically but the printing step for blue print signature is still required. In view of a paperless grant management in IMI the electronic signature for the electronic-only transmission of financial statements (Form C) and adjustments will be developed.

- Monitoring system for EFPIA In-Kind Contribution cap (Q1)

We will implement a monitoring system to allow easy verification that EFPIA non-EU In-Kind contributions remain within the caps defined by Special Clauses 13A and 13B.

- Ex-post Audit (Q2)

In 2014 it is envisaged to finalise the development of this module to support the ex-post audit sampling, implementation, analysis and follow-up.

- Interim Reviews (Q3)

EoI, FPP and ENSO evaluations are already managed via SOFIA. For 2014 it is envisaged to integrate in SOFIA the management of the Project Interim Reviews also, increasing efficiency and facilitating the capture of the output from project activities.

- Enhancements for Experts management (Q3)

In view of a paperless Call management it is envisaged to have in SOFIA the electronic-only administration of Experts including the appointment management.

Support to other IMI Business Tools

IMI has well established collaborative platforms to provide support to the Governance Bodies, namely the Governing Board, the Scientific Committee and the States Representatives Group. In 2014 such platforms will have continuous improvements whenever needed.

Regarding the Partner Search Tool (PST) in 2014 it is envisaged to enhance further its usability for coordinators and partners to team up.

The events registration tool has been extended to also help the management of events shared by other Joint Undertakings. Continuous improvements for the IMI events registration tool are envisaged to be implemented during 2014, such as a pre-event networking module and a workshop module.

ICT Tenders

2014 will be a demanding year concerning IT tenders as all Framework Contracts will be finishing. This also implies several planning and coordination of possible systems' handovers, should contracts be awarded to new operators.

ICT Internal Support

Further efficiency gains in the operations of the Office will be sought through improvements of IT systems. Key actions will include:

- Improvements to common file and email servers with other Joint Undertakings;
- Further development of DORA (DOcument Repository Application), the IMI JU's electronic document management system enabling full electronic processing, storage and fast retrieval of all official IMI documents, to manage the process flow for invoices approval;
- ISA (Information System for Absences) will be adapted to the new EU Staff Regulations;
- A new platform will be developed: eMA (electronic Missions Application) to manage the complete missions work flow, from the request up to expenses claim.

Following a request from other Joint Undertakings located in the same premises, in order to best exploit synergies towards enhanced efficiency and cost-effectiveness, IMI will make available its internal HR and other administrative IT applications for their own use.

In addition, staff portable laptops and printers shall be upgraded for the majority as they turn 3 years of usage.

5.5 Procurement and contracts

In order to reach its objectives and adequately support its operations and infrastructures, IMI JU will allocate funds to procure the necessary services and supplies. In order to make tender and contract management as effective and cost-efficient as possible, IMI makes use as much as possible of multi-annual framework contracts and inter-institutional tenders. All essential framework contracts IMI is using will be running beyond 2014 with the exception of the IT and telephony services framework contracts mentioned below.

The most important contracts to be concluded in 2014[18] are the renewals of the framework contracts for IT support services; telephony infrastructure and support services; and software development. The call for tenders will be launched in Q1. IMI is tendering for the contracts in a single tender jointly with four other Joint Undertakings located in the same building and sharing the same ICT infrastructure[19] .

As regards communication, in Q3 2013 IMI has expressed its interest to join a tender procedure carried out by European Commission's DG RTD for a framework contract for events' organisation. Therefore IMI has reversed its plan to launch its own procedure for a similar contract. For public relations consultancy, IMI intends to conclude a specific contract in 2014 under the framework contract of DG RTD.

On the operational side in 2013, IMI - concluded a contract for consultancy services to establish a platform to study the optimisation of exploitation of IMI's project results. This contract is likely to be renewed in 2014, a possibility foreseen in the original tender.

Furthermore, IMI JU will explore possible expansions of the KUL case study carried out in 2013 on IP and business outcomes of six IMI projects, notably by including a macroeconomic perspective.

Concerning the activities to support and monitor IMI projects, IMI JU will launch a tender procedure to provide projects with the necessary legal and financial expertise and support to explore and implement sustainability plans.

[18] I.e. tenders for contracts with a value exceeding €130,000, which is the statutory limit for publication of the tender in the S series of the Official Journal. In addition, IMI uses negotiated procedures for low-value contracts below this statutory threshold.

[19] ARTEMIS JU, Clean Sky JU, ENIAC JU and FCH JU.

5.6 Data protection and access to documents

Data protection

In 2014, IMI JU will continue to ensure that personal data are protected and that Regulation (EC) No 45/2011 is complied with. Key actions for 2014 will include:

- Raising awareness with the IMI JU Staff: the IMI Data Protection Officer will invest time in informing the staff in particular in relation to the implementation of the accountability principle and to the follow-up of the new thematic guidelines issued by the European Data Protection Supervisor;
- Finalising procedures internally for handling notifications related to standard administrative procedures or addressing new processing operations;
- Follow-up on developments and implementation of the revised EU legal framework for data protection, alongside a continuous analysis of the impact of technological developments on personal data protection, especially those connected to the Internet.

Access to documents

IMI will also continue to address requests for access to IMI documents according to Regulation (EC) No 1049/2001, in a spirit of openness and transparency in order to bring its activities and output closer to the public.

The objectives of actions in this field will continue, as a means to strengthen public confidence in IMI by giving the opportunity to the public to monitor its work. In addition, this will bring additional benefits such as improving public awareness of IMI activities and processes as well as stimulating the interaction on key issues and on the future of IMI.

6 INTERNAL CONTROL AND AUDIT ENVIRONMENT

IMI JU has in place an integrated management system of governance structures, internal controls and risk management procedures to plan and implement its strategic and operational goals and objectives. In addition, the organisation relies on a combination of internal and external audits, ex-post audits, performance measurement tools, continuous improvement initiatives and independent expert reviews to monitor and ensure that IMI JU remains efficient, effective and compliant with all relevant regulations, rules and procedures. The existing internal control and audit set-up and arrangements take into account the nature and objectives of the public-private partnership as well as its size and organisational needs.

IMI JU will continue to build on the experience and lessons learned from the past four years as well as respond and adapt to new challenges and developments. It will implement and enhance its established internal control measures, ensuring in the process that all critical risks are appropriately mitigated; key priorities are achieved; legal and regulatory requirements are complied with; and stakeholders' expectations are met. The annual risk assessment exercise carried out by the Executive Office in the second semester of 2013 signalled the need to take specific measures in 2014 to adequately manage the risks resulting from the envisaged transitional change to reflect Horizon 2020 objectives, obligations and *modus operandi,* as well as to mitigate the risk that IMI JU may continue to detect an average 'error rate' that is higher than the 2% threshold set for the programme.

More specifically, throughout 2014, management will pro-actively assess and ascertain the robustness of internal controls and ensure overall compliance with rules and procedures. This will be achieved mainly through the:

- Review, coordination and follow up of the annual action plan for the implementation of IMI JU's internal control standards (ICS);
- Maintenance of a systematic risk management process in the annual planning and the conduct of an annual risk assessment exercise;
- Identification and prioritisation of the ICSs that need to be improved taking also in consideration the recommendations resulting from internal and external audits;
- On-going self-assessment and reporting on IMI JU's formal compliance with the ICS and on the effectiveness of the ICS put in place.

The following ICSs will be therefore prioritised for the year 2014:

ICS 3,[20] ICS 7[21] and ICS 10[22]

Particular attention will be given to the impact of new challenges and developments on the organisation structure as well as on staff allocation and business continuity. This is crucial in order to ensure that the structure and resources in IMI JU continue to meet evolving organisational objectives and needs.

ICS 5

Objective and Performance Indicators: Management will ensure that annual goals and objectives as well as key performance indicators are updated to reflect changing strategic priorities.

ICS 8

Processes and procedures: Management will take measures to safeguard the integrity and maturity of IMI JU's internal control system as the organisation evolves to respond to new challenges and developments.

[20] Staff allocation and flexibility
[21] Operational structure
[22] Business continuity

Ex-Post Audits of beneficiaries and EFPIA companies

Throughout 2014, the Executive Office will carry on with the implementation of the Ex-post Audit Strategy adopted in 2010 to ensure the legality and regularity of the operational expenditure. This strategy complements ex-ante controls embedded in IMI JU's management processes and includes the correction of any amounts found to have been paid in excess. Errors of a systematic nature will also continue to be extended to cover unaudited financial statements ('Forms C') of the same participants.

Representative and, if necessary, risk-based audits of beneficiaries will be launched during the year to cover new cost claims received and validated by IMI JU since the last audited period. In parallel, independent reviews of submitted certificates of in-kind methodology as well as audits of accepted declarations of in-kind contributions by EFPIA companies will also be continued and followed-up.

Internal and External Audit

In 2014, the Internal Audit Service of the European Commission (IAS) and the Internal Audit Capability (IAC) of IMI JU will continue to implement the coordinated multi-annual audit strategy for 2012-2014. These activities will include the provision of independent, objective assurance as well as consulting engagements on various aspects of IMI JU's processes and activities.

In parallel, during the year, the European Court of Auditors will audit and report on the reliability of IMI JU's 2013 Annual Accounts as well as the legality and regularity of the underlying transactions.

Anti-fraud strategy

In 2014, IMI JU will prepare and implement a comprehensive anti-fraud strategy in line with the European Commission Anti-Fraud Strategy (COM(2011)376) applicable to its services and also extended to agencies and other EU bodies.

Anti-fraud measures are part of sound financial management required under the EU Financial Regulation. In essence, the anti-fraud strategy will outline specific objectives and pro-active actions for fraud protection and detection within the existing internal control system with the aim of further protecting IMI JU's financial interests, its compliance with ethical values and the protection of the JU's reputation. The strategy will cover the following features:

- preventive measures against fraud, corruption and any other illegal activities;
- carrying out effective checks;
- recovering amounts wrongly paid and
- imposing effective, proportionate and dissuasive administrative and financial penalties where appropriate.

ANNEX I - DRAFT BUDGET 2014, INCLUDING STAFF ESTABLISHMENT PLAN 2014 (version 27/06/2014)

STATEMENT OF REVENUE				
Heading Revenue		**Financial year 2014**		**Comments**
Chapter		Commitment Appropriation (CA)	Payment Appropriation (PA)	
10	EU contribution	217 973 700	165 627 993	Commitment appropriations include EUR 4,440,000 for running costs and EUR 213,533,700 for operational costs. Payment appropriations include running costs of EUR 4,440,000 and operational costs of EUR 161,187,993.
	Title 1 - Total	**217 973 700**	**165 627 993**	
20	EFPIA contribution	4 440 000	4 440 000	EFPIA contribution to IMI JU running costs
	Title 2 - Total	**4 440 000**	**4 440 000**	
C2	**Title 3 - Total**	**880 903**	**733 257**	
	Total EU (operational and running costs) and EFPIA (running costs) contribution	**223 294 603**	**170 801 250**	
STATEMENT OF EXPENDITURE				
Heading Title 1		**Financial year 2014**		**Comments**
Chapter		Commitment Appropriation (CA)	Payment Appropriation (PA)	
11	Staff in active employment	4 370 000	4 370 000	Salaries
12	Staff recruitment - miscellaneous expenditure	25 000	25 000	Miscellaneous expenditure on staff recruitment: travel expenses, etc.
13	Missions and duty travels	190 000	190 000	Mission expenses
14	Sociomedical structure	250 000	250 000	Other staff costs: training, language classes, medical service, interim staff
17	Entertainment and representation	20 000	20 000	Representation, receptions and internal meetings (EC/EFPIA)
	Title 1 - Total	**4 855 000**	**4 855 000**	
Heading Title 2		**Financial year 2014**		**Comments**
Chapter		Commitment Appropriations (CA)	Payment Appropriations (PA)	
20	Office building and associated costs	590 000	590 000	Rent, works, common/IMI charges and parking. Additional costs: indexation, insurance, water/gas, electricity, heating, maintenance + repairs, security and surveillance.
21	Information technology purchases	583 000	583 000	IT purchases, software licences, software development, IMI website
22	Office equipment (movable property and associated costs)	145 000	145 000	Purchases and rental of office equipment, maintenance and repair
23	Current administrative expenditure	130 000	130 000	Office supply, literature, subscriptions, translation services, bank charges and miscellaneous office expenditure
24	Telecommunication and postal expenses	67 000	67 000	Data communication such as telephones, video conferences and postal services
25	Expenditure on formal meetings	160 000	160 000	Official meetings such as SRG, Scientific committee, Governing Board and working groups created by GB
26	Running costs in connection with operational activities	500 000	500 000	Expenditure in connection with research activities and objectives of IMI (workshops, meetings and events targeting IMI projects)
27	External communication, information and publicity	650 000	650 000	External communication and events such as Info Days, Stakeholder forums
28	Service contracts	580 000	580 000	Studies, audits
29	Expert contracts and cost of evaluations	620 000	620 000	Costs linked to evaluations, expert contracts
	Title 2 - Total	**4 025 000**	**4 025 000**	
	Total Running Costs	**8 880 000**	**8 880 000**	
Heading Title 3		**Financial year 2014**		**Comments**
Chapter		Commitment Appropriation (CA)	Payment Appropriation (PA)	
30	Implementating the research agenda of IMI JU	213 533 700	161 187 993	Grant Agreements - Payments
C2	Carry over from 2013	880 903	733 257	
	Title 3 - Total	**214 414 603**	**161 921 250**	
	Total EU (operational and running costs) and EFPIA (running costs) contribution	**223 294 603**	**170 801 250**	

Figure 7

Staff establishment plan 2014

Grade	Establishment plan 2013			Year 2014														
				Posts evolution						Organisational evolution			Establishment Plan 2014			Modifications envisaged in application of flexibility rule		
				Promotion / Career advancement			Turn-over (departures/arrivals)			New posts (per grade)			Authorised					
	PERM	TEMP	TOTAL	Officials	TA - LT	TA - ST	Officials	TA - LT	TA - ST	Perm	Temp - LT	Temp - ST	Perm	Temp	Total	Perm	Temp	Total
AD16		0	0								0			0	0		0	0
AD15		0	0								0			0	0		0	0
AD14		1	1								0			1	1		1	1
AD13		0	0								0			0	0		0	0
AD12		1	1								0			1	1		1	1
AD11		4	4								0			4	4		4	4
AD10		0	0								0			0	0		0	0
AD9		2	2								0			2	2		2	2
AD8		9	9								0			9	9		9	9
AD7		5	5								0			5	5		7	7
AD6		0	0								0			0	0		0	0
AD5		1	1								10			11	11		3	3
Total AD	**x**	**23**	**23**	**0**	**0**	**0**	**0**	**0**	**0**	**x**	**10**	**x**	**x**	**33**	**33**		**27**	**27**
AST11		0	0								0			0	0		0	0
AST10		0	0								0			0	0		0	0
AST9		0	0								0			0	0		0	0
AST8		1	1								1			0	0		1	1
AST7		0	0								0			0	0		0	0
AST6		0	0								0			0	0		0	0
AST5		0	0								0			0	0		0	0
AST4		0	0								0			0	0		0	0
AST3		5	5								5			0	0		5	5
AST2		0	0								0			0	0		0	0
AST1		0	0								0			0	0		0	0
Total AST	**x**	**6**	**6**	**0**	**0**	**0**	**0**	**0**	**0**	**x**	**6**	**x**	**x**	**0**	**0**		**6**	**6**
Overall Total		**29**	**29**	**0**	**0**	**0**	**0**	**0**	**0**					**33**	**33**		**33**	**33**

Figure 8

ANNEX II - PRELIMINARY BUDGET 2015,
INCLUDING PRELIMINARY STAFF ESTABLISHMENT PLAN 2015 (version 26/06/2014)

STATEMENT OF REVENUE				
Heading Revenue		**Financial year 2015**		**Comments**
Chapter		Commitment Appropriation (CA)	Payment Appropriation (PA)	
10	EU contribution	222 034 267	190 182 443	Commitment appropriations include EUR 4,440,700 for running costs and EUR 217,593,567 for operational costs. Payment appropriations include running costs of EUR 4,440,700 and operational costs of EUR 185,741,743.
	Title 1 - Total	**222 034 267**	**190 182 443**	
20	EFPIA contribution	4 440 700	4 440 700	EFPIA contribution to IMI JU running costs
	Title 2 - Total	**4 440 700**	**4 440 700**	
	Total EU (operational and running costs) and EFPIA (running costs) contribution	**226 474 967**	**194 623 143**	
STATEMENT OF EXPENDITURE				
Heading Title 1		**Financial year 2015**		**Comments**
Chapter		Commitment Appropriation (CA)	Payment Appropriation (PA)	
11	Staff in active employment	4 392 760	4 392 760	Salaries
12	Staff recruitment - miscellaneous expenditure	20 000	20 000	Miscellaneous expenditure on staff recruitment: travel expenses, etc.
13	Missions and duty travels	190 000	190 000	Mission expenses
14	Sociomedical structure	230 000	230 000	Other staff costs: training, language classes, medical service, interim staff
17	Entertainment and representation	20 000	20 000	Representation, receptions and internal meetings (EC/EFPIA)
	Title 1 - Total	**4 852 760**	**4 852 760**	
Heading Title 2		**Financial year 2015**		**Comments**
Chapter		Commitment Appropriations (CA)	Payment Appropriations (PA)	
20	Office building and associated costs	661 640	661 640	Rent, works, common/IMI charges and parking. Additional costs: indexation, insurance, water/gas, electricity, heating, maintenance + repairs, security and surveillance.
21	Information technology purchases	561 000	561 000	IT purchases, software licences, software development, IMI website
22	Office equipment (movable property and associated costs)	153 000	153 000	Purchases and rental of office equipment, maintenance and repair
23	Current administrative expenditure	123 000	123 000	Office supply, literature, subscriptions, translation services, bank charges and miscellaneous office expenditure
24	Telecommunication and postal expenses	67 000	67 000	Data communication such as telephones, video conferences and postal services
25	Expenditure on formal meetings	158 000	158 000	Official meetings such as SRG, Scientific committee, Governing Board and working groups created by GB
26	Running costs in connection with operational activities	500 000	500 000	Expenditure in connection with research activities and objectives of IMI (workshops, meetings and events targeting IMI projects)
27	External communication, information and publicity	625 000	625 000	External communication and events such as Info Days, Stakeholder forums
28	Service contracts	580 000	580 000	Studies, audits
29	Expert contracts and cost of evaluations	600 000	600 000	Costs linked to evaluations, expert contracts
	Title 2 - Total	**4 028 640**	**4 028 640**	
	Total Running Costs	**8 881 400**	**8 881 400**	
Heading Title 3		**Financial year 2015**		**Comments**
Chapter		Commitment Appropriation (CA)	Payment Appropriation (PA)	
30	Implementating the research agenda of IMI JU	217 593 567	185 741 743	Grant Agreements - Payments
	Title 3 - Total	**217 593 567**	**185 741 743**	
	Total EU (operational and running costs) and EFPIA (running costs) contribution	**226 474 967**	**194 623 143**	

Figure 9

Staff establishment plan 2015

Grade	Establishment plan 2014				Year 2015														
					Posts evolution						Organisational evolution			Establishment Plan 2015			Modifications envisaged in application of flexibility rule		
					Promotion / Career advancement			Turn-over (departures/arrivals)			New posts (per grade)			Requested (Provisional Draft Budget)					
	Total	PERM	TEMP	TOTAL	Officials	TA - LT	TA - ST	Officials	TA - LT	TA - ST	Perm	Temp - LT	Temp - ST	Perm	Temp	Total	Perm	Temp	Total
AD16			0	0											0	0		0	0
AD15			0	0											0	0		0	0
AD14			1	1											1	1		1	1
AD13			0	0											0	0		0	0
AD12			1	1											1	1		1	1
AD11			4	4											4	4		4	4
AD10			0	0											0	0		0	0
AD9			2	2											2	2		2	2
AD8			9	9											9	9		9	9
AD7			7	7											5	5		7	7
AD6			0	0											0	0		0	0
AD5			3	3											1	1		5	5
Total AD	**x**	**x**	**27**	**27**	**0**	**0**	**0**	**0**	**0**	**0**	**x**	**x**	**x**	**x**	**23**	**23**		**29**	**29**
AST11			0	0											0	0		0	0
AST10			0	0											0	0		0	0
AST9			0	0											0	0		0	0
AST8			1	1											1	1		1	1
AST7			0	0											0	0		0	0
AST6			0	0											0	0		0	0
AST5			0	0											0	0		0	0
AST4			0	0											0	0		0	0
AST3			5	5											5	5		5	5
AST2			0	0											0	0		0	0
AST1			0	0											0	0		0	0
Total AST	**x**	**x**	**6**	**6**	**0**	**0**	**0**	**0**	**0**	**0**	**x**	**x**	**x**	**x**	**6**	**6**		**6**	**6**
Overall Total			**33**	**33**	**0**	**0**	**0**	**0**	**0**	**0**					**29**	**29**		**35**	**35**

Figure 10

Annex III – CALLS FOR PROPOSALS TO BE LAUNCHED IN 2014

The first calls for proposals of IMI2 will be launched to implement the 2014 Scientific Priorities. It is expected that at least 2 Calls for proposals will be launched covering at least 4 topics.

1st IMI2 CALL FOR PROPOSALS

The 1st Call of IMI2 shall be launched on 9th July 2014.

INTRODUCTION

The Innovative Medicines Initiative 2 (IMI2) Joint Undertaking has been created[23] following the below principles:

- Research related to the future of medicine should be undertaken in areas where societal, public health and biomedical industry competitiveness goals are aligned and require the pooling of resources and greater collaboration between the public and private sectors, with the involvement of small and medium-sized enterprises (SMEs).
- The scope of the initiative should be expanded to all areas of life science research and innovation.
- The areas should be of public health interest, as identified by the World Health Organisation report on priority medicines for Europe and the World (2013 update: http://www.who.int/medicines/areas/priority_medicines/en/).

The initiative should therefore seek to involve a broader range of partners, including mid-caps[24], from different sectors e.g. biomedical imaging, medical information technology, diagnostic and/or animal health industries (while ensuring gender matters are considered). Involving the wider community in this way should help to advance the development of new approaches and technologies for the prevention, diagnosis and treatment of diseases with high impact on public health.

The IMI2 Strategic Research Agenda (SRA) is the main reference for the implementation of research priorities for IMI2. Based on the SRA the 2014 scientific priorities for IMI2 have been prepared, which include themes on metabolic disorders and neurodegeneration which are addressed in this call.

[23] The Council Regulation (EU) No 557/2014 of 6 May 2014 establishing the Innovative Medicines Initiative 2 Joint Undertaking.
[24] Under the IMI2 JU, mid-sized companies having an annual turnover of EUR 500 million or less, established in anand EU Member State or an associated country, are eligible for funding.

Applicant consortia are invited to submit short outline proposals to one of the topics. These proposals should address all aspects of the topic to which the applicant consortia are applying. The size of each consortium should be adapted to the scientific goals and the expected key deliverables.
While preparing their short outline proposals, applicant consortia should ensure that needs of patients are adequately addressed and, where appropriate, patient involvement is encouraged. Synergies and complementarities with other EU funded projects should be explored in order to avoid overlaps and duplications and to maximize European added value in health research.

Before submitting a short outline proposal, applicant consortia should familiarize themselves with all call documents such as the IMI2 Manual for evaluation, submission and grant award, and the IMI2 evaluation criteria.

1. TRANSLATIONAL APPROACHES TO DISEASE MODIFYING THERAPY OF TYPE 1 DIABETES MELLITUS (T1DM)

BACKGROUND AND PROBLEM STATEMENT

The global prevalence of diabetes has risen dramatically over the past decades. Whilst the connection between change in lifestyle patterns and type 2 diabetes mellitus (T2DM) seems undisputed, the connection between increased urbanization and type 1 diabetes remains a conundrum. Type 1 diabetes mellitus (T1DM) is a chronic disease affecting worldwide around 17 million people (World Health Organization's Priority Medicines for Europe and the World 2013 update, p.88). Type 1 disease has its peak incidence at puberty, but may occur at any age. The incidence rate is highest in Europe affecting altogether 22/100.000 per year, with major regional differences and an overall 25% higher incidence rate than in the United States of America (USA) (www.diapedia.org). The incidence of childhood T1DM is rapidly on the rise worldwide, especially in the under 5 year old age group.

T1DM is characterized by hyperglycemia due to destruction and loss of insulin-producing pancreatic beta cells and function over time. Furthermore, T1DM can be differentiated from the more common T2DM based on one or several autoantibodies directed towards antigens of the endocrine pancreatic islets. The emergence of islet autoantibodies as biomarkers preceding clinical islet beta cell failure has led to the generally held view that T1DM is an autoimmune disease and that immunologic abnormalities occur well ahead of clinical onset. The precise cause of type 1 diabetes is unknown, and believed to be due to one or more of the following: genetic susceptibility, dysfunctional programming of immune tolerance,

diabetogenic trigger(s) and/or exposure to a driving antigen. Recent analyses of pancreatic autopsy specimens from individuals with longstanding T1DM surprisingly demonstrate a heterogeneous but unexpected persistence of residual pancreatic beta cells despite insulin deficiency and active autoimmunity. These unexpected findings highlight the need for additional translational research to enable a deeper understanding of the pathophysiology, heterogeneity, and natural history of T1DM in humans.
The disease is currently not preventable and no cure is available. The only available pharmacotherapy for T1DM patients is the lifelong injection of insulin. Management of T1DM is not trivial as it is associated with multiple daily "finger pricks" to control blood glucose and requires multiple injections of insulin replacement therapy. A significant further burden is the risk of insulin induced hypoglycaemia which is currently considered the most significant barrier for optimization of adherence. An alternative approach to subcutaneous insulin replacement therapy is pancreas or pancreatic islet cell transplantation but existing cell replacement therapies require immunosuppression and are limited to very few recipients.

NEED AND OPPORTUNITY FOR PUBLIC-PRIVATE COLLABORATIVE RESEARCH

For almost a century, pharmacotherapy of T1DM has been synonymous with insulin therapy. Although undisputedly very successful, insulin therapy is associated with recognized limitations, such as adherence and drug induced hypoglycaemia. Stakeholders involved in care of people with T1DM as well as patients themselves agree that truly disease modifying therapy remains the ultimate approach to solve the challenge. Very few experimental alternatives to insulin therapy have been approached and clinical experimentation in the field of T1DM care has been modest at best. Considering the rapid growth of T1DM prevalence and the gravity of the problem, stakeholders in the T1DM community agree that is about time to intensify innovation in the field of T1DM therapy.

The pharmaceutical industry represented through EFPIA is highly motivated to play a leading role in establishing the widest possible cross-functional consortium with representatives from patient advocacy groups, health authorities, diabetes care givers, innovators, and industrialists. The objective is clearly to launch discovery programs in the field of T1DM that could lead to prevention as well as disease modifying and ultimately curative therapy. To achieve this ambitious goal deeper insight into the heterogeneous, phenotypic characteristics of people either at risk of developing T1DM or having manifest disease is required. This goal can only be achieved by pooling the knowledge, expertise and resources of all key stakeholders in the area, both public and private. Using state of the art technologies it is envisioned that this initiative will focus on a complete mapping of interactions between the immune system and pancreatic beta cells in humans and on the environmental changes that has led to increased disease incidence.

Through a thorough mapping of environmental and molecular mechanisms leading to T1DM, it will become possible to draft preventive strategies and to design future disease modifying therapies. The research strategy of the call shall embrace a strong focus on translational medical activities initiated at the bedside, refined at the workbench, and then finally brought back to the bedside for clinical validation of potential therapeutic approaches aiming at fundamentally preventing, halting, and reversing the β-cell destructive course of T1DM.

OVERALL OBJECTIVES

The overall aim of the initiative is to significantly progress the understanding of T1DM disease by bringing together patients, health authorities, leading clinicians, and researchers from the areas of immunology, beta cell biology, and biomarker research from both academia and industry.

Based on the assumption that T1DM is primarily driven by immunological dysfunction leading to beta cell destruction, it is expected that this initiative will significantly progress the understanding of the pathophysiology, heterogeneity, and natural history of T1DM in humans.

Translational medicine efforts mapping all stages of the disease are considered a pre-requisite for the initiation of rational drug discovery programs. As the program progresses, leading to the formulation of hypotheses of central pathophysiological processes in the development of T1DM, it is envisioned that the consortium will initiate clinical experimental studies that focus on validation in clinical studies of the newly acquired insights of dysfunctional molecular pathways leading to manifest T1DM.

POTENTIAL SYNERGIES WITH EXISTING EU SPONSORED CONSORTIA

It is expected that the project generated by this call will synergise and build on the results and assets of previous and ongoing European effort in diabetes including IMI projects in the diabetes area. The IMIDIA project (http://www.imidia.org/) has established a unique standardized, continuously growing human biorepository of biofluids (plasma, serum), pancreatic tissue and pancreatic beta cells from mostly adult diabetes and non-diabetic control subjects (predominantly T2DM).
The DIRECT project (http://www.direct-diabetes.org/index.php), while focussing on type 2 diabetes also is establishing a comprehensive collection of biosamples and clinical information on non-diabetic control subjects that can be of high value for the T1DM call.

In addition synergies with FP7-supported consortia in the fields of T1DM can be seen, e.g. to BIOSID (http://ec.europa.eu/research/health/medical-research/diabetes-and-obesity/projects/biosid_en.html), DIABIL_2 (http://www.diabil-2.eu/), DIABIMMUNE (http://www.diabimmune.org/), DIAMAP (http://www.diamap.eu/), DIAPREPP (http://www.diaprepp.eu/), NAIMIT (http://naimit.eu/), PREPOBEDIA (http://www.prepobedia.org/).

In addition synergies in the field of type 1 diabetes could be established with BBMRI (http://bbmri.eu/).

Another important synergy can be envisaged with the efforts of the global TRIALNET initiative (https://www.diabetestrialnet.org/about/index.htm).

The JDRF nPOD resource (http://www.jdrfnpod.org) of tissues (pancreas and other organs) from donors with diabetes, at-risk of developing T1DM, as well as non-diabetes controls, will also synergize with the efforts of this program.

EXPECTED KEY DELIVERABLES

Disease Biology and Translational Medicine (Target & Biomarker Identification)

It is envisioned that a pan-European clinical trial and translational research network will be built, including creation of a T1DM patient registry of readily accessible cohorts of T1DM patients willing to participate in future clinical research in the field. The network will facilitate a systematic and comprehensive functional and molecular profiling of disease heterogeneity, and identification of high-risk subjects beyond the use of islet-autoantigens.

The expanding on existing patient registries and prospective cohorts as well as the establishment of new cohorts shall be used to focus on:

- Systematic prospective and retrospective launch of broad "–omics" characterization of human biological samples from new-borns/infants/children/adolescents/adults at risk of developing diabetes as well as from newly diagnosed T1DM patient cohorts undergoing standard glucose control therapy. Such "full –omics" analysis should include both "at risk" subjects (HLA+AA-, HLA+AA+), as well as new onset T1DM patients to identify molecular markers in patient biofluids (blood, plasma, serum, lymph, urine)
    - Transcriptome assessment from enriched cells / particular fluid samples (including short RNAs and microRNA profiling)
    - SNP mapping & eQTL analysis, next generation sequencing of fast progressing, "at risk" subjects
    - Analysis of the gut microbiome
    - Metabolomics assessment (from available biofluids)

  - Proteomics and phosphoproteomics assessment (from exosome/biofluids)
  - Systematic epigenetic analysis (incl. methyl- & acetylation profiles).
- Phenotypic characterization (in silico based on medical records, as well as through active experimental clinical studies)
  - Identification of the glucose responsiveness as an indicator for patient beta cell status (OGTT, fasting blood sugar, hypoglycaemia propensity)
  - Pilot studies of imaging pancreatic inflammation
  - Behavioural phenotypes (therapeutic adherence, dietary preferences, exercise, cognitive)
- Establishment of systematic large-data and bio-bank repositories enabling extensive cross functional data mining and modelling of disease incidence and progression.
- Long term glucose control (HbA1c) status in recent onset patients as well as in relevant controls
- Exploration of imaging technologies for the use of identification and stratification of high-risk patients and as a surrogate end point in clinical studies.

Further activities could embrace novel methods to measure auto reactive T cell functional responses. Characterization of leukocytes obtained from patient blood, lymph or tissue samples to identify immune cell targets and surrogate end points are desired. A goal will be to define, standardize, and ultimately approve biomarker and immune profiling analysis that could be implemented for staging participants in future T1DM clinical trials in Europe. Prerequisite for successful outcome of such standardization effort is active participation of innovators, regulatory authorities, health care providers, and patient representatives.

In parallel, the project must focus on the metabolic characterisation of T1DM patients, such as the status of ß-cell function, or changes and defects in β-cell proliferation mechanisms (glucose, glucokinase, PDGF(R), WNTs), and beta cell stress/death in people with T1DM. Leveraging and enabling access to human pancreatic beta cells, islets, and pancreatic tissue from T1DM patients, through direct or collaborative efforts, should be prioritized by the consortium. In some instances implementation of surrogate assays of immune system interaction with islet function may be required, and it is suggested that the consortium integrate learnings from previous IMI and EU funded projects.

Qualification of identified biomarkers as diagnostics, as well as detailed characterization of the prediabetic period using novel diagnostics such as implantable micro-devices and early detection of autoantibodies (“Lab on a chip“) should be considered. Innovation of technically viable diagnostics solutions may require involvement of specialized entrepreneurs not traditionally represented by EFPIA members.

Identification and validation of biomarkers reflective of the disease progression including β-cell specific "ID tag" to quantify/monitor beta cell mass is also of high interest as it will assist novel disease taxonomy.

Defining and refining disease taxonomy for T1DM may create the foundation for personalized therapy of T1DM by the use of novel biomarker candidates and imaging technologies for the identification and stratification of high-risk patients and as a surrogate end point in clinical studies (consolidate health authority acceptance of T1DM disease classification as basis for medical decision making and approval of novel T1DM therapies).

Furthermore, the initiative will consider the development and characterization of most translatable preclinical T1DM models for discovery of novel clinical therapies to verify the newly acquired molecular knowledge for their human disease translatability.
Translational medicine efforts mapping all stages of the disease are considered a pre-requisite for the initiation of rational drug discovery programs aiming at treating the underlying causes of β-cell failure in people with T1DM.

Innovative clinical trial paradigms

During the past decade, a limited number of clinical trials have tested a variety of therapeutic approaches aimed at modifying immune function in people at risk for developing T1DM or with manifest disease. Therapeutic approaches have included attempts to induce immune tolerance to known islet autoantigens (proinsulin, GAD65), immune suppression through T cell modifying therapies (e.g. anti CD3), and anti-inflammatory antibodies (e.g. anti-Il-1β and anti-TNFα). These therapeutic approaches have been characterized by highly diverse clinical trials protocols and inconsistent primary end-points, rendering direct comparisons of efficacy and safety difficult. Guided by translational insights to the disease, the program is expected to facilitate the development of standardized clinical trial protocols with clearly defined, clinically meaningful, evidence based end-points providing indisputable medical value for people with T1DM as well as society.

As it is expected that the thorough characterization of "at risk" populations and newly diagnosed T1DM patients will consolidate existing as well as spur novel hypotheses for T1DM aetiology and pathophysiology, a clinical trial network shall also be used as vehicle for clinical research aiming at validating potential novel therapies.

Existing evidence suggest that a highly targeted T-cell mediated immune response is responsible for the islet destruction seen in T1DM. Therefore, modelling sequential T cell activation, T cell mediated cytotoxicity, and dysfunctional T cell regulation has led to a number of possible immunomodulatory approaches that have yet to be tested in people with new onset T1DM. In particular, in silico modelling based on in vitro and on animal data suggest that sequential combination of immunomodulatory agents (T cell specific antibodies, modulators of chemotaxis, inducers of immunological tolerance) may provide rational approaches for clinical trials aimed at halting the progression of the immune based destruction of beta cells and ultimately inducing tolerance to the triggering autoimmune event. It is expected that the established clinical trial network will engage in testing such novel immunomodulatory and tolerance inducing principles. The following deliverables are envisioned:

- Generation of a European comprehensive network of clinical and translational research centres capable of recruiting and conducting clinical trials in people with T1DM (providing a prospective clinical trials database for T1DM).
- Development of standardized entry criteria and endpoints for T1DM trials (both metabolic and immune profiles) preferably in collaboration with clinical centers in the US and with participation of patient advocacy groups, and regulatory authorities.
- Implementing the use of electronic data capture devices to collect an array of "real world data" useful for verification of therapeutic area hypotheses, regulatory rapports, etc.
- Testing and development of novel bio-statistical methodologies applicable to new compositions of relevant end points for T1DM clinical trials.
- Evaluation of novel mono- and combination approaches (i.e. combining multiple immune modulatory approaches, immune cell migration modification, immune tolerance inducers, β-cell enhancing therapeutics) in people with T1DM.
- The pan-European clinical trial and translational research network is expected to make important contributions to the evaluation of new emerging biomarkers and diagnostics indicative of T1DM disease progression or disease modification in clinical settings.

Patient participation

To aid in making the projects generated by this call more patient-centric, the project will be expected to establish a T1DM Patient Advisory Committee to enable input from patients and family members into the research involving subjects with T1DM and their biosamples and research around the development of innovative clinical trial paradigms. The T1DM Advisory Committee should include patients with T1DM of varying age and varying duration of disease, individuals at-risk of developing T1DM, and family members of children and adults with T1DM.

INDUSTRY CONSORTIUM

From the pharmaceutical industry consortium it is expected that specialists from the areas of molecular biology, chemistry, biologics, preclinical & clinical pharmacology, bioinformatics, translational medicine and clinical trials will actively participate in the projects work packages.

EFPIA PARTICIPANTS AND ASSOCIATED PARTNERS

Sanofi (coordinator), Juvenile Diabetes Research Foundation (JDRF) (co-coordinator), Novo Nordisk, Eli Lilly, GSK, Helmsley Charitable Trust. The EFPIA partners have invited the JDRF and Helmsley Charitable Trust to participate as equal partners in the steering group formulating this T1DM focused call. The JDRF (http://jdrf.org/) is a not for profit organisation focusing on patient advocacy as well as funding of research in the field of T1DM. The Helmsley Charitable Trust (http://helmsleytrust.org/) is a charitable organisation supporting research in health, selected place-based initiatives, education and human services. Both organisations participate in the present topic as Associated Partners to IMI2.
Additional companies are under consideration and the final list is to be confirmed.

INDICATIVE DURATION OF THE PROJECT

The indicative duration of the project is 84 month (7 years). This duration allows in depth systematic molecular analysis and immune and metabolic phenotyping of retrospective and prospective collected biological samples from T1DM patient cohorts. Further, the obtained insights will be integrated into novel to be established and existing models. Finally, the comprehensive patient characterization will be thoroughly integrated in to be defined prospective clinical trials.

FUTURE PROJECT EXPANSION

Potential applicants must be aware that the Innovative Medicines Initiative 2 (IMI2) Joint Undertaking, if so foreseen in the applicable annual work plan, may publish at a later stage another call for proposals restricted to those projects already selected under this call in order to enhance their results and achievements by extending their duration and funding. Consortia will be entitled to open to other beneficiaries as they see fit.

In the context of this topic, the EFPIA companies already envision the possibility to expand the project scope, during its implementation, to support clinical trials with immune-modulatory compounds in development. A restricted call would allow achieving this in the most efficient way by timely building on the progress and outcomes of the deliverables related to innovative clinical trial paradigms (e.g. clinical trial networks, identification of at risk patient population, definition of standardized entry criteria and endpoints, and novel bio-statistical methodologies for T1DM clinical trial). The detailed scope of the call will be described in the relevant annual work plan.

INDICATIVE BUDGET

The indicative contribution from EFPIA companies and Associated Partners is EUR 17 630 000.
The financial contribution from IMI2 JU will be a maximum of EUR 17 630 000.

Justification for Sanofi and JDRF non-EU in-kind contribution

Sanofi´s non-EU in-kind contribution amounts to EUR 3 000 000. Studies in preclinical models for the evaluation of the role of the autoimmune system in the development of T1DM are available at Sanofi sites based in the US (Genzyme). The inclusion of these autoimmune models in the project and the linkage of their results to the outcome from studies on beta-cell function are required to evaluate novel translatable preclinical models mimicking human T1DM. Comparable preclinical autoimmune models are not available at EU-based Sanofi sites. Furthermore, non-EU contribution will be generated by the partial manufacture of the autoimmune antibody that will be investigated in a clinical trial of the “Innovative Clinical Trial Paradigms in T1DM” part of the project.
JDRF non-EU contribution amount to EUR 420 000, to cover costs of their US based personnel.

TYPE OF ACTION

Research and Innovation action

APPLICANT CONSORTIUM

The applicant consortium is expected to address all the research objectives and make key contributions on the defined deliverables in synergy with the industry consortium.

To address the complex tasks of the call adequately, the project is expected to build a pan-European clinical trial and translational research network including a clinical registry of eligible people with T1DM. Such network will include:

- Academic endocrine clinics and associated supporting departments
- Basic, translational, and clinical researchers from the fields of T1DM autoimmunity and β-cell biology,
- Drug discovery and medical staff in Pharmaceutical Industry and Small and Medium size Enterprises.
- Hands-on data base specialists and big data managers
- Patient organizations/representatives
- Experts in regulatory science and health technology assessment preferably representing European health authorities.

Cross fertilization in this team of experts is the key for the success of the initiative.

SUGGESTED ARCHITECTURE OF THE FULL PROPOSAL

The above described cross functional and cross sector team members are recommended to work together in dedicated work packages addressing the different aspects of the overall call. Each work package team is recommended to consist of academic and industrial/biotech members with regular interactions to ensure knowledge exchange between the different expertise. Inter-work package knowledge transfer should be ensured at all times via regular management board meetings. The jointly used data documentation tool is considered a key piece for the success of the overall call ensuring maximum information gain by applying systems biology.

In addition a plan for interactions with Regulatory Agencies/Health Technology Assessment bodies with relevant milestones and appropriate resource allocation should be built into the project architecture as well as aspects related to dissemination and sustainability, facilitating continuation beyond the duration of the project.

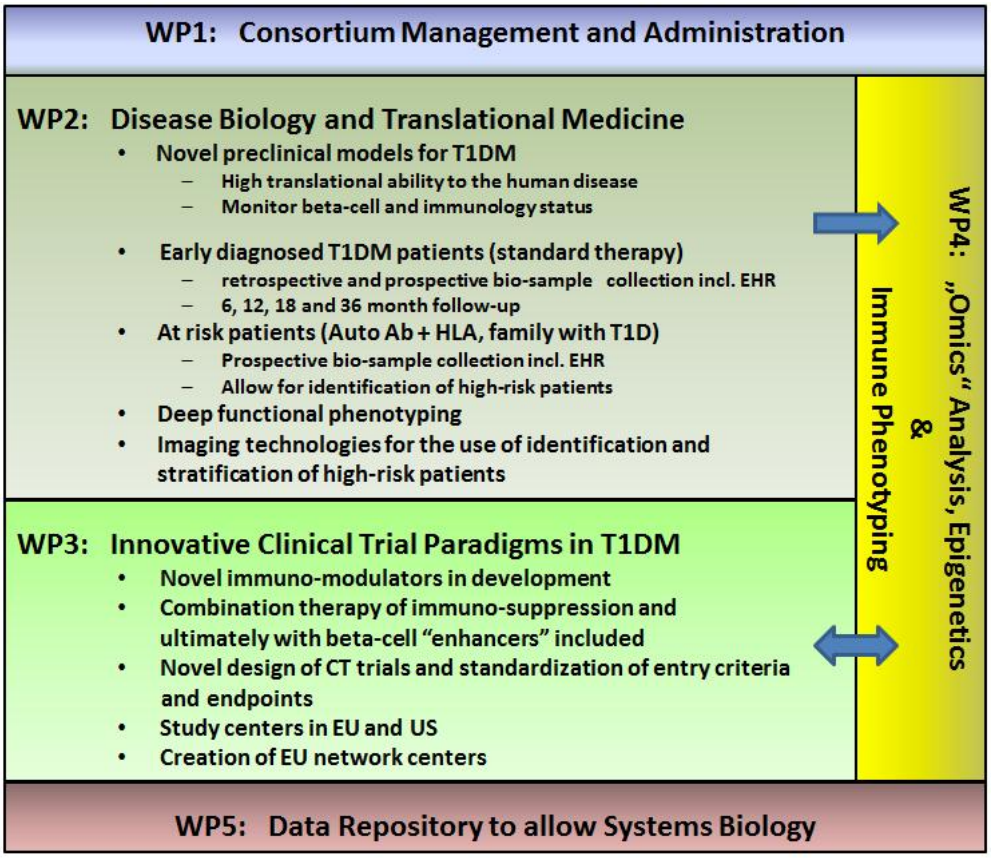
Please also note that the following outline of the architecture for the full proposal is a suggestion; different innovative project designs are welcome, if appropriate.

Note: Data collection and data management should be conducted according to established data standards and/or in collaboration with a data standards organization (e.g. CDISC), to develop new data standards if no established data standards exist.

Suggestion for project structure

This project is suggested to be organized in 4 major work packages:

- WP2: Disease Biology and Translational Medicine
- WP4: "Omics" Analysis, Epigenetics and Immune Phenotyping
- WP3: Innovative Clinical Trial Paradigms in T1DM
- WP5: Data Repository to allow Systems Biology



As a result of this, the project will:

- significantly progress the understanding of the pathophysiology, heterogeneity and natural history of T1DM in humans,
- improve the knowledge on translatable preclinical models for T1DM,
- facilitate the development of standardized clinical trial protocols with defined clinically relevant, evidence based entry- and end-point criteria and the evaluation of novel mono & combination treatment approaches.

2. DISCOVERY AND VALIDATION OF NOVEL ENDPOINTS IN DRY AGE-RELATED MACULAR DEGENERATION AND DIABETIC RETINOPATHY

BACKGROUND AND PROBLEM STATEMENT

Diseases of the retina are among the leading causes of blindness world-wide. Substantial progress has been made in the treatment of neovascular age-related macular degeneration (neovascular AMD) and diabetic macular edema (DME). However, for other common retinal conditions such as the dry form of AMD (dry AMD) or diabetic retinopathy (DR) treatment options remain limited. One major development hurdle is the lack of suitable, patient-relevant study endpoints with clinical relevance both in early exploratory and pivotal trials. Moreover, there are significant gaps in the understanding of how pre-clinical findings translate into outcomes. This results in the following problem statements:

- Best corrected visual acuity (BCVA) and derived variables are the only endpoints that have served as basis for regulatory approval of retinal drugs. However, BCVA captures only a small portion of visual function. Dry AMD or DR patients may have good BCVA, in spite of significant clinical impairment resulting in difficulties with daily activities such as reading or driving. There is a lack of methodology/instrumentation to quantify this type of vision impairment robustly and reliably.

- There is a lack of short-term endpoints predictive for visual acuity outcomes that would qualify as sufficiently predictive proxy in an early proof-of-concept or dose-finding study or even as surrogate endpoints in pivotal trials.

- There is a lack of predictive markers and models (animal models and cellular systems) translating from the preclinical to the clinical setting. It needs to be evaluated to what extent novel visual function measures will translate from pre-clinical to clinical studies as well as to what extent preclinical effect sizes will translate into clinical effects.

- There is a gap in understanding of endophenotypes in diseases like dry AMD or DR that are currently perceived as close disease entities, but in reality may have very different natural courses or response to therapy. This may have significant medical and health-economic implications.

In ophthalmology there are many and very diverse techniques that allow to measure functional and anatomic parameters. Despite this methodological wealth, the relevance of different parameters for the assessment of disease severity remains uncertain, and so does their translation into outcomes relevant for patient daily activities and Quality of Life (QoL). For example, in neovascular AMD and other well-evaluated

indications, it has been shown that many promising imaging parameters are weakly or not-at-all correlated with patient relevant visual function. It is obvious that significant methodological validation work needs to be done. Therefore, an important focus on endpoint research is to validate existing technologies and to leverage the large armamentarium of contemporary ophthalmological examination techniques.

NEED AND OPPORTUNITY FOR PUBLIC-PRIVATE COLLABORATIVE RESEARCH

The topic tackles a problem of a scale that cannot be achieved by a single institution and requires combination of expertise and collaboration of stakeholders across different sectors:

- **Pharmaceutical companies** have expertise of drug discovery, drug development as well as regulatory and HTA requirements.
- **Academia** has expertise in methods to assess visual function and structural (bio-) markers that may correlate with visual impairment both pre-clinically and clinically. They have access to databases on the natural history and the course under treatment of the diseases in-scope that would allow a retrospective analysis of potential correlations.
- **Imaging and medical device companies** have expertise in development and application of contemporary examination methods.
- **Hospitals/practicing physicians** have access to dry AMD and/or DR patients. They have a good understanding of epidemiology, pathophysiology, or other evidence to predict clinical benefit.
- **Patients, users and caregivers** can also play an important role in the establishing the value of new endpoints.
- **Regulators, Health Technology Assessment (HTA) bodies and payers** could provide guidance on prerequisites for acceptability of endpoints.
- **Others such as technological centres and Contract Research Organisations** may be able to contribute to the deliverables of the project.

OVERALL OBJECTIVES

The aim of the project is to evaluate novel endpoint candidates for dry AMD and DR for use in clinical trials investigating drug or other therapies. The evaluation should cover the technical, medical and health economic appropriateness of a method and bridge preclinical and clinical studies. The following methods are in scope:

- **Novel approaches to subjective visual function testing beyond BCVA:** Methods falling into this category include methods of visual acuity testing under different conditions such as dim light or low contrast. Additional methods may comprise parameters such as microperimetry, motion or pattern detection, contrast sensitivity, color vision, visio-motor coordination or reading speed. The main research objective on this type of endpoints is the validation of patient relevance and/or predictive strength for each potential endpoint.
- **Electrophysiology:** Electrophysiological methods offer a broad array of largely objective parameters to quantify visual function. They are less dependent on patient co-operation than subjective visual function tests. Electrophysiological methods can be used in animal models and as such they have an inherent potential in translational research settings. The key objective of electrophysiological studies is the translation of pre-clinical results into clinical outcomes as well as correlation with patient-relevant endpoints.
- **Imaging:** Imaging devices that quantify anatomic changes in the retina have evolved tremendously in the last decade and have revolutionized disease diagnosis and monitoring. The further development of the techniques by means of image processing, detectable biomarkers in the retina and potentially photonics will further change the diagnostics and follow-up of retinal diseases. It would be important that such parameters are put into perspective and correlated to patient-relevant outcomes and prognosis of the disease.
- **Patient reported outcome (PRO) tools and QoL-related endpoints:** There are few validated PRO tools and the most prominent example, the NEI-VFQ-25[25], is only well-correlated to the BCVA of the better-seeing eye, therefore being of little additional value. Studies in that field should focus on development of better-designed and researched PRO tools capturing the patient-relevant impact of visual impairment, beyond visual acuity.
- **Soluble and genetic biomarkers:** Several soluble and genetic biomarkers correlate with progression of diabetes and its complications as others do with age-related-macular degeneration. Activities in this field should focus on putting these and novel markers like proteomic and metabolomics biomarkers into perspective with outcomes, prognosis and severity of the ocular disease.
- **A combination of the aforementioned methods:** The consensus is that the likelihood of a single method fulfilling all the above criteria is low and therefore research on combinations of the aforementioned approaches will be required.

[25] National Eye Institute Visual Functioning Questionnaire 25 (www.nei.nih.gov)

POTENTIAL SYNERGIES WITH EXISTING CONSORTIA

Synergies and complementarities with existing initiatives, both in Europe and globally should be considered, building on achievements, and incorporating when possible data and lessons learnt, while avoiding unnecessary overlapping and doubling of efforts.

Applicants should include considerations in their proposal how the interactions with ongoing consortia, such as the following ones, are envisaged.

The SUMMIT is an ongoing IMI project on diabetes complications (http://www.imi.europa.eu/content/summit; www.imi-summit.eu). One of the work packages is dedicated to characterisation of retinal phenotype in diabetic patients and thorough documentation of the eye status along with the status of the systemic condition (including soluble bio-markers). There are clear opportunities for synergies with this project.

In addition, there are potential synergies with on-going FP7 projects within the field of macular degeneration and diabetic retinopathy, for example, HELMHOLTZ[26], ENDHOMRET[27] and REDDSTAR[28].

The proposal should also build on achievements and learnings from any relevant European and Member state initiatives and aim to create synergies with H2020 generated projects and global initiatives.

EXPECTED KEY DELIVERABLES

The key deliverable will be the generation of adequate data resulting from robust retrospective and/or prospective studies in patients that could serve as basis for initial discussion with regulatory agencies and/or HTA-bodies for acceptance of the resulting outcomes as endpoints for future clinical programmes. Interactions and advice from regulatory authorities will be sought early-on during set-up of the studies.

It is expected that the proposed research programme delivers data for each of the proposed conditions on:

- Technical evaluation of potential methods in regards to validity, repeatability, reliability, interpretability, and translatability from preclinical to clinical. The technical evaluation includes also an assessment whether a method is acceptable for patients with the disease.
- Development of novel methods (e.g. imaging, proteomics, metabolomics, genomics, epigenetics) and models, including animal models, and tools as applicable (e.g. disease/endophenotype specific patient reported outcome tools or novel visual function testing protocols).

[26] http://www.vision-research.eu/index.php?id=909
[27] http://erc.europa.eu/erc-funded-projects
[28] http://www.reddstar.eu

- Clinical validation of methods/tools in patient studies for dry AMD and DR. Preferentially, the studies should evaluate several candidate methods head-to-head. The collection of biomarkers (e.g. genomic or soluble biomarkers including proteomic and metabolomics markers) during the study will permit to explore the selection of high risk populations.

It is expected that each proposed study focuses either on a translational aspect or on patient-relevance of a given outcome parameter or combines both if applicable. If translational aspects are studied, the investigation should be set-up to show the correlation of data from an experimental model with the clinical outcome parameter. For studies aiming to show patient-relevance, a concept should be provided on how to link the novel parameter to an accepted parameter (e.g. a PRO tool), either previously validated or to be validated within the proposed project.

Wherever there are synergies between dry AMD and DR these should be leveraged, e.g. by combining both conditions within one study. However, it is also important to clearly address how the applicant consortium intends to investigate condition-specific aspects.

INDUSTRY CONSORTIUM

The industry consortium will comprise pharmaceutical and imaging companies. Industry contribution will include study support with central study functions (data management, statistics, project/study management, regulatory etc.).

EFPIA PARTICIPANTS

Bayer HealthCare (coordinator), Sanofi, Novo Nordisk, Zeiss

INDICATIVE DURATION OF THE PROJECT

The indicative duration of the project is 5 years (60 months).

INDICATIVE BUDGET

The indicative EFPIA contribution is EUR 7 000 000.

The financial contribution from IMI2 JU will be a maximum of EUR 7 000 000.

TYPE OF ACTION

Research and Innovation action

APPLICANT CONSORTIUM

The applicant consortium is expected to address all the research objectives and make key contributions on the defined deliverables in synergy with the industry consortium.

The applicant consortium is expected to be multidisciplinary and have a proven track record of:

- Strong clinical expertise in ophthalmology (including advanced examination techniques)
- Strong clinical research experience
- Access to patients and databases
- Public health expertise
- Health economic expertise
- Understanding of pre-clinical models in ophthalmology
- Biomarker expertise (biomarkers research and development)
- Data and knowledge management
- Regulatory, ethics, patients and project management.

It is intended that an advisory panel to the consortium, which comprises payers, regulatory agencies and other relevant expert advisors is instituted for this project.

The contribution from the applicant consortium should be the setting-up and running of the studies that are required to meet the call's objectives. These activities will be supported by in-kind and financial contribution from the EFPIA companies.

SUGGESTED ARCHITECTURE OF THE FULL PROPOSAL

The consortium is expected to suggest architecture for the full proposal addressing all objectives and key deliverables.

A plan for interactions with Regulatory Agencies/health technology assessment bodies with relevant milestones, and appropriate resources allocation, should be built into the project architecture as well as aspects related to dissemination and sustainability, facilitating continuation beyond the duration of the project.

Note: Data collection and data management should be conducted according to established data standards and/or in collaboration with a data standards organization (e.g. CDISC), to develop new data standards if no established data standards exist.

CONDITIONS FOR THIS CALL

Applicants intending to submit a short outline proposal in response to the IMI2 Call 1 should read the topic text, above, the IMI2 Manual for submission, evaluation and grant award and the IMI2 Evaluation Criteria.

Call Identifier: H2020-JTI-IMI2-2014-01

Publication Date: 9 July 2014

Stage 1 Submission start date: 9 July 2014

Stage 1 Submission deadline: 12 November 2014 – 17:00:00 Brussels time

Stage 2 Submission deadline: 21 April 2015 – 17:00:00 Brussels time

Indicative Budget: From EFPIA and Associated Partners: EUR 24 630 000
From the IMI2 JU: EUR 24 630 000

IMI2-2014-01-01	The indicative contribution from EFPIA companies and Associated Partners EUR 17 630 000. The financial contribution from IMI2 JU is a maximum of EUR 17 630 000	Research and Innovation action Two stage submission and evaluation process Only the applicant consortium whose proposal is ranked first at stage 1 is invited for stage 2

IMI2-2014-01-02	The indicative EFPIA contribution is EUR 7 000 000 The financial contribution from IMI2 JU is a maximum of EUR 7 000 000	Research and Innovation action Two stage submission and evaluation process Only the applicant consortium whose proposal is ranked first at stage 1 is invited for stage 2

Eligibility and admissibility conditions

The conditions are described in parts B and C of the General Annexes to the work programme.

Evaluation criteria, scoring and threshold

The criteria, scoring and threshold are described in the IMI2 Evaluation Criteria, with the following exception:

IMI2-2014-01-01 IMI2-2014-01-02	If a proposal fails to achieve the threshold for a criterion, the evaluation of the proposal will be stopped.

Evaluation procedure

The full evaluation procedure is described in the IMI2 Manual for submission, evaluation and grant award.

The procedure for setting priority order for proposals with the same score is given in the IMI2 Evaluation Criteria.

The applicant consortium of the highest ranked proposal (stage 1) for each topic will be invited to discuss with the relevant industry consortium the feasibility of jointly developing a full proposal (stage 2).

The applicant consortia of the second and third-ranked proposal (stage 1) for each topic may be invited for preliminary discussions with the industry consortium if the preliminary discussions with the higher ranked proposal and the industry consortium fail. Such contacts should be done in priority order, i.e. the second ranked proposal should be contacted only after failure of pre-discussions with the first ranked, and the third after the second ranked.

Indicative timetable for evaluation and grant agreement

	Information on the outcome of the evaluation (first stage)	Information on the outcome of the evaluation (second stage)	Indicative date for the signing of grant agreements
IMI2-2014-01-01 IMI2-2014-01-02	Maximum 5 months from the date of submission to the first stage.	Maximum 5 months from the date of submission to the second stage.	Maximum 3 months from the date of informing the applicants following the second stage evaluation.

Consortium agreements

In line with the Rules for Participation and Dissemination applicable to IMI2 actions[29] and the IMI2 model grant agreement, participants in Research and Innovation actions are required to conclude a consortium agreement prior to grant agreement.

Submission Tool

Please note: The IMI electronic submission tool **SOFIA** (Submission OF Information Application) is to be used for submitting a short outline proposal in response to a topic of the IMI2 Call 1; no other means of submission will be accepted. SOFIA will be opened for submission of proposals on 9 July 2014. Updates of the proposals may be submitted online until the Call submission deadline. Only the most recent version shall be considered for the evaluation procedure (including eligibility check).

To access the IMI electronic submission tool SOFIA, applicant consortia wishing to submit a short outline proposal will need to complete a request for access to the tool.

[29] Regulation (EU) No 1290/2013 of 11 December 2013 and Commission Delegated Regulation (EU) No 622/2014 of 14 February 2014.

2nd IMI2 CALL FOR PROPOSALS

The following topics are currently being considered for the second call to be launched in Quarter 4, 2014 (subject to final confirmation):

- Remote Assessment of Disease and Relapse: A platform based on biosensors;
- Immunology: A platform to accelerate drug development for immune-mediated disorders and vaccines;
- Translational safety: Improving predictivity of unwanted drug effects;
- Multiple sclerosis: New approaches for drug development in multiple sclerosis based on patients registries and imaging biomarkers;
- Type 1 and type 2 diabetes: Building the IMI2 diabetes portfolio;
- New pathways to accelerate access of patients to innovative medicines;
- Standardization of batch release process in drug manufacturing;
- Towards an Aetiology based Taxonomy for Neuropsychiatric disorders.

Additional topics might be considered according to emerging industry or public-health needs.