Annual Work Plan of IMI2 JU for 2015

Annex I to the Decision of the IMI2 JU Governing Board
No IMI2-GB-DEC-2015-01
Document approved by the IMI2 JU Governing Board
on 21.01.2015
Last update: 22.12.2014
Document reference: IMI2/INT/2014-02881

Table of Contents

FOREWORD 4
1 OBJECTIVES AND KEY PERFORMANCE INDICATORS 5
1.1 Strategic objectives 5
1.2 Annual objectives, key performance indicators and related targets 6
2 SCIENTIFIC PRIORITIES FOR 2015 13
2.1 Introduction 13
2.2 Diabetes/Metabolic disorders 15
2.2.1 Specific challenge: Towards precision medicine in diabetes and metabolic disorders 15
2.3 Neurodegeneration 17
2.3.1 Specific challenge: Development of a comprehensive strategy for neurodegenerative disorders R&D. 17
2.4 Prevention and treatment of immuno-mediated disease 19
2.4.1 Specific challenge: Multiple Sclerosis 19
2.4.2 Specific Challenge: Understanding the risks and benefits of glucocorticoid treatment. 20
2.5 Infection control including incentives for reinvestment in antimicrobials, antivirals, and vaccines 21
2.5.1 Specific challenges: Antimicrobial resistance 21
2.5.2 Specific challenge: Ebola and other filoviral haemorrhagic fevers (Ebola +) programme 22
2.5.3 Specific challenge: Innovation in vaccines 23
2.6 Translational Safety 24
2.6.1 Specific challenge: Better tools and models for safety monitoring before and beyond product launch 24
2.7 Data and Knowledge Management 25
2.7.1 Specific challenge: Enhancing of data and knowledge management 26
2.7.2 Specific challenge: Remote Assessment of Disease and Relapse 27
2.8 Medicines Adaptive Pathways to Patients (MAPPs) 28
2.8.1 Specific challenge: MAPPs implementation 28
2.9 Other Areas of Priority 29
2.9.1 Specific challenge: Respiratory Diseases 29
2.9.2 Specific Challenge: Towards a Quantitative Biological Approach for Neuropsychiatry 29
3 MANAGEMENT OF CALLS AND PROJECTS 30
3.1 Activities related to proposals evaluation and grant preparation 30
3.2 Activities to support and monitor ongoing projects 30
3.3 Monitoring and analysis of projects' results 32
3.4 Stakeholders' engagement and external collaborations 33
3.4.1 Goals of IMI's patient engagement strategy 34
3.4.2 Ways that patients can engage with IMI 34
3.4.3 Outreach to researchers 36
3.4.4 People involved & roles 36

3.4.5 Timeline 38
4 COMMUNICATION AND EVENTS 41
4.1 Communication activities 41
4.2 Key audiences 41
4.3 Key messages 41
4.4 Increasing the engagement of patients and SMEs in IMI's activities 42
4.5 Communication channels 42
4.6 Media outreach 43
4.7 Key events planned in 2015 43
4.8 Resources 44
4.9 Analysing the impact of the IMI communication activities 44
5 MANAGEMENT OF THE EXECUTIVE OFFICE 45
5.1 Support to governance and advisory bodies 45
5.2 Budget and finance 46
5.3 Human resources 47
5.4 INFORMATION AND COMMUNICATION TECHNOLOGY 48
5.5 Procurements and contracts 49
5.6 Data protection and access to documents 50
6 INTERNAL CONTROL AND AUDIT ENVIRONMENT 51
ANNEX I Calls for proposals to be launched in 2015 53
ANNEX II General conditions for the Calls for proposals 68
ANNEX III - Indicators of Results and Impact as specified in the Legislative Financial Statement of IMI2 JU for monitoring implementation of the initiative 72
ANNEX IV - Standard H2020 Performance Indicators (Annex I and II of the Council Decision 2013/743/EU of 3 December 2013 establishing the specific programme implementing Horizon 2020 - the Framework Programme for Research and Innovation (2014-2020) 74

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 European scale and beyond.

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.

In 2015, the IMI JU Programme Office will continue managing the portfolio of projects initiated under the 7th Research Framework Programme. It will also carry out the evaluation and kick-off of projects resulting from Calls for proposals launched in late 2013 and 2014. As running projects are progressing and maturing, continued 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 implement all adaptations resulting from its new legal framework under Horizon 2020, the new EU Research Framework Programme. This will include widening the scope of participation to IMI notably through the Associated Partnership scheme. In addition, recommendations arising from the second interim evaluation will be fully implemented, and most notably a more articulate communication strategy with clear and measurable goals and objectives, addressing both the key stakeholders and a wider audience as well as implementing a new key performance indicators (KPI) framework aimed at better demonstrating IMI JU impacts and socio-economic benefits. Furthermore, further enhancement of the efficiency and effectiveness of the Programme Office will be implemented, in a spirit of continuous improvement.

I am confident that the achievements of IMI JU to date will enable the partnership to tackle future challenges with pride and enthusiasm.

Irene Norstedt

…….

Acting Executive Director

1 OBJECTIVES AND KEY PERFORMANCE INDICATORS

1.1 Strategic objectives

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 PPPs 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.

On 6 May 2014, 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 was adopted. IMI2 JU 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 annual scientific priorities for 2015 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. These expected outcomes will be important in the longer term as IMI2 JU implements the programme under the framework of Horizon 2020.

1.2 Annual objectives, key performance indicators and related targets

A set of annual objectives of IMI for 2015, have been updated for the measurement of performance and progress in 2015, together with the associated KPIs and targets. These take into account:

- The continued implementation of actions related to the first phase of IMI concerning the FP7 programme and the execution of actions related to Horizon 2020 programme in 2015;
- The experience gained so far in developing KPIs, metrics and other qualitative assessment for measuring the results and achievements of IMI;
- The collection and analysis, during 2015, of baseline data for measuring the impact of IMI for patients, on European competitiveness, on healthcare system, on regulatory framework and new standards and practices. The compiled data will be used in subsequent years as the basis for setting targets and reporting on key KPIs on the longer term impact of IMI and progress against its strategic objectives.
- The planned further development of SOFIA in 2015 to integrate and automate the submission and extraction of data for the selected KPIs, but only as regards the ongoing IMI1 projects. For IMI2 projects as from 2015 IMI JU will make full use of the Horizon 2020 IT environment. KPI-related information for IMI2 projects will be collected through this Horizon 2020 IT environment.

The 2015 annual objectives and KPIs, presented in Table 1 overleaf, are linked to the main policy objectives of IMI 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 focus on performance in 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 annual scientific priorities,
2. the degree of progress of IMI projects in delivering pre-set results and achieving targeted research performance,
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,
6. the extent of communication and awareness of IMI among all target groups, and
7. the overall efficiency, budget execution and the level of awareness of the Programme Office IMI.

For the purpose of monitoring of IMI's contribution to the achievement of the H2020 objectives, the Programme Office will start to collect data for:

1. Reporting against the Indicators of Results and Impact as specified in the Legislative Financial Statement included in the European Commission's proposal for IMI2 Council Regulation. These are presented in Annex II of the AWP 2015.
2. Reporting against the relevant standard H2020 performance indicators for assessing the results and impacts of the specific objectives of the programme, as detailed in Annex I and II of the Council Decision 2013/743/EU establishing Horizon 2020 - the Framework Programme for Research and Innovation. These indicators are listed in the in Annex III of the AWP 2015.

The Programme Office will continue to measure and track, with the assistance of external consultants and service providers, all aspects of the Joint Undertaking's 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 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.

Key Strategic Focus	Annual Objectives 2015	Link to the Council Regulations setting up IMI JU & IMI2 JU		Selected Key Performance Indicator (KPI)	Method	2015 Target
		73/2008 of 20.12.2007[1]	557/2014 of 6.05.2014[2]			
Portfolio	IMI'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 2015 that are addressed by IMI's calls for proposals launched in 2015	Extent of coverage of priority areas for 2015 as defined in Section 2.	**KPI 1:** ≥4 priority areas from IMI2 JU's Annual Scientific Priorities for 2015
Scientific Output	IMI projects effectively deliver and disseminate high quality outputs	▪ Article 2(a) and 2(b)	▪ Article 2(a) and 2(b)	**KPI 2:** Target estimated percentage of IMI 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 assessed 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[3] per €10 million of total IMI funding requested by the projects **KPI 4:** Target to measure extent to which IMI's 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 the citation impact of IMI publications[5] is higher than the EU average **KPI 6**: Target to measure the extent to which IMIs bibliometric indicators compare with those of other	The main source of information is the independent bibliometric analysis and results as last compiled and reported to the Programme Office by an external contractor, 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. The benchmarking analysis with other international funding bodies to be	**KPI 3:** ≥20 publications **KPI 4:** ≥10% higher than EU average **KPI 5:** ≥20% higher than EU average

[1] OJ L 30 of 4.2.2008

[2] OJ L159 of 7.6.2014

[3] 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 2015	Link to the Council Regulations setting up IMI JU & IMI2 JU		Selected Key Performance Indicator (KPI)	Method	2015 Target
		73/2008 of 20.12.2007[1]	557/2014 of 6.05.2014[2]			
				international funding bodies. Target to compare the citation impact of IMI publications[5] with the one of other international funding bodies (**KPI 6.1**), Target to compare the percentage of highly cited papers of IMI programme with the one of other international funding bodies[4] (**KPI 6.2**).	performed by external contractor, applying internationally recognised standards and criteria.	**KPI 6.1:** ≥15% higher than the average of sampled institutions **KPI6.2** ≥5% higher than than the average of sampled institutions
Impact on regulatory framework and standardization	IMI 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 and compiled in 2015	**KPI 7:** ≥ 5 **KPI 8:** Baseline data will be collected in 2015 **KPI 9:** Baseline data will be collected in 2015

[4] Publications that belong to the world's top decile of papers for journal category and year of publication.

Key Strategic Focus	Annual Objectives 2015	Link to the Council Regulations setting up IMI JU & IMI2 JU		Selected Key Performance Indicator (KPI)	Method	2015 Target
		73/2008 of 20.12.2007[1]	557/2014 of 6.05.2014[2]			
Business development and sustainability	IMI 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[5] **KPI 11:** Target to measure impact on EU 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 and compiled in 2015	**KPI 10:** ≥2 patent applications per € 10 million of costs accepted and reimbursed by IMI JU. [6] **KPI 11:** Baseline data will be collected in 2015 **KPI 12:** 25% of finalised projects

[5] During 2015, initial baseline data will continue to be collected and analysed on the number of patents resulting from IMI JU projects, particularly on the first 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 2015	Link to the Council Regulations setting up IMI JU & IMI2 JU		Selected Key Performance Indicator (KPI)	Method	2015 Target
		73/2008 of 20.12.2007[1]	557/2014 of 6.05.2014[2]			
				KPI 13: Target to measure the estimated number of reported Full-Time Equivalents (FTEs) based in the EU that can be considered as directly related to the IMI programme	The estimated total number of FTEs reported by the projects as being directly related to the IMI programme will be reported for KPI 17. The data will be collected directly from the consortia through SOFIA or via an annual survey.	**KPI 13: ≥ 1500**
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 14:** Target percentage of participants in signed Grant Agreements that are SMEs **KPI 15:** 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 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 up the end of the year under review are considered in this calculation	**KPI 14:** ≥20% **KPI 15:** ≥20%
Patient participation	IMI JU projects promote the involvement of patient organisations	▪ Article 2	▪ Article 2(a) ▪ Article 1(c) in Statutes of IMI2	**KPI 16:** 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	Calculation is based on the latest available data extracted from IMI applications SOFIA and QlikView for the project partners Participations in IMI projects may count the same organisation multiple times	**KPI 16:** 100%

Key Strategic Focus	Annual Objectives 2015	Link to the Council Regulations setting up IMI JU & IMI2 JU		Selected Key Performance Indicator (KPI)	Method	2015 Target
		73/2008 of 20.12.2007[1]	557/2014 of 6.05.2014[2]			
			JU	**KPI 17**: Target to measure impact for patients	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 in coordination with the European Commission in 2015	**KPI 17:** Baseline data will be collected in 2015
Impact on society	IMI JU projects address the unmet healthcare needs, e.g. chronic, emerging or diseases lacking effective treatment	▪ Article 2	▪ Article 2	**KPI 18:** Target to measure additional impact on society	For KPI 18, the methodology for capturing the information and the baseline data for establishing the target will be determined in 2014-2015	**KPI 18:** Baseline data will be collected in 2015
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 2015	**KPI 19:** ≥10 000 **KPI 20:** Baseline data will be collected in 2015 and used to determine the appropriate target

Key Strategic Focus	Annual Objectives 2015	Link to the Council Regulations setting up IMI JU & IMI2 JU		Selected Key Performance Indicator (KPI)	Method	2015 Target
		73/2008 of 20.12.2007[1]	557/2014 of 6.05.2014[2]			
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) and Article 32 of the IMI Financial Rules	**KPI 25:** ≤30 days **KPI 26:** ≤90 days

2 SCIENTIFIC PRIORITIES FOR 2015

2.1 Introduction

The Scientific Priorities for 2015 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 framework that underpins the development of specific projects or research programmes to be prioritised for funding is set up by Scientific Research Agenda (SRA) for IMI2 (see http://www.imi.europa.eu/content/imi-2). On the bases of the WHO Priority Medicines Report, The SRA identifies twelve key health priorities, and it is anticipated that throughout the lifetime of IMI2, many of these health priorities will be addressed.
To progress towards the achievement of IMI2 Objectives the actions developed in 2015 will seek to:

- increase the success rate in clinical trials
- where possible, reduce the time to reach clinical proof of concept in medicine development
- develop new therapies for diseases for which there is a high unmet need and limited market incentives
- develop diagnostic and treatment biomarkers for diseases clearly linked to clinical relevance
- and approved by regulators;
- reduce the failure rate of vaccine candidates in phase III clinical trials through new biomarkers for initial efficacy and safety checks;
- Develop tools, standards and approaches to assess efficacy, safety and quality of regulated health products

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 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-7):

[7] MAPPs refers to a flexible development and access pathway within the current regulatory framework that maximizes the positive impact of new medicines on public health by balancing timely access for patients with the need to provide evolving information on benefits and risks. It requires the early marketing authorisation of a product focused on a well-defined and targeted population identified by predictive preclinical and clinical evidence as well as various sources of real world evidence. It implies a clear safety and efficacy profile and may integrate a number of elements such as adaptive clinical trial design, patient centric benefit/risk assessments and the continuous evaluation of a therapy as new evidence (including real-world evidence) becomes available. MAPPs, therefore, relate to the entire life cycle of a medicine from development, through licensing to patient access (pricing/reimbursement and healthcare delivery).
Please refer also to: 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=WC0b01ac058004d5c

- target validation based on human biology (efficacy and safety);
- 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);
- patient-centric approach -effect on medical practice and outcomes (health & disease management);
- regulatory framework (including pharmacovigilance);
- reimbursement & patient access.

As already showed for the Calls launched in 2014, the initiative will continue to seek involving a broader range of partners, including micro, small and medium sized enterprises[8], 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 among others. 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.

Using the framework of the SRA, the 2015 Priorities for the design of the IMI2 Call topics have been selected on the basis of their potential to foster a set of high impact initiatives, in areas where the maximum number of stakeholders can join forces. In the scientific priorities, where appropriate, attention would also be given to relevant rare forms of diseases.. To facilitate their development Strategic Advisory/Governing Groups (SGG) in the key priority areas of immunology, metabolism, neurodegeneration, translational safety data and knowledge management as well as infections control[9], have been established in 2014. The contribution that EFPIA companies make to these groups represents eligible contributions to the operational costs of the IMI2 JU.

In addition to these priority areas, EFPIA and/or other industries active in health care may propose further activities under one or more of the 12 key health areas, identified in the Scientific Research Agenda[10] or based on emerging needs. Topics will be selected based on their ability to address unmet medical 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. Additional topics might also be considered according to very urgent public-health needs.

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[11]. 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 and associated 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.

[8] 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)

[9] Subject to formal confirmation by the IMI2 JU Governing Board.

[10] Antimicrobial Resistance, Osteartritis, Cardiovascular Diseases, Diabetes, Neurodegeretaive dieseases, psychiatric diseases, respiratory diseases, autoimmune diseases, ageing associated diseases, oncology, rare diseases, vaccines

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

2.2 Diabetes/Metabolic disorders

Activities in this priority area should seek progress towards novel diagnostic and treatment paradigms for the mechanisms being involved and triggering the early onset and progression of diabetes (type 1 and type 2)/metabolic disorders and their complications. This should aim to enable an early diagnosis with novel and predictive biomarkers, to allow the development of novel experimental medicine approaches to safe and efficacious treatments, considering also health system sustainability of treatment intervention.

2.2.1 Specific challenge: Towards precision medicine in diabetes and metabolic disorders

In order to address the most relevant and important shortcomings and medical needs of existing therapies a strategic mapping of the mechanisms, approaches and research activities being associated with Diabetes/Metabolic Disorders was developed in order to create within IMI2 a portfolio of call topics and consortia including co-morbidities associated with diabetes such as the metabolic syndrome, rare diseases with diabetic phenotype, cardiovascular diseases with focus on lipid and lipoprotein metabolism, obesity and metabolic liver diseases.

Synergies will have to be created with several on-going EU-wide and global initiatives including on-going IMI projects such as SUMMIT, IMIDIA, EMIF and DIRECT. All these efforts are already generating large scale sequencing and other data, including in some projects genome-wide association studies (GWAS), 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 approach for Diabetes/Metabolic Disorders.

Scope:

According to the strategic and holistic approach a continuous flow of aligned and interconnected call topics and consortia will tackle the most relevant tasks and challenges to improve diagnosis, prevention and treatment of diabetic patients, including when relevant collaboration with care providers and public health aspects, and accordingly the launch of 2 call topics in the field of Diabetes/Metabolic Disorders is envisaged for 2015. It is expected that at least some of the following aspects will be covered:

- 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 rare immune mechanisms in type 1 diabetes and other autoimmune 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.

- Development of new, cost-effective diagnostic methodologies to monitor treatment effects and disease progression and complications for use in clinical practice and in the development of new compounds based on the integrate perspectives of the regulatory agencies and Health Technology Assessment bodies (HTAs).
- Development of individual screening programs to identify persons at risk for diabetes and confirm suspected diabetes thus providing improved disease surveillance and disease management. Furthermore development of adherence programs will be considered with a focus on predictors of non-adherence, designs of interventions depending upon risk of non-adherence, and measures outcomes.
- Further project ideas currently in discussion at an early stage may focus on Diabetic Nephropathy, metabolic liver diseases like Non-alcoholic fatty liver disease and Non-alcoholic Steatohepatitis (NASH) as well as a comprehensive analysis of patient data from placebo trials in diabetes to elucidate and stratify the heterogeneity of type 2 diabetic patients.

Expected impact:

- Delivery of tools and capabilities required to develop and implement stratified medicine approaches for diabetes/metabolic disorders, moving into an era of targeted therapies with improved patient outcomes.
- More efficient R&D process, more rapid uptake of scientific advances by regulators and HTAs and new medicines by healthcare providers, based on increased operational excellence.
- The ability to diagnose and treat patients with diabetes/metabolic disorders at an earlier stage in the disease, to find treatments that addresses the narrow therapeutic window for insulin treatment, to monitor treatment success and to better estimate the risk of developing disease complications.
- Increased quality of healthcare options, more integrated healthcare solutions lowering the cost of healthcare.
- Enabling delivery of a range of treatment options and programmes tailored to individual patient needs leading to potential to delay disease progression, lower mortality and increase quality of life.
- Tailor made adherence programmes to support patients in managing their treatment and maximise the benefit gained from interventions.

Type of action:
Research and innovation actions

2.3 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, and a series of call topics are envisioned to be launched in the field of neurodegenerative disorders by IMI in 2015.

2.3.1 Specific challenge: Development of a comprehensive strategy for neurodegenerative disorders R&D.

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 and EPAD projects, 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.

Scope:

It is expected that at least some of the following aspects will be covered:

- The identification and validation of drug targets in Alzheimer's disease (AD) by capitalizing on specific GWAS/risk genes (LOAD) leading from pathway understanding/analysis to validated and druggable targets
- The identification and validation of drug targets based on protein misfolding spreading in neurodegeneration, taking common as well as AD-specific mechanisms of spreading into account.
- The Creation, development and/or expansion of drug development centre(s) focused on dementia and dealing with novel targets in new spaces, including phenotypical screens.
- Activities to Increase confidence for progressing treatments to late clinical development including Innovative AD trial designs and regulatory approaches as well as biomarkers and outcome measures.
- Actions to advance efficiency and capabilities of clinical trials and to improve the quality and relevance of evidence available to help patients, caregivers, clinicians, employers, insurers, and policy makers make informed health decisions in AD.
- Coordination and support for activities and studies/actions related to implications of AD prevention, including elements of the ethical and practical implications regarding informing individuals of their risk of developing AD (based on risk stratification model, biomarkers, genetics, etc), the Regulatory pathway for AD prevention studies and the assessment of the impact of AD prevention approaches for patients, caregivers, physicians, regulators, payers, and policy-makers
- Actions related to improve understanding of predictive value of treatment-related biomarker changes on AD disease progression.

- Actions related to nonclinical models that are predictive of treatment effect on slowing disease progression in AD, including aspects to improve the technologies and a broader access to those models.
- Actions to increase understanding of the blood brain barrier and the glymphatic system in AD/ND, to elucidate the underlying mechanisms leading to changes/malfunctioning and exploit this knowledge for development of novel brain delivery technologies.
- Activities related to real world evidence across the disease continuum of AD including disease interception.
- Actions related to the understanding and evaluation of targets and treatment options in the area of degenerative and eventually regenerative aspects of MS and neuropathic pain.

Expected impact:

- The tools and capabilities required to develop and implement stratified medicine approaches for neurodegenerative disease, moving into an era of targeted therapies with improved patient outcomes.
- A more efficient R&D process with a higher probability of success, leading to a more rapid uptake of scientific advances by regulators and HTAs and of new medicines by healthcare providers.
- An overall reduction in the direct and indirect costs associated with the management of neurodegenerative disease through more accurate patient risk assessment and earlier therapeutic intervention.
- Better understanding of the individual risk of developing a neurodegenerative disease and therefore the ability to actively manage this risk.
- Access for patients to better treatment programmes, treatment delivery and adherence programmes tailored to individual needs.

Type of action:
Research and innovation actions and Coordination and support actions.

2.4 Prevention and treatment of immuno-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.

The proposed work will focus on a key set of immune mediated disease or disease mechanisms where working in partnership will benefit the knowledgebase and accelerate delivery of drug treatments to patients. 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,BLUEPRINT 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.

2.4.1 Specific challenge: Multiple Sclerosis

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. Although there is considerable variation in the severity and symptoms of among people affected by MS, progress has been made in defining subgroups with different disease courses and needs within the MS population. Health services for MS patients need to improve substantially to optimally counteract the consequences of MS and to maximise quality of life equitably across Europe.
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. Thus limited robust evidence exists to guide health professionals in how to use disease modifying drugs in individual patients to optimize the long term outcome (personalized medicine).

Scope:

- 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. Full potential will only be achieved by broader geographic coverage, high documentation rate per country, high data quality and – in addition to the retrospective approach – aligned prospective data consistently collected across all (or at least most) countries in Europe.
- 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.
- Progress in assessing the consequences of MS and the effectiveness of services, including treatment, necessitates systematic data on much larger numbers of MS patients than is so far available.
- The observation of a differing response to the same treatment in the different phases of Multiple Sclerosis (MS) provides clear evidence that pathophysiological mechanisms change along the course of the disease and calls for new therapeutic strategies for progressive disease. It is now considered that the progressive phase of MS is dominated by neurodegeneration at least partially determined by

compartmentalized inflammation in the CNS driven by microglial activation. The relatively poor understanding of the pathogenesis and clinical features of progressive MS (compared with Remitting Relapsing MS), together with the objective difficulty of targeting neurodegeneration (as witnessed by the lack of therapies for the other major neurodegenerative diseases such as Alzheimer's), are major roadblocks to the development of therapies. Moreover the absence of reliable surrogate measures of the degenerative processes impedes the development of new treatments.

Expected impact:

- The identification of therapeutic opportunities and the design and implementation of clinical strategies which will transform the diagnosis and management of autoimmune diseases.
- The linkage and expansion of real life data to 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).

Type of action:
Research and innovation actions

2.4.2 Specific Challenge: Understanding the risks and benefits of glucocorticoid treatment.

Glucocorticoids, or 'steroids' as they commonly are referred to, are the backbone of care for many autoimmune and inflammatory conditions. Despite their ubiquitous use, they have been implicated in the occurrence of life limiting adverse events and negative impacts on quality of life. These adverse effects lead many to conclude that long term steroid use is undesirable. However steroids also can have beneficial effects, and in some instances play a crucial role in disease management. Understanding the risks and benefits of glucocorticoid treatment, dependent upon disease, dose and longevity of use, would inform the debate about their value and also how they should be best utilized in treatment.
A number of new medicines under development have the potential to reduce the use of steroids. However, the uncertainty in the benefit / risk profile of glucocorticoids in the management of disease, casts uncertainty over the clinical, commercial and economic benefits of steroid sparing and limits the value of such a claim in the label of a medicine.

Scope

- The biomarkers and patient focused outcomes required to predict and monitor steroid induced side effects versus disease related side effects supporting better care management for patients.
- New treatment guidelines for the use of steroids in patient care.
- Integration of the numerous already existing clinical data on steroids.
- Educational materials for clinicians to translate new treatment guidelines into daily clinical practice and for tools patients to make more informed decisions about steroid use, other treatment options available to them and their own management of their disease.
- Economic models capable of assessing the healthcare costs associated with steroid induced side effects.

Expected impact:

- A more informed and appropriated use of steroids therefore improving patient care
- An enhanced understanding of the improvement in the quality of clinical care that new steroid sparing medicines can offer to patients.

Type of action:
Research and innovation actions

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

An expansion in the IMI New Drug for Bad Bugs (ND4BB) programme will be sought including looking for synergies with the ND4BB IMI programme and other ongoing and planned EU-wide and global initiatives. In this context activities will aim to establish a strategy for antimicrobial resistance (AMR) in collaboration with the EC and other key stakeholders to define and execute an implementation plan, and considering elements of global collaboration. In addition 2015 will see the expansion of the programme to other areas such as vaccines, viral and fungal infections and epidemiology and novel diagnostics. During late 2014 the IMI2 2nd Call focused on Ebola and the 3rd Call will launch 2 vaccine topics. During 2015 at least 1-2 topics related to Ebola and 1-2 topics related to AMR are envisoned to be launched in the Infection control field.

.

Scope

- Gram negative bacterial infections has emerged as the consensus target pathogen area (both prevention and treatment),

  Of significant priority will be novel approaches to the treatment of biofilm, ie deep-seated infections, pathogen specific approaches to treatment and potentially adjunctive therapeutics, immunostimualtory agents and Multi Drug Resitant (MDR) gram negative rods
- The gram positive infections. Staphylococcus aureus remains an important pathogen and novel means of treatment and prevention are needed with infection control prioritized over novel therapeutics.
- Vaccines both prophylactic and therapeutic for the prevention and treatment of infectious diseases
- Viral infections with focus on:

  Zoonotic infections, including Ebola virus

  Filoviradae

  Hepatitis B

  Opportunistic infections that may emerge
- Fungal infections both prophylactic and therapeutic treatments.
- Epidemiology & novel (rapid point of care) diagnostics as well as discovery and development of biomarkers for infection. As well as a better understanding of epidemiology (e.g. the etiology of infections).

2.5.1 Specific challenges: Antimicrobial resistance

AMR has been declared a major global public health threat. In Europe 25,000 deaths were reported in 2007 as a result of AMR of which 2/3 being due to gram-negative bacteria. In US deaths due to AMR is estimated to a minimum of 23.000 deaths per year. The clinical burden is associated with soaring treatment and societal costs with a cost of AMR being estimated at around 1.5 billion per year only in Europe. The incidence of infections due to Gram-negative bacteria continues to rise at a time when drug companies have more or less withdrawn from antibiotic research and the number of newly approved antibiotics is low. Despite the recognised need for new antimicrobials the reality is that as a society we faced with the potential situation where prescribers could have few, if any, therapeutic options to treat certain bacterial infections.

Continues efforts are required if key barriers to the development and delivery of effective antibiotics are to be overcome.

Type of action:
Research and innovation actions and coordination and support action

2.5.2 Specific challenge: Ebola and other filoviral haemorrhagic fevers (Ebola +) programme

IMI2 plans to expand and extend its EBOLA + programme started in 2014 with one or more topics to be launched in 2015.

Scope:

- *Immunotherapy:* Ebola is a highly fatal disease, for which no efficient therapy is available today. There is increasing evidence that transfusion of blood from patients recovered from EVD has therapeutic effect, most likely related to the presence of neutralising antibodies, opening the potential for immune therapy. A potential future topic would be aimed at developing therapeutic products for filovirus infections based on passive immunisation (such as monoclonals, hyperimmune gammaglobulines, etc...), which should result in sufficient treatment regimens available at affordable price.
- *Formulations for cold chain:* A potential future project will focus on the development of alternative formulations (for clinically active vaccines) that would improve thermo-stability to simplify the vaccine distribution logistics, taking into account real-world field conditions and the health systems context.
- *Rapid diagnostic tests – long term:* A potential future project would follow the initial effort (current Topic 5) of developing affordable rapid diagnostics to detect Ebola and other haemorrhagic fevers allowing long term surveillance. The project may address developing new tests through early development, analytical validation, clinical validation, registration and launch.
- *Antivirals development and repurposing:* Ebola virus is a negative sense ssRNA virus with a 19kb genome encoding just 7 genes. As such there is comparatively limited scope for the development of anti-viral small molecules, with the polymerase and viral entry processes likely to form the most amenable druggable targets. There are also currently a very limited number of facilitates globally with the infrastructure to run CAT4 Ebola virus cell based assays, which is a critical component for progression of any repurposing program. A potential future topic would aim at creating a co-ordinated and collated tool-box of molecules from across the Industry, which are known to have anti-viral efficacy against a range of viral targets and may have been discontinued from development against their primary target. The project would seek to repurpose these molecules by testing in a CAT4 efficacy cell based Ebola virus assay, to determine whether these molecules have any utility in the blockade of Ebola viral entry or replication. If molecule(s) with potential anti-viral activity are identified, then depending upon their readiness for clinical development, a series of pre-clinical and clinical safety studies may be required to underwrite further clinical development.
- *Multivalent filovirus vaccine development:* Multivalent filovirus vaccine candidates might be better able to protect against a range of current (Zaire) and future filovirus outbreaks. A potential future topic would aim at developing promising multivalent filovirus vaccine candidates. The project would deliver efficacy data in relevant animal models, toxicology data to support entry into clinical studies, and Phase I, II, and III clinical studies.

Expected Impact:

The topics of the proposed IMI2 Ebola and other filoviral haemorrhagic fevers programme (the Ebola+ programme) cover actions that will address:

- short term challenges of the current epidemic as well as actions needed to address EVD and other filoviral haemorrhagic fevers in a sustainable way for the long-term (see also conclusions from the high level WHO meeting on Ebola Vaccines Access and Financing of 23 October 201412).

Type of action:
Research and innovation actions.

[12] http://www.who.int/medi acentre/news/ebola/23-october-2014/en/

2.5.3 Specific challenge: Innovation in 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.

Scope:

- Identify novel biomarkers for vaccine efficacy and safety through systems biology approaches, enabling the screening of multiple candidates vaccines in pre-clinical and early clinical trials, which may include human challenge trials
- Establish integrated data base and additional surveillance system to identify the burden of infectious and non-infectious diseases in different populations and across countries. Epidemiological studies are valuable to understand and assess correlates of protection and inform design of immunogenicity and/or efficacy trials

Expected impact:

- The development of alternatives approaches to the use of animal testing contributing to a reduced use of animals
- Better tests and models for monitoring of vaccine quality
- Better understanding of correlates of protection

Type of action:
Research and innovation actions, and Coordination and Support Actions

2.6 Translational Safety

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, HESI/ILSI and NIH driven projects) and from data management initiatives.

2.6.1 Specific challenge: Better tools and models for safety monitoring before and beyond product launch

There is still a critical need for tools and methods that will facilitate the monitoring of safety issues, contributing to the safety of patients before and 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.

Scope:

- The concordance of toxicity of pharmaceuticals in humans and in animals should be re-assessed in order to check whether current practices have the appropriate performance, identify areas of improvement, and communicate with Health Authorities and Public on undisputable grounds.
- 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, should 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. Lastly, biomarkers allowing longitudinal, non-invasing follow-up such as in vivo bioimaging should be promoted either for safety monitoring ,biodistribution or for stratification of patients;
- New platforms should be developed reflecting the complexity of human organ physiology (e.g. 3D, or organ-on-chip models, single cell-type or co-culture, static or dynamic systems…) 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, and should compare already commercially available platforms in order to select to most promising one(s), on the basis of agreed criteria. 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 and ideally, their regulatory acceptance. This would also participate to Replacement, Reduction and Refinement of animal use;
- 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 silico and 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 (or exposure at site of action), a further activity should include the evaluation and optimisation of existing or new toxicokinetic techniques (such as imaging) and models with the aim of predicting adaptive and adverse changes based on in vitro/in vivo 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. In particular, the development of a "cloud"-type database would allow preclinical and clinical experts to have easy access to normative animal and human data, visualize them, and help making decisions on safety risk.

Expected impact:

- Progress in more integrated preclinical and clinical data analysis.
- A more efficient use of biomarkers and bio-imaging.
- The addressing of the contribution of animal studies to safety evaluation, in the spirit of 3Rs.
- An impact in the area of mechanistic toxicology.
- The delivery of improved (human) cell based systems for use in translation safety assessment.

Type of action:
Research and innovation actions

2.7 Data and Knowledge Management

The IMI2 2015 activities will expand upon work from existing IMI projects including EMIF, eTRIKS, DDMORE 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. This area will also cover initiatives aimed to the development of tools and methods for real-time identification of behavioural and physiological patterns (biosignatures) for better disease monitoring and management.

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. 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. Here there will be inks with activities in the strategic areas of Metabolic disorders and neurodegeneration. 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. In addition, 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. Finally further actions to enhance and support the involvement and central role of patients in pharmaceutical research & development and regulatory approval of medicines and vaccines will be sought.

2.7.1 Specific challenge: Enhancing of data and knowledge 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.

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.

Scope:

- research of diseases & mechanisms
- (therapeutic) development optimization
- platforms for research, translational, adaptive informatics, real world data, digital business
- sustainability & data governance (both for IMI 1 and IMI 2 projects)
- 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.
- An open access, integrated resource for the discovery of molecular biomarkers of biological processes and diseases
- A Smart Clinical Program design- a web based tool with a structured information model for pre-competitive and public clinical program design information
- Generation of a public and Pre-Competitive Patient Derived Xenograft Molecular Database
- Informatics for medicines research and development
- Novel approaches towards better patient adherence and compliance

Expected impact:

- Robust KM solutions and operational excellence required to allow integration and analysis of diverse data sets, addressing long-term sustainability, accessibility and re-use of generated research data for future studies;
- Innovative IT/analytical solutions required to support new clinical trial paradigms and monitoring devices.
- Increased value and return on biomedical research investment through operational excellence and collaboration and re-use of public research infrastructures;
- More cost effective, improved R&D processes, enabled by fit- for-purpose KM infrastructures, with the potential of improved scientific insight , leading to downstream healthcare improvements for Europe.
- A coherent and transparent framework to address data privacy and personal integrity issues inherent in the use of health records and personal genomic data;
- Improved transparency of data re-use and impact on R&D.

Type of action:
Research and innovation actions and Coordination and support actions

2.7.2 Specific challenge: Remote Assessment of Disease and Relapse

With rising health-care costs, all health care stake-holders (payers, physicians, patients) are shifting the onus from a 'pay for intervention' to a 'pay for performance' model. This change in focus towards overall outcomes will drive a paradigm shift towards disease interception, i.e. move from a 'diagnose and treat' to a 'predict and pre-empt' approach. In this model, Pre-emption, i.e. intervening early enough in the disease process to prevent serious effects of the disease associated with progression, becomes a critical component of managing chronic disease. Additionally, as the trajectory of chronic diseases is often cyclical, this offers multiple interception opportunities to prevent serious decline — for example, predicting and pre-empting recurrence/suicidality in severe depression, hypoglycaemic event in diabetes, or exacerbations in COPD or Asthma.

Measuring physiological and activity-based parameters remotely and continuously via unobtrusive on-body sensors or smartphones has the potential to revolutionize our ability to predict and pre-empt harmful changes in disease trajectory. By developing methods for real-time identification of behavioural and physiological patterns (biosignatures) that culminate in 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.

Scope:

- The Remote Assessment of Disease and Relapse (RADAR) programme aims to overcome two key bottlenecks in developing such methods: 1) a lack of fundamental disease understanding into the signals and fluctuations in disease state and 2) the lack of clear policy, guidelines and pathways to develop and license "pre-emptive" therapeutic strategies that use such digital monitoring and remote assessment technology.
- To address these bottlenecks, topics in multiple therapeutic areas are expected to be launched under the RADAR platform. These topics will study the fluctuation of chronic disease using remote monitoring technology to provide a foundation for developing novel digital interventions. Such research needs to bring together physicians, patient groups, sensor manufactures, ICT providers, data management and analyst specialists with the pharmaceutical industry to undertake such research.

Expected impact:

- By exploring new pre-emptive therapeutic strategies based on remote continuous monitoring, the programme should establish if such approaches are scientifically and practically feasible, as part of a wider healthcare system.
- An increase in the understanding of chronic disease should be delivered.
- The development of a policy for the regulatory and licensing pathways to deliver a digital intervention should be sought.
- A framework to support a new digital based interactions between patients and health care providers should be built.

Type of action:

Research and innovation actions

2.8 Medicines Adaptive Pathways to Patients (MAPPs)

2.8.1 Specific challenge: MAPPs implementation

The regulatory environment is lagging behind evolving science; conventional R&D models are no longer financially viable and have become a major hurdle to efficient drug development; general response rates to modern medicines are not satisfactory. A more flexible pathway within the current regulatory/reimbursement framework would not only accelerate access of crucial therapies to patients but would also increase the probability of success as therapies would be oriented towards those patients deemed most likely to respond. The cost of drug development for industry and for healthcare providers could significantly reduce.

Medicines Adaptive Pathways to Patients (MAPPs) defines a flexible development and access pathway within the current regulatory framework that maximizes the positive impact of new medicines on public health by balancing timely access for patients with the need to provide evolving information on benefits and risks. However a pre-requisite for the success of MAPPs implementation lies in full and common understanding of its value, not just for industry but across the entire innovation life cycle: for regulators, HTAs, payers, governments, clinicians and, most importantly, patients. Although MAPPs is already discussed in many public forums and broadly supported, further coordination and integration is needed to clearly define the approach, as well as its applicability within the current legislative framework and its viability for all stakeholders.

The Coordination and Support Action "' Enabling Platform on Medicines Adaptive Pathways to Patients resulted from the call launched in 2014, will also inform research activities by facilitating inclusion of MAPPs enablers in new IMI2 activities as part of actions covered by other priority areas or as specific actions as relevant.

Scope

It is expected that at least some of the following aspects will be covered:

- Modelling potential benefit/risks for stakeholders along the health care value chain, highlight changes in prescription /use conditions, and determine new benefit/risk assessment and patient access processes, including an overall approach for the progressive reduction of HTA and financial uncertainty of adaptive pathways
- Novel methodologies for adaptive clinical trial design
- Methodologies for patient perspective elicitation in benefit/risk assessment of medicinal products from development through the entire life cycle.

Expected impact

- The development of tools, methodologies, infrastructures that will allow changes in R&D, regulatory and medical practice to enable early patient access to innovative prevention and treatment options.

Type of action:
Research and innovation actions and coordination and support actions

2.9 Other Areas of Priority

2.9.1 Specific challenge: 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).

2.9.2 Specific Challenge: Towards a Quantitative Biological Approach for Neuropsychiatry

The development of novel pharmacological treatments for neuropsychiatric disorders has stagnated over the last two decades. This statement holds true across the whole field; cognitive decline in dementia, the control of psychosis, affect, the core symptoms of autism spectrum disorders. In addition to the need to treat traditional psychiatric patient groups we have an aging population. This group presents with more complex pathologies and comorbid conditions thus the need for accurate diagnosis, treatment selection and novel therapeutics will become increasingly important and complex. Indeed, if the current efforts to develop disease modifying approaches are successful then these challenges will be faced by potentially a dramatically larger, longer surviving patient population. To reverse this stagnation a new approach is required.
The development of a quantitative biological approach to the understanding and hence classification of neuropsychiatric diseases should significantly facilitate more successful drug discovery and development. This approach would link behavioural symptoms, ideally better quantified, to maladaptive brain circuitries, molecular changes, disease stage and genetic risk regardless of any existing disease classification. A developing understanding of the biological substrates is thus expected to lead to translatable, quantifiable biomarkers or endophenotypes that allow us to effectively treat the right patient population. The aim of this challenge is to initiate the process that is needed to move towards a quantitative biology based framework for neuropsychiatry disorders. This is timely both to reverse the stagnation in the development of treatments for classical psychiatric disorders, but also to address the challenges offered by the need to treat neuropsychiatric issues associated with the increasing burden of neurodegenerative disease.

Scope:

The overall scope will be to explore the same set of quantifiable biological parameters across selected symptom constellations common to distinctly classified syndromes by classical taxonomy.
These studies would be driven from clinical quantitative biology back through appropriate translation to the measurement of homologous pre-clinical quantitative biological indices.

Expected impact:

- New classification of the disease would allow stratification of patients to facilitate more effective treatment and design of clinical trials, including the standardisation of measurement across sites.
- Identify the best predictive systems- clinical, non-clinical and pre-clinical - for the exploration of the underlying biological process and the identification and development of novel therapies or targets.
- Utilise new biomarkers to drive the development of new innovative trial designs for the conduct of preventative and disease modifying trials.

Type of action: Research and innovation actions

3 MANAGEMENT OF CALLS AND PROJECTS

3.1 Activities related to proposals evaluation and grant preparation

Key activities in 2015 will comprise the evaluation of Short Proposals and Full Proposals submitted for the topics of IMI2 Calls 1 and 2, launched in 2014.

The next calls of IMI2 will be launched to implement the 2015 Scientific Priorities. It is expected that at least 2 Calls for proposals will be launched covering at least 4 topics. Besides the launch of competitive Calls for proposals, IMI2 JU will explore any other necessary procedures to evaluate proposals and award funding to actions.

Timelines for completion of the evaluation process and of preparation will be kept as lean as possible with the aim of completing signature of the Grant Agreements for IMI2 Call 1 and 2 actions by Q3 2015, for IMI2 Call 3 and 4 actions by Q4 2015. In any case the timelines prescribed for Horizon 2020 will be adhered to.

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 ongoing projects

56 ongoing actions will be running at different stages of their life cycle in 2015. IMI will continue to provide support and advice to the consortia, including on amendments to Grant Agreements. These will include 1 new project from Call 10, as 7 projects from Call 11 and 2 actions from the IMI2C1 that should all start in 2015.

An overview of the project support and monitoring activities for 2015 is provided in the table below (status of projects as forecasted for 1st January 2015).

IMI Calls	ongoing	completing 1st year in 2015	completing 2nd year in 2015	completing 3rd year in 2015	completing 4th year in 2015	completing 5th year in 2015	completing 6th year in 2015	finishing in 2015	Final report due 2015
1	12						2	10	10
2	8				6			2	1
3	7			7					
4	7			7					
5	1			1					
6	2			2					
7	2		2						
8	4	2	2						
9	3	3							
10	1								
11	7								
IMI2C1	2								
IMI2C2									
Totals	**56**	**5**	**4**	**17**	**6**	**0**	**2**	**12**	**11**

10 out of 12 of the projects generated from **Call 1** will complete the final year of activities in 2015 and will submit their final activity reports.

The 8 projects generated from **Call 2** will complete the 4th year and enter their fifth and final year of activities, with two of these finishing their activities and one submitting its final activity report. Quick-Concept, the latest starting project from Call 2, will undergo an interim review.
The 7 projects generated from Call 3 will complete their 3rd year of activities and will all start the final post-interim review phase.

The 7 projects generated from **Call 4** will be in their third year of activities in 2015, with five [13] of them due for their interim review.

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. The projects generated by the 2014 IMI2 Call 1 and 2 will start in Q3-Q4 of 2015.

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. Many IMI projects are discussing how to sustain their results (tools, databases, guidelines, etc.) after the IMI project duration. Some discuss the founding of a not-for-profit organisation with an appropriate business model that would allow continuation of the project. Cross-project meetings to discuss potential solutions for sustainability by learning from each other are therefore considered important and the IMI Programme Office might facilitate the organisation of such meetings in 2015.

Likewise, many IMI projects deal with ethical considerations including but not limited to code-of-conduct in public-private collaboration. Cross-project meetings to exchange and discuss potential solutions on how issues around ethics are handled are therefore considered important and the IMI Programme Office might facilitate the organisation of such meetings in 2015.

The ND4BB programme comprises 7 topics, and more topics might follow in 2015. The IMI Programme Office considers that it is important to ensure that ND4BB projects collaborate with each other and therefore might facilitate the organisation of cross-project meetings of ND4BB and related projects.

Cross projects interactions are planned for the below 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 projects in the portfolio of psychiatric disorders on one side and the projects of the portfolio of neurodegenerative diseases on the other. In particular a symposium to launch an IMI Alzheimer's Platform among the 3 projects EMIF

[13] ETRIKS was reviewed in 4Q2014 immediately following the submission of the Year 2 periodic report. EMIF had a 1year review in 2014.

(EMIF-AD), AETIONOMY and EPAD is planned during the AD/PD Congress 2015 (http://www2.kenes.com/adpd/Pages/Home.aspx). Knowledge Management (KM): In 2015, the Code of Practice for the Secondary Use of Medical Data in Scientific Research Projects is expected to be issued as guidance for IMI Actions. A cross projects meeting will be organized to develop a strategy regarding long term consent management and sustainability of the Data and Knowledge Repositories generated by the IMI projects. Activities will be continued to foster implementation and development of standards for clinical data (CDISC and CFAST) as well as non-clinical data (see collaboration with CDISC).

- Antimicrobial resistance: activities are planned to boost integration of projects under the ND4BB programme. To this effect, dedicated meetings will be organised in 2015 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 will facilitate in 2015 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 will also:
- Explore any other necessary procedure to evaluate proposals
- Launch a tender procedure to make available the necessary legal and financial expertise and support to projects.
- Launch a tender procedure to support projects with 1) data citation, and 2) the submission of research data to a trusted digital repository including long term consent management.

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 programme there is a need to develop an online platform that would allow for customisable, analytics on all project outputs; 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. For the IMI2 projects this monitoring can be done using the functionalities of the Horizon 2020 IT infrastructures, which will be used for all IMI2 grants.

In 2015 the analysis of the IMI project scientific outputs in terms of publications and collaboration among IMI researchers will be continued.

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.

3.4 Stakeholders' engagement and external collaborations

Patients

For many years, patient involvement in research was restricted to participating in clinical studies and trials as research subjects. Today, it is widely recognised that patients can and should be much more involved in all aspects of research, including agenda setting, study design, communication, and ethics. This change has prompted a lot of organisations to change the way they work, and many now describe themselves as 'patient-centric'. Despite this evolution, much more can and should be done to involve patients more fully in research; too many researchers and organisations still see patients as primarily research subjects. At the same time, there are voices in the patient community that are increasingly sceptical of organisations' claims to be 'patient-centric'.

At IMI, it has always been clear that patients have an essential role to play in the organisation's activities, and over the years the Programme Office has taken active steps to engage with patients and promote patient involvement in its projects and activities.

These include:

- Inclusion of a patient representative in the IMI Scientific Committee since its creation.
- Regular involvement of patients and patient representatives as speakers and panellists in IMI events.
- Surveys, carried out by the London School of Economics (LSE) in 2013, on patient involvement in IMI projects and patients' opinion of IMI.
- An event (in summer 2013) dedicated to building bridges between ongoing IMI projects and patients.
- An event (in spring 2014) designed to gather patients' input on what should be the priorities for IMI in the area of diabetes.

The LSE surveys of patient involvement in and opinion of, IMI revealed some important points:

- Around 40% of those surveyed had heard of IMI, and of these, around half expressed an interest in providing input on IMI's research agenda.
- A majority (89%) thought patients could contribute to research and development in various ways.
- Barriers to greater patient input identified by respondents include the perceptions that patient knowledge is less important than that of clinicians or scientists, and that researchers do not give patients the opportunity to get involved in research.
- Patients are involved in around 60% of IMI projects in some way.
- 25 patient organisations are involved in projects funded under the first eight IMI Calls for proposals.

IMI projects with particularly strong patient involvement are:

- EUPATI is developing training materials and courses to help patients engage more effectively in medical research and development.
- U-BIOPRED is paving the way for more personalised treatments for severe asthma. As well as taking part in the project's clinical study, patients have advised the project on ethical, scientific, and communication issues.
- PROactive is developing methods to incorporate the impact of chronic obstructive pulmonary disease (COPD) on patients' daily lives into drug development.
- Patient organisation Alzheimer Europe is an active partner in the IMI projects Pharma-Cog, EMIF-AD, AETIONOMY and EPAD.
- EU-AIMS is paving the way for new treatments for autism spectrum disorder. US-based patient advocacy group Autism Speaks is a partner in the project and is contributing €1 million to its work.
- Diabetes charity and patient organisation JDRF has contributed to IMI's IMIDIA and SUMMIT projects and is now an associate partner in IMI 2 as it is contributing to the IMI 2 – Call 1 project on type 1 diabetes, together with the charity Helmsley Charitable Trust.

In addition, it is worth noting that IMI is strongly supported by a number of key opinion leaders among patients and in the patient advocacy community.

The need for an IMI patient engagement strategy

All of these activities reveal that IMI's patient outreach efforts until now have been largely successful. Nevertheless, so far this work has been largely ad hoc, and this, combined with the enthusiasm of patients for IMI's work, suggests that there is considerable scope for IMI to do more.

It is therefore timely for IMI to put together a comprehensive patient engagement strategy. Such a strategy will both ensure that IMI's work in this area is coherent, and that IMI's claims to be patient-centric are credible.

3.4.1 Goals of IMI's patient engagement strategy

IMI's core activity is setting up and managing competitive Calls for proposals and overseeing the management of the resulting projects. Patients can and should be involved in all aspects of these activities – a key focus of IMI 2. With this in mind, IMI's goals with respect to patients are twofold:

- To **raise awareness** of IMI's activities and successes among patients and explain what IMI is doing for them. This is both an important goal on its own, and a step towards IMI's second goal with regards to patients.
- To **engage** patients in IMI's activities and projects
- To ensure IMI maintains credibility among patients, IMI must endeavour to lead by example and gain patient input in all aspects of its activities as a research-funding organisation, and promote their involvement in IMI projects.

Key messages

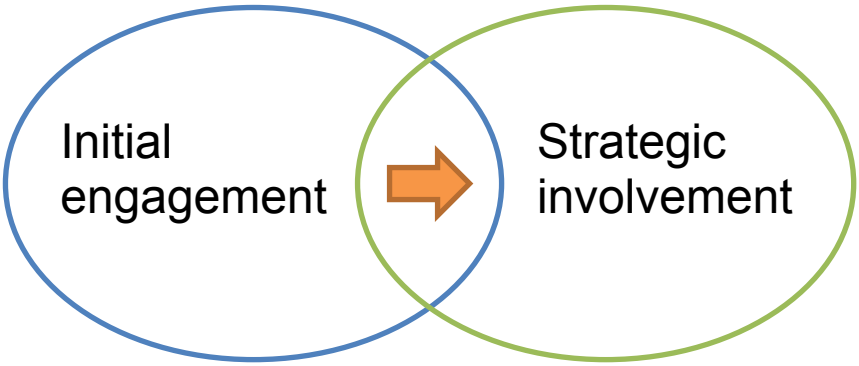
Bearing in mind the above goals, the key message to patients is:

> **IMI works to ensure its projects are focused on patients' expectations and needs, by offering patients opportunities to contribute to and engage in its projects and activities**

In addition, if patients are to be accepted as project partners, IMI must convince the wider research community of the value of working with patients as experts, and not just research subjects.

3.4.2 Ways that patients can engage with IMI

As highlighted in the goals of this strategy, patients can engage with IMI on two levels. Providing opportunities for **initial engagement** with IMI (such as on social media, through information leaflets, videos, attending events etc.) will assist in **awareness raising** and **credibility building** which can then lead on to a deeper and ongoing **strategic involvement** (such as involvement in topic selection, committees and research projects).



Initial engagement

In order to raise awareness among patients, IMI must:

- develop materials that transmit complex ideas and information in language that patients and the general public can understand and avoiding scientific jargon;
- ensure that information is relevant by identifying the point of relevance for the patient (what this actually means for them);
- identify the appropriate channels for dissemination of the information.

Channels / materials

- **Website** section dedicated to patients with information materials, links to latest Calls, testimonials, etc.
- **Information leaflets** to be distributed at events and via partners such as hospitals, health charities, patient organisations etc. Covering topics such as *What can IMI do for you*, *How you can make a difference* etc.
- **Patient voice newsletter** that interested parties can subscribe to, to be kept informed of developments and initiatives on a quarterly basis.
- **Videos** providing engaging information in a nutshell, raising interest and directing viewers to where they can learn more. To be used online and at events.
- **Social media platforms** such as Facebook, Twitter and LinkedIn that are used regularly by patients/general public to communicate and find out information.
- **Media relations** - preparing a series of press releases using a story-telling approach, with testimonials, success stories etc. directed at traditional mainstream media and bloggers.
- **Events** – including IMI events for both patients and wider audiences, as well as external events where IMI is giving a presentation.
- **Multipliers –** including patient organisations themselves as well as the IMI Scientific Committee and States Representatives Group (SRG).

Strategic involvement of patients

Patients can potentially be deeply involved in IMI's activities in a number of ways. It should be noted that patient involvement will inevitably be more important in some projects than others. Nevertheless, IMI's procedures should be designed to ensure that the question of patient involvement relevance is always raised.

IMI activities that would benefit from the strategic involvement of patients are as follows:

- **IMI governance committees** – IMI has had a patient representative on its Scientific Committee since its inception. This should be maintained.
- **Idea generation** – although most Call topics are generated by EFPIA companies, there is scope for other organisations to propose and/or consult on Call topics.
- IMI should encourage patient organisations working in areas that are aligned with IMI's scientific priorities to come forward with ideas for projects. If ideas seem promising, EFPIA and IMI should support patient organisations wishing to put forward ideas to the EFPIA Research Directors Group.
- IMI should encourage greater involvement of patients in the Strategic Governance Groups.
- **Input into consultations on Call topics** - all IMI Scientific Officers should consider inviting patient experts to participate in early consultations on draft topics.
- **Promote new IMI Calls for proposals** – Patient organisations, especially pan-European ones, can help to promote IMI's Calls for proposals to their members.
- **Participation in applicant consortia** – Patient organisations should be encouraged to apply for funding as part of consortia.

- **Participation in evaluations and reviews** – Where relevant, IMI should invite patient experts to participate in panels that review project proposals and ongoing projects.
- **Events** – IMI should continue to invite patients to provide their perspective at relevant events via presentations or participation in panel discussions.

Strategic involvement of patients – actions required

To advance patient involvement in its activities, IMI needs to:

- develop tailored materials and channels outlined in the 'initial engagement' section above;
- ensure Call texts clearly explain how patients can contribute to each topic (where relevant) and, if necessary, translate relevant parts of the text into lay language;
- continue to forge and maintain good working relationships with relevant patient organisations and key opinion leaders from the patient community, for example through personal contacts and one-on-one meetings;
- adapt its internal procedures and templates to ensure patient involvement is considered and facilitated in all activities;
- ensure procedures and associated briefings/materials are patient friendly, so that patients invited to act as experts are clear on their role and what is expected of them.
- In 2015 we already anticipate to organise another meeting of the patient focus series. Alzheimer disease is a potential topic. The other disease areas as well as horizontal patient related topics are also under consideration.

3.4.3 Outreach to researchers

One important goal of IMI's patient engagement strategy is promoting patient involvement in its own projects. However, to achieve this, IMI must:

- inform and convince those writing the topic texts (usually representatives from the pharmaceutical industry) and those leading applicant consortia (usually academic researchers) of the value of working with patients.

To achieve this, IMI will need to:

- develop communication materials targeting scientists (in both academia and industry) highlighting the benefits of working with patients, and explaining the many different ways patients can contribute to research projects;
- ensure that where relevant, topic texts clearly specify cases where patient involvement in projects is considered essential;
- ensure reviewers are briefed to check whether or not this has been addressed in proposals;
- highlight patient involvement success stories in broader communication materials.

3.4.4 People involved & roles

IMI's patient engagement work is a joint effort between the science teams (primarily the officer responsible for patient outreach) and the communication teams.

IMI Scientific Officer responsible for patient outreach:

- Together with the communications team, lead in the development and maintenance of IMI's patient engagement strategy.
- Lead efforts to ensure patient involvement is embedded in procedures surrounding preparation of Call topics, proposal evaluation, and project review.

- In collaboration with the communications team, develop guidance for patients taking part in IMI activities.
- Identify patient organisations relevant to new topics, both for awareness raising and engagement purposes.
- Lead efforts to continue building links and good working relationships with key patient organisations.
- Identify areas of the Call topics that could be particularly well suited to patient organisations.
- Together with the communications team, lead in the organisation of events targeting patients.
- Identify success stories of patient involvement in IMI projects.
- Contribute to materials targeting patients and other researchers.
- Present IMI's work for and with patients at scientific conferences.

IMI Communication Team

- Together with the patient liaison officer, lead in the development and maintenance of IMI's patient engagement strategy.
- Lead the drafting of materials targeting patients and written in an appropriate language (both general materials and Call/project-specific materials).
- Lead the drafting of materials targeting researchers.
- In collaboration with the patient outreach officer, develop guidance for patients taking part in IMI activities.
- Together with the patient outreach officer, lead in the organisation of events targeting patients.
- Oversee the layout and publication of all materials.
- Ensure materials are distributed via the appropriate channels.
- Present IMI's work for and with patients at scientific conferences.

Other scientific officers

- Ensure Call/project procedures are followed correctly so that patients are involved where relevant.
- Ensure topic texts highlight the importance of patient involvement where relevant.
- Assist the patient outreach officer in identifying areas of their topic texts and project activities that are relevant for patients.
- Assist the patient outreach officer in identifying relevant patient organisations and patient experts that should be informed of Calls for proposals / contribute to IMI activities.
- Help to identify patient involvement success stories in their projects.
- Highlight work with patients during presentations at scientific conferences.

Executive Director

- Provide input on the patient engagement strategy.
- Together with the patient outreach officer, forge links with key patient organisations.
- Highlight work with patients during presentations at external events.

Governing Board and Founding Members

- Provide input on the patient engagement strategy.
- As ambassadors and multipliers, promote IMI's work with patients in their communications.

Other multipliers (Scientific Committee, States Representatives Group)

- Assist in disseminating IMI's patient-friendly materials.
- Assist in identifying relevant patient organisations at the national level and promoting IMI's work to them (especially the SRG).

The success of the strategy can be monitored in a number of ways.

Initial milestones will be:

- Implementation of more patient-friendly procedures.

- Publication of certain initial materials.
- Identification of and successful outreach to key organisations and opinion leaders.

Once these are in place, IMI can monitor:

- Levels of patient interest in IMI, as measured by involvement in committees and panels, visits to patient pages of the website, interest on social media, attendance at events.

This will provide IMI with baseline levels of interest against which SMART targets can be set. As the strategy evolves and more materials are released, IMI will amend these targets as needed.
In the longer term, IMI could consider repeating the patient survey which was carried out in 2013. This would give a good indication of patient awareness and perception of IMI.

3.4.5 Timeline

In 2014, IMI developed a patient engagement strategy. First actions for its implementation started in 2014 and will continue in 2015.

Regulators

The strengthening of the relations with regulatory agencies in particular with EMA and FDA will continue in 2015 to:
- ensure that IMI projects benefit from the Regulators' input.
- maximize the impact of IMI projects outputs to progress regulatory science.

This engagement with Regulators will be even greater considering the SRA vision of delivering the right treatment to the right patient at the right time for priority diseases and the activities to progress the implementation of MAPPs. In this context, IMI will consider to extend this interaction with health technologies bodies/payers. In addition IMI will expand the dialogue with other regulatory agencies in the world, in particular PMDA.
IMI will therefore continue raising awareness of the IMI consortia on the regulatory relevance of their activities, the subsequent regulatory processes to follow particularly with the qualification advice/opinions procedures and on supporting early liaison with the Regulators. To this end, IMI will consider the need to develop further guidance towards consortia or complement those already available.

IMI will continue to organize the annual IMI Regulatory Summit with the EMA and FDA, which in particular aims to critically review the interactions between IMI projects and Regulators, identify recommendations for improvement and potential opportunities for future collaborative research. In 2015, IMI, together with EFPIA/EMA/FDA, will also follow-up on any actions and activities that would be agreed at the 4th IMI Regulatory Summit to be hosted in December 2014 by the FDA.

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 Entreprises

Based on past activities IMI has been successful in encouraging SME participation in IMI Calls. As of the end of Call8, 15% of the successful applicants to IMI were SMEs. Furthermore, SMEs that have successfully applied have been allocated 18.4% of the IMI budget for the projects launched. To build on this success, IMI 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.

Building on the success of previous IMI events additional 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.

Health Care Professionals

In light with the aims and objectives of the SRA of IMI2 in 2015 the Programme Office will start developing a strategy for outreach to Health Care Professionals. This first preparatory work will focus on identifying the best channels to use to promote their engagements in IMI actions.

CDISC

The collaboration with the Clinical Data Interchange Standards Consortium (CDISC) will continue in 2015 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 may be organized for the projects. Any novel data standards needed for the implementation of IMI Actions will, where possible, be developed according to a standards development methodology such as the process followed by CDISC. The latter will be discussed through participation in 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 collaboration with C-Path Institute will continue in 2015 notably with a potential third joint IMI & C-Path meeting scheduled in Q4 of 2015. The objective remains to foster synergy in areas of common interest such as modeling and simulation, and to maintain the collaborations between specific projects and research areas as follows:

- 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 have a continued 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 continue in 2015.

FNIH Biomarker Consortium

Collaboration will continue between the IMI EU-AIMS project and FNIH Biomarkers Consortium's Autism Initiative to align the two initiatives to achieve harmonized biomarkers qualification by EMA and FDA and link biobanking and clinical research initiatives.

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

In addition opportunities will be explored to align the IMI initiatives in diabetes and neurodegeneration with parallel initiatives launched as part of AMP (Accelerated Medicines Platform).

The Global CEO initiative for Alzheimer's Disease

Collaboration will be strengthened between the global CEO initiative for Alzheimer's Disease and the IMI Platform for Alzheimer's Disease towards the implementation of an aligned and synergistic Global Alzheimer's Platform (GAP) as an agreed action point from the Global Action against Dementia launched at the G8 Dementia Summit of 2013 (http://dementiachallenge.dh.gov.uk/category/g8-dementia-summit/). This will include seeking a Memorandum of Understanding between the GAP and IMI.

The Sackler Institute of the New York Academy of Science

Interactions will start with the Sackler Institute of the NY Academy of Science in order to facilitate synergies in the area of nutrition research relevant to key priorities of IMI2 SRA such as aging, metabolic disorders and neurodegenerative disorders. This will include seeking a Memorandum of Understanding between the Sackler Institute and IMI.

4 COMMUNICATION AND EVENTS

4.1 Communication activities

The IMI Communication and External Relations Strategy for 2015 will focus on the following objectives:

- Promote the launch of IMI 2 and raise awareness levels and perception of IMI among all target groups
- Raise awareness levels in particular among mid-sized enterprises, and industries other than pharmaceutical companies
- Attract the best researchers from relevant target groups to apply for funding under IMI 2 Calls for proposals
- Increase the engagement of patients in IMI's activities
- Increase the engagement of SMEs in IMI's activities

In addition, IMI works to promote networking between the different target groups, particularly with regard to the creation of applicant consortia responding to IMI's Calls for proposals.

4.2 Key audiences

- Academic researchers – convince them of the excellence and applicability of research coming out of IMI projects, convince them of the added-value of participating in an IMI project, 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) and mid-sized companies– convince them that IMI provides opportunities to not only receive funding, but to work with networks of the leading experts in their area, raise their profile in the sector, and develop new business opportunities;
- Patients and 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 – raise awareness of IMI as an initiative is speeding up the development of better, safer medicines including for diseases that affect a large proportion of the population.

4.3 Key messages

IMI's key messages have been developed and revised over a number of years, and will continue to evolve as IMI develops. Currently IMI has a set of 'top level' messages for all audiences, as well as specific messages for different audiences. The full list of messages as well as supporting information and success stories to illustrate all messages can be found in the separate 'key messages' document.

The top level messages are:

- IMI is evolving, and the IMI 2 programme has 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

In addition, in 2015 IMI will continue to highlight what is new in IMI 2 JU in its communications, particularly those directed to potential applicants.

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

Patients and carers have an important role to play in research. Throughout 2013 and 2014, IMI made significant efforts to reach out to patients and explore ways of boosting their involvement in IMI projects. As this initiative was warmly welcomed by patients and projects alike, it is now timely to take a more strategic approach to patient engagement. A strategy for this has been drafted and will be implemented gradually throughout 2015. The goal of this strategy is to both raise awareness of IMI's activities and encourage patients to get involved in both IMI's projects and its broader activities.

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 JU, 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 order to achieve the new, higher target, it would be important to put in place a more strategic approach to SME recruitment, and defining this strategy will be an important activity for the communication team, in collaboration with the science team, in 2015.

4.5 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 / Governing Board, members of advisory bodies (States Representatives Group, Scientific Committee), National Contact Points, relevant scientific, patient,

business 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

4.6 Media outreach

In recent years, IMI has enjoyed increased positive visibility in key general and specialist media. In 2015, 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 Programme 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. Media Consulta may also run media training for new staff that requires it in 2015.

4.7 Key events planned in 2015

Activity	Timeline
Create new IMI website	Q4 2014 – Q1/2 2015
Promote launch of IMI 2 – Call 2	Q1
Promote launch of 11th Call projects (via website, newsletter, social media, press, etc.)	Q1
IMI session at AD/PD congress, Nice, France	March 2015
SME / Venture Capitalist networking event	Spring 2015
Event with and for patients at European Parliament	Spring 2015
IMI Stakeholder Forum 2015 on Infections diseases	Spring / early summer 2015
Promote further IMI 2 Calls for proposals	tbc

IMI will also look into other events, such as BIO and BioFit, in the months to come.

4.8 Resources

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. Plans are in place to recruit a fourth team member – this will allow IMI to fully implement its patient engagement strategy; devise an SME engagement strategy; and reach out to new target groups such as potential Associated Partners and mid-sized companies. It will also allow the office to develop new networking activities, most notably for potential applicants.

Other IMI staff contributes 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, 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.

4.9 Analysing the impact of the 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 2015 IMI will have the results of 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 and set broader communications goals based on awareness and perception of IMI among different target groups.

5 MANAGEMENT OF THE EXECUTIVE OFFICE

5.1 Support to governance and advisory bodies

IMI will continue to provide support to the 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 addition, monthly teleconferences between the Chair, Vice-Chair and IMI Programme Office management will be held for information purposes.

The **Scientific Committee** is an advisory body to the Governing Board. It will meet at least twice. The Scientific Committee will be consulted on the Annual Work Plans, will advise on Call texts and will participate to interim reviews. Based on IMI2 legal framework, the Chair of the Scientific Committee may now participate to the meetings of the Governing Board on issues of specific interest to the Committee.

The **States Representatives Group** will be consulted on the Annual Work Plans and will receive the evaluation outputs. At least two meetings of the States Representatives Group are foreseen for 2015. The Chair will participate in Governing Board meetings.
In addition, as part of the new governance features of IMI2 JU, strategic advisory groups to the Governing Board (called Strategic Governing Groups) were established by the Governing Board in 2014, will further develop their activities. Those were 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 in various thematic areas as follows:

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

A scientific member of the Programme Office has been allocated to each of the Strategic Governing Group and will continue also in 2015 to support their activities. Specific IT tools to support the activities of the SGGs will be implemented in 2015.

Continuous attention will be given to enhance communication with these bodies and seek and feedback on any significant IMI activities and developments. 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 and global 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 IT tool that generates statistics and data.

5.2 Budget and finance

Draft Budget Plan 2015

The forecast put forward in the preliminary annual budget plan (PDB) for 2015 approved by the Governing Board in July 2014, as part of the revised Annual Work Plan for 2014, has been re-evaluated based on the available information.

Commitment appropriations (in EUR)	
Administrative expenditure	8,881,400
*Operational expenditure	217,593,567

*Excluding amounts carried over from 2014

Payment appropriations (in EUR)	
Administrative expenditure	8,881,400
*Operational expenditure	143,000,000
Operational expenditure – carry over from 2014 (estimate)	31,000,000

*Excluding amounts carried over from 2014

	Budget* - administrative expenditure (in EUR)
Title 1 – costs related to IMI staff	
Salaries, missions, training and recruitment costs	4,852,760
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 IMI projects).	4,028,640

*It is without prejudice to the outcome of the procedure with the Budgetary Authority

While the budget of administrative expenditure and of operational commitment appropriations remains the same, the need for operational payment appropriations is adjusted by EUR 42.7 mil. The decrease in payment appropriations is due to the suspension of a large workpackage in one of the on-going projects. In addition, the amount in PDB 2015 was partly based on the estimate of pre-financing needs of IMI2 projects set out in the legislative financial statement annexed to the draft IMI2 regulation. This had to be adapted taking into account calculation of pre-financing level under the new model grant agreement.

Due to the delays in negotiations of two projects and the suspension of a workpackage mentioned above, EUR 31 million of the payment appropriation 2014 is expected to be carried over to 2015. The exact amount will be specified once the budgetary year 2014 is closed and will be entered into the budget 2015 based on the Governing Board decision at the beginning of 2015. The estimated expenditure mentioned in this section will be balanced by the revenue from the IMI Founding members.

Financial Management

During 2015, 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.

In 2015, the work programme will be implemented around four main themes:

Staffing

The staffing needs of IMI Programme Office will be carefully assessed, under the direction of the Governing Board, along the growth projection set out in IMI2 JU Legislative Financial Statement.

Human Resources team will implement the selection and recruitment actions accordingly.

Organisation development

Changes of staff population, including at management level, associated with the development of IMI2 JU and related Horizon 2020 objectives and obligations will involve adapting the organisational structure to further enhance effectiveness and flexibility, in a spirit of continuous improvement.

Human Resources will be fully associated to these activities, notably by advising management on means to enhance operational efficiency and effectiveness, through the following::

- Identify activities required to achieve organizational objectives;
- Assignment of duties and responsibilities to best achieve fulfilment of objectives and tasks
- Establishment of clear and efficient reporting lines and set up necessary delegations of authority.
- Enhancement of co-ordination between the different activity cluster areas.

HR management

As part of HR core functions, the team will deal with issues related to people such as performance management and assessment, safety, compensation and benefits, employee motivation, communication, administration, and training.

Apart from the day-to-day management of administrative workflows and process the HR function will deal and follow up in particular with:

- Full implementation of the new EU Staff Regulation (entered into force on 1 January 2014) through the adaptation of the EC implementing rules to the specificities and size of IMI2 JU and their adoption by the Governing Board;
- The performance management of the work environment to enable staff members to perform to the best of their abilities including a rational learning and development policy for better efficiency and staff retention.

Inter-JU cooperation

The efficiency and cost effective management of IMI2 JU is also based on a close collaboration with other Joint Undertakings through flexible arrangements and experienced mechanisms of pooling expertise for specific time-bound tasks. In 2015, IMI will be willing to go further notably through sharing of human resources IT tools, common calls for tender, common approach on implementing rules.

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. A strong element in achieving this goal will be the rollout of the use of the full suite of Horizon 2020 IT tools for the management of IMI2, from the launch of calls for proposals to the follow-up of the grants.

The following table sets out an overview of ICT developments and activities planned in 2015.

IMI Core Business	
SOFIA (Submission OF Information Application)	– Migration to systems after ICT tender. (Q1+Q2) – Audit implementation (Q1) – Integration in H2020 IT tool (Q3)
ICT Internal Support	
DORA (Document Repository Application)	– Migration to systems after ICT tender (Q1+Q2)
ISA (Information System for Absences)	
eMA (electronic Missions Application)	
IMI Intranet	
ICT Tenders	
File, email and Print Servers plus support services	– Implementation of FWC as tendered in 2014Q3+4
sTesta	– Handover to new supplier already selected by EC
Internet	– Implementation of FWC as tendered in 2014Q3+4
Software development	– Current FWC finishing in Q4 2014; continuation will be acquired via EC FWC
Other IMI Business tools	
Support to Governance Bodies (Governing Board, Scientific Committee, States Representatives Group)	– Platform for Strategic Governance Groups (SGGs)
PST (Partner Search Tool)	– Maintenance (continuous improvements)
Events Registration Tool (IMI and JTIs platforms)	– Maintenance (continuous improvements)
IMI website	– Redevelopment of IMI2 website, based on up-to-date technology

ICT Tenders
2015 will see the implementation of the results of the IT tender for in-house ICT. This also implies planning and coordination of system handovers. Migration will have to be done the core business platform SOFIA as well as IMI in-house tools.

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.

Development of SOFIA continues to facilitate the electronic representation of IMI processes, which will also support the audit process.

The European Commission has offered that IMI can use the systems (SEP, SYGMA, COMPASS) to manage calls and projects under the Horizon 2020 framework. IMI will therefore start evaluation of these tools as soon as they can be accessed (expected: end 2014). Nevertheless, development and maintenance of SOFIA will continue in 2015.
Provided the evaluation turns out favourably, IMI considers to have the Call 1 data migrated via the EC submission tool (SEP) into SYGMA, where project management would be continued. For Call 3 and later calls, IMI would use SEP for both stages of submission and evaluation (in SEP), and then SYGMA for project management. SOFIA will continue to support IMI1 projects and potentially as a fall-back-solution for IMI2 Calls 1 to 4.

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, the States Representatives Group and the newly formed Strategic Governance Groups. In 2015, the platforms will enjoy continuous improvements and increase of scope.
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.

IMI website
The website of IMI will be redeveloped from scratch. This is driven by two sources: The evolution from IMI to IMI2 and advancements in technology. The use of contemporary technology is expected to improve the interaction with the site. Moreover, it will likely reduce the need for custom-made software components and increase security.

5.5 Procurements and contracts

In order to reach its objectives and adequately support its operations and infrastructures, IMI will allocate funds to procure the necessary services and supplies. 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. Most essential framework contracts IMI is using will be running beyond 2015.

Two of the larger framework contracts of IMI will expire in 2015: The framework contract for ex-post audits will be replaced by a framework contract of the Commission. For the framework contract for interim staff services, IMI will launch a new tender procedure in 2015.

On the operational side in 2014, 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 2015, a possibility foreseen in the original tender.

Furthermore, IMI will explore possible expansions of the KUL case study carried out in 2015 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.

5.6 Data protection and access to documents

Data protection

IMI will continue to ensure that personal data are protected and that Regulation (EC) No 45/2001 is complied with. Key actions for 2015 will include:

- Raising awareness with the IMI Staff: in particular in relation to the implementation of the accountability principle, to the follow-up of the new thematic guidelines issued by the European Data Protection Supervisor and to support the implementation of the IMI Code of practice on Secondary use of medical data in scientific research projects;
- Adapting procedures internally for handling notifications related to standard administrative procedures and for processing operations related to IMI2 JU and the amended Staff Regulations;
- 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 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 keep high level of public confidence in IMI2 JU 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;
- Stimulating the interaction on key issues.

6 INTERNAL CONTROL AND AUDIT ENVIRONMENT

IMI has in place an effective and robust internal control framework that complies with its rules and procedures and contributes towards the achievement of the Joint Undertaking's strategic objectives.

The Programme Office will continue in 2015 to build on the experience and lessons learned from the past years to 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 evolving stakeholders' expectations are met.
Due consideration will also be given during the year to the conclusions of the annual risk assessment exercise carried out by the Programme Office in the second semester of 2014 which signalled the need to take specific measures to respond and adapt to new challenges and developments brought about with the transition to IMI2 JU and the incorporation of Horizon 2020 objectives, obligations and *modus operandi*.

More specifically, throughout 2015, the Programme Office plans to:

- Update its Internal Control Standards in order to reflect the evolving needs of the organisation and better meet the expectations of its members and stakeholders in terms of efficiency, effectiveness and flexibility. During the year, management will draw up and propose to the Governing Board a renewed set of management standards;

- Establish and monitor the annual action plan for the implementation of IMI's internal control system, which is based on ICSs that have been prioritised for the year as well as on implementation of recommendations resulting from internal and external audits or other reviews;

- Maintain an integrated and systematic risk management process in its annual planning cycle, including the conduct of an annual full risk assessment exercise;

- Assess and formally report on IMI's compliance with the ICS and on the overall effectiveness of the internal control framework. The results of this exercise will also contribute to the annual reporting and declaration of reasonable assurance of the Executive Director.

The following ICSs have been prioritised by management for the year 2015:

- **ICS 3 and ICS 7 (Staff allocation and Organisational structure)**

Developments and obligations described above, including the continued transition to IMI2, have a significant impact on the way IMI should be organised in the future in order to continue to meet evolving organisational and stakeholder needs and expectations. These changes will also have an impact on the human resource requirements, IT development and support as well as workspace arrangements. It is therefore proposed to maintain the priority of the standards related with staff allocation and recruitment (ICS 3) as well as on the effectiveness of the operational structure (ICS 7).

- **ICS 6 (Risk management)**

The transition towards a new entity implementing a new programme in parallel with the management of the previous one based on different rules and objectives imply, *per se,* a number of risks that need to be carefully monitored and addressed both at operational level (Programme Office) and at Governing Board level. Furthermore, to better deal with risks related to the individual projects in IMI's broad portfolio, it is planned to maintain a risk register, at project level, for the timely identification, documentation, mitigation and follow up of critical issues affecting projects.

- **ICS 8 and 9 (Processes and procedures and management supervision)**

IMI's internal operating procedures are also being duly revised and updated to reflect the new environment and requirements of H2020. In 2015 this will also require close monitoring and management supervision in order to ensure that the changes adhere to the new applicable legal and procedural provisions and requirements and that the appropriate measures are being taken to continue to safeguard the interests of IMI.

Ex-Post Audits of beneficiaries and EFPIA companies

The Programme Office will carry on with the implementation of its Ex-post Audit Strategy to ensure the legality and regularity of the operational expenditure. This strategy complements ex-ante controls embedded in IMI'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. During the year the Strategy will also be updated to reflect changes and developments. 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 since the last audited period. In parallel, independent reviews of submitted certificates of in-kind methodology as well as risk-based audits of accepted declarations of in-kind contributions by EFPIA companies will also be continued and followed-up.

Internal and External Audit

The Internal Audit Service of the European Commission (IAS) and the Internal Audit Capability (IAC) of IMI will jointly implement a new coordinated multi-annual audit strategy for 2015-2017. The new risk-based audit strategy is expected to be reviewed and approved by the Executive Director and the Governing Board by Q1 2015.

During the year, the internal audit activities of the IAS and the IAC will continue to examine and evaluate specific risk-management, governance and the internal control processes of the Joint Undertaking and provide, to the Executive Director and to the Governing Board, with independent and objective assurance and consulting services designed to add value and improve IMI's operations. Audit capability will also be enhanced, when necessary, with co-sourcing arrangements to cover specialised areas of review.

In parallel, during the year, the European Court of Auditors will audit and report on the reliability of IMI's 2014 Annual Accounts as well as the legality and regularity of the underlying transactions.

Anti-fraud strategy

IMI will implement an 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 an essential part of sound financial management required under the EU Financial Regulation. In essence, IMI's anti-fraud strategy, which will be finalised by the end of 2014, will outline specific objectives and pro-active actions to be taken by the Joint Undertaking for fraud protection, early detection and immediate correction within the existing internal control framework.

The strategy will aim to further protect IMI's financial interests, its compliance with ethical values and the protection of the Joint Undertaking's reputation. Its implementation will cover the following four elements:

- preventive measures against fraud, corruption and any other illegal activities;
- the conduct, as necessary, of checks and verifications to detect any possible wrongdoings or irregularities;
- applying corrective actions, including the recovery of wrongly paid amounts; and
- imposing, where appropriate, effective, proportionate and dissuasive administrative and financial penalties.

ANNEX I Calls for proposals to be launched in 2015

The framework that underpins the development of specific projects or research programmes to be prioritised for funding is set up by Scientific Research Agenda (SRA) for IMI2 (see http://www.imi.europa.eu/content/imi-2). On the basis of the WHO Priority Medicines Report, the SRA identifies twelve key health priorities, and it is anticipated that throughout the lifetime of IMI2, many of these health priorities will be addressed.

To progress towards the achievement of IMI2 Objectives the actions developed in 2015 will seek to:

- increase the success rate in clinical trials
- where possible, reduce the time to reach clinical proof of concept in medicine development
- develop new therapies for diseases for which there is a high unmet need and limited market incentives
- develop diagnostic and treatment biomarkers for diseases clearly linked to clinical relevance
- and approved by regulators;
- reduce the failure rate of vaccine candidates in phase III clinical trials through new biomarkers for initial efficacy and safety checks;
- develop tools, standards and approaches to assess efficacy, safety and quality of regulated health products

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[18]. 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 and associated 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.

1. Diabetes/Metabolic disorders

Activities in this priority area should seek progress towards novel diagnostic and treatment paradigms for the mechanisms being involved and triggering the early onset and progression of diabetes (type 1 and type 2)/metabolic disorders and their complications. This should aim to enable an early diagnosis with novel and predictive biomarkers, to allow the development of novel experimental medicine approaches to safe and efficacious treatments, considering also health system sustainability of treatment intervention.

Specific challenge: Towards precision medicine in diabetes and metabolic disorders

In order to address the most relevant and important shortcomings and medical needs of existing therapies a strategic mapping of the mechanisms, approaches and research activities being associated with Diabetes/Metabolic Disorders was developed in order to create within IMI2 a portfolio of call topics and consortia including co-morbidities associated with diabetes such as the metabolic syndrome, rare diseases with diabetic phenotype, cardiovascular diseases with focus on lipid and lipoprotein metabolism, obesity and metabolic liver diseases.

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

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

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 approach for Diabetes/Metabolic Disorders.

Scope:

According to the strategic and holistic approach a continuous flow of aligned and interconnected call topics and consortia will tackle the most relevant tasks and challenges to improve diagnosis, prevention and treatment of diabetic patients, including when relevant collaboration with care providers and public health aspects, and accordingly the launch of 2 call topics in the field of Diabetes/Metabolic Disorders is envisaged for 2015. It is expected that at least some of the following aspects will be covered:

- 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 rare immune mechanisms in type 1 diabetes and other autoimmune 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.
- Development of new, cost-effective diagnostic methodologies to monitor treatment effects and disease progression and complications for use in clinical practice and in the development of new compounds based on the integrate perspectives of the regulatory agencies and Health Technology Assessment bodies (HTAs).
- Development of individual screening programs to identify persons at risk for diabetes and confirm suspected diabetes thus providing improved disease surveillance and disease management. Furthermore development of adherence programs will be considered with a focus on predictors of non-adherence, designs of interventions depending upon risk of non-adherence, and measures outcomes.
- Further project ideas currently in discussion at an early stage may focus on Diabetic Nephropathy, metabolic liver diseases like Non-alcoholic fatty liver disease and Non-alcoholic Steatohepatitis (NASH) as well as a comprehensive analysis of patient data from placebo trials in diabetes to elucidate and stratify the heterogeneity of type 2 diabetic patients.

Expected impact:

- Delivery of tools and capabilities required to develop and implement stratified medicine approaches for diabetes/metabolic disorders, moving into an era of targeted therapies with improved patient outcomes.
- More efficient R&D process, more rapid uptake of scientific advances by regulators and HTAs and new medicines by healthcare providers, based on increased operational excellence.

- The ability to diagnose and treat patients with diabetes/metabolic disorders at an earlier stage in the disease, to find treatments that addresses the narrow therapeutic window for insulin treatment, to monitor treatment success and to better estimate the risk of developing disease complications.
- Increased quality of healthcare options, more integrated healthcare solutions lowering the cost of healthcare.
- Enabling delivery of a range of treatment options and programmes tailored to individual patient needs leading to potential to delay disease progression, lower mortality and increase quality of life.
- Tailor made adherence programmes to support patients in managing their treatment and maximise the benefit gained from interventions.

Type of action:
Research and innovation actions

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, and a series of call topics are envisioned to be launched in the field of neurodegenerative disorders by IMI in 2015.

Specific challenge: Development of a comprehensive strategy for neurodegenerative disorders R&D.

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 and EPAD projects, 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.

Scope:

It is expected that at least some of the following aspects will be covered:
- The identification and validation of drug targets in Alzheimer's disease (AD) by capitalizing on specific GWAS/risk genes (LOAD) leading from pathway understanding/analysis to validated and druggable targets
- The identification and validation of drug targets based on protein misfolding spreading in neurodegeneration, taking common as well as AD-specific mechanisms of spreading into account.
- The Creation, development and/or expansion of drug development centre(s) focused on dementia and dealing with novel targets in new spaces, including phenotypical screens.
- Activities to Increase confidence for progressing treatments to late clinical development including Innovative AD trial designs and regulatory approaches as well as biomarkers and outcome measures.

- Actions to advance efficiency and capabilities of clinical trials and to improve the quality and relevance of evidence available to help patients, caregivers, clinicians, employers, insurers, and policy makers make informed health decisions in AD.
- Coordination and support for activities and studies/actions related to implications of AD prevention, including elements of the ethical and practical implications regarding informing individuals of their risk of developing AD (based on risk stratification model, biomarkers, genetics, etc), the Regulatory pathway for AD prevention studies and the assessment of the impact of AD prevention approaches for patients, caregivers, physicians, regulators, payers, and policy-makers
- Actions related to improve understanding of predictive value of treatment-related biomarker changes on AD disease progression.
- Actions related to nonclinical models that are predictive of treatment effect on slowing disease progression in AD, including aspects to improve the technologies and a broader access to those models.
- Actions to increase understanding of the blood brain barrier and the glymphatic system in AD/ND, to elucidate the underlying mechanisms leading to changes/malfunctioning and exploit this knowledge for development of novel brain delivery technologies.
- Activities related to real world evidence across the disease continuum of AD including disease interception.
- Actions related to the understanding and evaluation of targets and treatment options in the area of degenerative and eventually regenerative aspects of MS and neuropathic pain.

Expected impact:

- The tools and capabilities required to develop and implement stratified medicine approaches for neurodegenerative disease, moving into an era of targeted therapies with improved patient outcomes.
- A more efficient R&D process with a higher probability of success, leading to a more rapid uptake of scientific advances by regulators and HTAs and of new medicines by healthcare providers.
- An overall reduction in the direct and indirect costs associated with the management of neurodegenerative disease through more accurate patient risk assessment and earlier therapeutic intervention.
- Better understanding of the individual risk of developing a neurodegenerative disease and therefore the ability to actively manage this risk.
- Access for patients to better treatment programmes, treatment delivery and adherence programmes tailored to individual needs.

Type of action:
Research and innovation actions and Coordination and support actions.

3. Prevention and treatment of immuno-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.

The proposed work will focus on a key set of immune mediated disease or disease mechanisms where working in partnership will benefit the knowledgebase and accelerate delivery of drug treatments to patients. 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,BLUEPRINT 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.

Specific challenge: Multiple Sclerosis

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. Although there is considerable variation in the severity and symptoms of among people affected by MS, progress has been made in defining subgroups with different disease courses and needs within the MS population. Health services for MS patients need to improve substantially to optimally counteract the consequences of MS and to maximise quality of life equitably across Europe.
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. Thus limited robust evidence exists to guide health professionals in how to use disease modifying drugs in individual patients to optimize the long term outcome (personalized medicine).

Scope:

- 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. Full potential will only be achieved by broader geographic coverage, high documentation rate per country, high data quality and – in addition to the retrospective approach – aligned prospective data consistently collected across all (or at least most) countries in Europe.
- 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.
- Progress in assessing the consequences of MS and the effectiveness of services, including treatment, necessitates systematic data on much larger numbers of MS patients than is so far available.
- The observation of a differing response to the same treatment in the different phases of Multiple Sclerosis (MS) provides clear evidence that pathophysiological mechanisms change along the course of the disease and calls for new therapeutic strategies for progressive disease. It is now considered that the progressive phase of MS is dominated by neurodegeneration at least partially determined by compartmentalized inflammation in the CNS driven by microglial activation. The relatively poor understanding of the pathogenesis and clinical features of progressive MS (compared with Remitting

Relapsing MS), together with the objective difficulty of targeting neurodegeneration (as witnessed by the lack of therapies for the other major neurodegenerative diseases such as Alzheimer's), are major roadblocks to the development of therapies. Moreover the absence of reliable surrogate measures of the degenerative processes impedes the development of new treatments.

Expected impact:

- The identification of therapeutic opportunities and the design and implementation of clinical strategies which will transform the diagnosis and management of autoimmune diseases.
- The linkage and expansion of real life data to 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).

Type of action:
Research and innovation actions

Specific Challenge: Understanding the risks and benefits of glucocorticoid treatment.
Glucocorticoids, or 'steroids' as they commonly are referred to, are the backbone of care for many autoimmune and inflammatory conditions. Despite their ubiquitous use, they have been implicated in the occurrence of life limiting adverse events and negative impacts on quality of life. These adverse effects lead many to conclude that long term steroid use is undesirable. However steroids also can have beneficial effects, and in some instances play a crucial role in disease management. Understanding the risks and benefits of glucocorticoid treatment, dependent upon disease, dose and longevity of use, would inform the debate about their value and also how they should be best utilized in treatment.
A number of new medicines under development have the potential to reduce the use of steroids. However, the uncertainty in the benefit / risk profile of glucocorticoids in the management of disease, casts uncertainty over the clinical, commercial and economic benefits of steroid sparing and limits the value of such a claim in the label of a medicine.

Scope

- The biomarkers and patient focused outcomes required to predict and monitor steroid induced side effects versus disease related side effects supporting better care management for patients.
- New treatment guidelines for the use of steroids in patient care.
- Integration of the numerous already existing clinical data on steroids.
- Educational materials for clinicians to translate new treatment guidelines into daily clinical practice and for tools patients to make more informed decisions about steroid use, other treatment options available to them and their own management of their disease.
- Economic models capable of assessing the healthcare costs associated with steroid induced side effects.

Expected impact:

- A more informed and appropriated use of steroids therefore improving patient care
- An enhanced understanding of the improvement in the quality of clinical care that new steroid sparing medicines can offer to patients.

Type of action:
Research and innovation actions

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

An expansion in the IMI New Drug for Bad Bugs (ND4BB) programme will be sought including looking for synergies with the ND4BB IMI programme and other ongoing and planned EU-wide and global initiatives. In this context activities will aim to establish a strategy for antimicrobial resistance (AMR) in collaboration with the EC and other key stakeholders to define and execute an implementation plan, and considering elements of global collaboration. In addition 2015 will see the expansion of the programme to other areas such as vaccines, viral and fungal infections and epidemiology and novel diagnostics. During late 2014 the IMI2 2nd Call focused on Ebola and the 3rd Call will launch 2 vaccine topics. During 2015 at least 1-2 topics related to Ebola and 1-2 topics related to AMR are envisoned to be launched in the Infection control field.

Scope

- Gram negative bacterial infections has emerged as the consensus target pathogen area (both prevention and treatment),

  Of significant priority will be novel approaches to the treatment of biofilm, ie deep-seated infections, pathogen specific approaches to treatment and potentially adjunctive therapeutics, immunostimualtory agents and Multi Drug Resitant (MDR) gram negative rods
- The gram positive infections. Staphylococcus aureus remains an important pathogen and novel means of treatment and prevention are needed with infection control prioritized over novel therapeutics.
- Vaccines both prophylactic and therapeutic for the prevention and treatment of infectious diseases
- Viral infections with focus on:

  Zoonotic infections, including Ebola virus

  Filoviradae

  Hepatitis B

  Opportunistic infections that may emerge
- Fungal infections both prophylactic and therapeutic treatments.
- Epidemiology & novel (rapid point of care) diagnostics as well as discovery and development of biomarkers for infection. As well as a better understanding of epidemiology (e.g. the etiology of infections).

Specific challenges: Antimicrobial resistance
AMR has been declared a major global public health threat. In Europe 25,000 deaths were reported in 2007 as a result of AMR of which 2/3 being due to gram-negative bacteria. In US deaths due to AMR is estimated to a minimum of 23.000 deaths per year. The clinical burden is associated with soaring treatment and societal costs with a cost of AMR being estimated at around 1.5 billion per year only in Europe. The incidence of infections due to Gram-negative bacteria continues to rise at a time when drug companies have more or less withdrawn from antibiotic research and the number of newly approved antibiotics is low. Despite the recognised need for new antimicrobials the reality is that as a society we faced with the potential situation where prescribers could have few, if any, therapeutic options to treat certain bacterial infections.

Continues efforts are required if key barriers to the development and delivery of effective antibiotics are to be overcome.

Type of action:
Research and innovation actions and coordination and support action

Specific challenge: Ebola and other filoviral haemorrhagic fevers (Ebola +) programme

IMI2 plans to expand and extend its EBOLA + programme started in 2014 with one or more topics to be launched in 2015.

Scope:

- *Immunotherapy:* Ebola is a highly fatal disease, for which no efficient therapy is available today. There is increasing evidence that transfusion of blood from patients recovered from EVD has therapeutic effect, most likely related to the presence of neutralising antibodies, opening the potential for immune therapy. A potential future topic would be aimed at developing therapeutic products for filovirus infections based on passive immunisation (such as monoclonals, hyperimmune gammaglobulines, etc...), which should result in sufficient treatment regimens available at affordable price.
- *Formulations for cold chain:* A potential future project will focus on the development of alternative formulations (for clinically active vaccines) that would improve thermo-stability to simplify the vaccine distribution logistics, taking into account real-world field conditions and the health systems context.
- *Rapid diagnostic tests – long term:* A potential future project would follow the initial effort (current Topic 5) of developing affordable rapid diagnostics to detect Ebola and other haemorrhagic fevers allowing long term surveillance. The project may address developing new tests through early development, analytical validation, clinical validation, registration and launch.
- *Antivirals development and repurposing:* Ebola virus is a negative sense ssRNA virus with a 19kb genome encoding just 7 genes. As such there is comparatively limited scope for the development of anti-viral small molecules, with the polymerase and viral entry processes likely to form the most amenable druggable targets. There are also currently a very limited number of facilitates globally with the infrastructure to run CAT4 Ebola virus cell based assays, which is a critical component for progression of any repurposing program. A potential future topic would aim at creating a co-ordinated and collated tool-box of molecules from across the Industry, which are known to have anti-viral efficacy against a range of viral targets and may have been discontinued from development against their primary target. The project would seek to repurpose these molecules by testing in a CAT4 efficacy cell based Ebola virus assay, to determine whether these molecules have any utility in the blockade of Ebola viral entry or replication. If molecule(s) with potential anti-viral activity are identified, then depending upon their readiness for clinical development, a series of pre-clinical and clinical safety studies may be required to underwrite further clinical development.
- *Multivalent filovirus vaccine development:* Multivalent filovirus vaccine candidates might be better able to protect against a range of current (Zaire) and future filovirus outbreaks. A potential future topic would aim at developing promising multivalent filovirus vaccine candidates. The project would deliver efficacy data in relevant animal models, toxicology data to support entry into clinical studies, and Phase I, II, and III clinical studies.

Expected Impact:

The topics of the proposed IMI2 Ebola and other filoviral haemorrhagic fevers programme (the Ebola+ programme) cover actions that will address:

- short term challenges of the current epidemic as well as actions needed to address EVD and other filoviral haemorrhagic fevers in a sustainable way for the long-term (see also conclusions from the high level WHO meeting on Ebola Vaccines Access and Financing of 23 October 201419).

Type of action:
Research and innovation actions.

[19] http://www.who.int/medi acentre/news/ebola/23-october-2014/en/

Specific challenge: Innovation in 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.

Scope:

- Identify novel biomarkers for vaccine efficacy and safety through systems biology approaches, enabling the screening of multiple candidates vaccines in pre-clinical and early clinical trials, which may include human challenge trials
- Establish integrated data base and additional surveillance system to identify the burden of infectious and non-infectious diseases in different populations and across countries. Epidemiological studies are valuable to understand and assess correlates of protection and inform design of immunogenicity and/or efficacy trials

Expected impact:

- The development of alternatives approaches to the use of animal testing contributing to a reduced use of animals
- Better tests and models for monitoring of vaccine quality
- Better understanding of correlates of protection

Type of action:
Research and innovation actions, and Coordination and Support Actions

5. Translational Safety

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, HESI/ILSI and NIH driven projects) and from data management initiatives.

Specific challenge: Better tools and models for safety monitoring before and beyond product launch

There is still a critical need for tools and methods that will facilitate the monitoring of safety issues, contributing to the safety of patients before and 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.

Scope:

- The concordance of toxicity of pharmaceuticals in humans and in animals should be re-assessed in order to check whether current practices have the appropriate performance, identify areas of improvement, and communicate with Health Authorities and Public on undisputable grounds.
- 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, should 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. Lastly, biomarkers allowing longitudinal, non-invasing follow-up such as in vivo bioimaging should be promoted either for safety monitoring ,biodistribution or for stratification of patients;
- New platforms should be developed reflecting the complexity of human organ physiology (e.g. 3D, or organ-on-chip models, single cell-type or co-culture, static or dynamic systems…) 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, and should compare already commercially available platforms in order to select to most promising one(s), on the basis of agreed criteria. 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 and ideally, their regulatory acceptance. This would also participate to Replacement, Reduction and Refinement of animal use;
- 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 silico and 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 (or exposure at site of action), a further activity should include the evaluation and optimisation of existing or new toxicokinetic techniques (such as imaging) and models with the aim of predicting adaptive and adverse changes based on in vitro/in vivo 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. In particular, the development of a "cloud"-type database would allow preclinical and clinical experts to have easy access to normative animal and human data, visualize them, and help making decisions on safety risk.

Expected impact:

- Progress in more integrated preclinical and clinical data analysis.
- A more efficient use of biomarkers and bio-imaging.
- The addressing of the contribution of animal studies to safety evaluation, in the spirit of 3Rs.
- An impact in the area of mechanistic toxicology.
- The delivery of improved (human) cell based systems for use in translation safety assessment.

Type of action:
Research and innovation actions

6. Data and Knowledge Management

The IMI2 2015 activities will expand upon work from existing IMI projects including EMIF, eTRIKS, DDMORE 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. This area will also cover initiatives aimed to the development of tools and methods for real-time identification of behavioural and physiological patterns (biosignatures) for better disease monitoring and management.

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. 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. Here there will be inks with activities in the strategic areas of Metabolic disorders and neurodegeneration. 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. In addition, 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. Finally further actions to enhance and support the involvement and central role of patients in pharmaceutical research & development and regulatory approval of medicines and vaccines will be sought.

Specific challenge: Enhancing of data and knowledge 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.

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.

Scope:

- research of diseases & mechanisms
- (therapeutic) development optimization
- platforms for research, translational, adaptive informatics, real world data, digital business
- sustainability & data governance (both for IMI 1 and IMI 2 projects)
- 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.
- An open access, integrated resource for the discovery of molecular biomarkers of biological processes and diseases
- A Smart Clinical Program design- a web based tool with a structured information model for pre-competitive and public clinical program design information
- Generation of a public and Pre-Competitive Patient Derived Xenograft Molecular Database
- Informatics for medicines research and development
- Novel approaches towards better patient adherence and compliance

Expected impact:

- Robust KM solutions and operational excellence required to allow integration and analysis of diverse data sets, addressing long-term sustainability, accessibility and re-use of generated research data for future studies;
- Innovative IT/analytical solutions required to support new clinical trial paradigms and monitoring devices.
- Increased value and return on biomedical research investment through operational excellence and collaboration and re-use of public research infrastructures;
- More cost effective, improved R&D processes, enabled by fit- for-purpose KM infrastructures, with the potential of improved scientific insight , leading to downstream healthcare improvements for Europe.
- A coherent and transparent framework to address data privacy and personal integrity issues inherent in the use of health records and personal genomic data;
- Improved transparency of data re-use and impact on R&D.

Type of action:
Research and innovation actions and Scientific Coordination Actions

Specific challenge: Remote Assessment of Disease and Relapse

With rising health-care costs, all health care stake-holders (payers, physicians, patients) are shifting the onus from a 'pay for intervention' to a 'pay for performance' model. This change in focus towards overall outcomes will drive a paradigm shift towards disease interception, i.e. move from a 'diagnose and treat' to a 'predict and pre-empt' approach. In this model, Pre-emption, i.e. intervening early enough in the disease process to prevent serious effects of the disease associated with progression, becomes a critical component of managing chronic disease. Additionally, as the trajectory of chronic diseases is often cyclical, this offers multiple interception opportunities to prevent serious decline — for example, predicting and pre-empting recurrence/suicidality in severe depression, hypoglycaemic event in diabetes, or exacerbations in COPD or Asthma.

Measuring physiological and activity-based parameters remotely and continuously via unobtrusive on-body sensors or smartphones has the potential to revolutionize our ability to predict and pre-empt harmful changes in disease trajectory. By developing methods for real-time identification of behavioural and physiological patterns (biosignatures) that culminate in 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.

Scope:

- The Remote Assessment of Disease and Relapse (RADAR) programme aims to overcome two key bottlenecks in developing such methods: 1) a lack of fundamental disease understanding into the signals and fluctuations in disease state and 2) the lack of clear policy, guidelines and pathways to develop and license "pre-emptive" therapeutic strategies that use such digital monitoring and remote assessment technology.
- To address these bottlenecks, topics in multiple therapeutic areas are expected to be launched under the RADAR platform. These topics will study the fluctuation of chronic disease using remote monitoring technology to provide a foundation for developing novel digital interventions. Such research needs to bring together physicians, patient groups, sensor manufactures, ICT providers, data management and analyst specialists with the pharmaceutical industry to undertake such research.

Expected impact:

- By exploring new pre-emptive therapeutic strategies based on remote continuous monitoring, the programme should establish if such approaches are scientifically and practically feasible, as part of a wider healthcare system.
- An increase in the understanding of chronic disease should be delivered.
- The development of a policy for the regulatory and licensing pathways to deliver a digital intervention should be sought.
- A framework to support a new digital based interactions between patients and health care providers should be built.

Type of action:

Research and innovation actions

7. Medicines Adaptive Pathways to Patients (MAPPs)

Specific challenge: MAPPs implementation
The regulatory environment is lagging behind evolving science; conventional R&D models are no longer financially viable and have become a major hurdle to efficient drug development; general response rates to modern medicines are not satisfactory. A more flexible pathway within the current regulatory/reimbursement framework would not only accelerate access of crucial therapies to patients but would also increase the probability of success as therapies would be oriented towards those patients deemed most likely to respond. The cost of drug development for industry and for healthcare providers could significantly reduce.

Medicines Adaptive Pathways to Patients (MAPPs) defines a flexible development and access pathway within the current regulatory framework that maximizes the positive impact of new medicines on public health by balancing timely access for patients with the need to provide evolving information on benefits and risks. However a pre-requisite for the success of MAPPs implementation lies in full and common understanding of its value, not just for industry but across the entire innovation life cycle: for regulators, HTAs, payers, governments, clinicians and, most importantly, patients. Although MAPPs is already discussed in many public forums and broadly supported, further coordination and integration is needed to clearly define the approach, as well as its applicability within the current legislative framework and its viability for all stakeholders.

The Coordination and Support Action "' Enabling Platform on Medicines Adaptive Pathways to Patients resulted from the call launched in 2014, will also inform research activities by facilitating inclusion of MAPPs enablers in new IMI2 activities as part of actions covered by other priority areas or as specific actions as relevant.

Scope

It is expected that at least some of the following aspects will be covered:

- Modelling potential benefit/risks for stakeholders along the health care value chain, highlight changes in prescription /use conditions, and determine new benefit/risk assessment and patient access processes, including an overall approach for the progressive reduction of HTA and financial uncertainty of adaptive pathways
- Novel methodologies for adaptive clinical trial design
- Methodologies for patient perspective elicitation in benefit/risk assessment of medicinal products from development through the entire life cycle.

Expected impact

- The development of tools, methodologies, infrastructures that will allow changes in R&D, regulatory and medical practice to enable early patient access to innovative prevention and treatment options.

Type of action:
Research and innovation actions

8. Other Areas of Priority

Specific challenge: 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).

Specific Challenge: Towards a Quantitative Biological Approach for Neuropsychiatry
The development of novel pharmacological treatments for neuropsychiatric disorders has stagnated over the last two decades. This statement holds true across the whole field; cognitive decline in dementia, the control of psychosis, affect, the core symptoms of autism spectrum disorders. In addition to the need to treat traditional psychiatric patient groups we have an aging population. This group presents with more complex pathologies and comorbid conditions thus the need for accurate diagnosis, treatment selection and novel therapeutics will become increasingly important and complex. Indeed, if the current efforts to develop disease modifying approaches are successful then these challenges will be faced by potentially a dramatically larger, longer surviving patient population. To reverse this stagnation a new approach is required.
The development of a quantitative biological approach to the understanding and hence classification of neuropsychiatric diseases should significantly facilitate more successful drug discovery and development. This approach would link behavioural symptoms, ideally better quantified, to maladaptive brain circuitries, molecular changes, disease stage and genetic risk regardless of any existing disease classification. A developing understanding of the biological substrates is thus expected to lead to translatable, quantifiable biomarkers or endophenotypes that allow us to effectively treat the right patient population. The aim of this challenge is to initiate the process that is needed to move towards a quantitative biology based framework for neuropsychiatry disorders. This is timely both to reverse the stagnation in the development of treatments for classical psychiatric disorders, but also to address the challenges offered by the need to treat neuropsychiatric issues associated with the increasing burden of neurodegenerative disease.

Scope:

The overall scope will be to explore the same set of quantifiable biological parameters across selected symptom constellations common to distinctly classified syndromes by classical taxonomy.
These studies would be driven from clinical quantitative biology back through appropriate translation to the measurement of homologous pre-clinical quantitative biological indices.

Expected impact:

- New classification of the disease would allow stratification of patients to facilitate more effective treatment and design of clinical trials, including the standardisation of measurement across sites.
- Identify the best predictive systems- clinical, non-clinical and pre-clinical - for the exploration of the underlying biological process and the identification and development of novel therapies or targets.
- Utilise new biomarkers to drive the development of new innovative trial designs for the conduct of preventative and disease modifying trials.

Type of action: Research and innovation actions

ANNEX II General conditions for the Calls for proposals

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 JU http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32014R0622&from=EN.

The following general conditions shall apply to the IMI2 Calls for Proposals:

LIST OF COUNTRIES AND APPLICABLE RULES FOR FUNDING

By way of derogation[20] from Article 10(1) of Regulation (EU) No 1290/2013, only the following participants shall be eligible for funding from the Innovative Medicines Initiative 2 Joint Undertaking:

(a) legal entities established in a Member State or an associated country, or created under Union law; and

(b) which fall within one of the following categories:

(i) 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; the definition of 'affiliated entities' within the meaning of Article 2(1)(2) of Regulation (EU) No 1290/2013 shall apply *mutatis mutandis*;

(ii) secondary and higher education establishments;

(iii) non-profit organisations, including those carrying out research or technological development as one of their main objectives or those that are patient organisations.

(c) the Joint Research Centre;

(d) international European interest organisations.

ADMISSIBILITY CONDITIONS FOR GRANT PROPOSALS, AND RELATED REQUIREMENTS

Part B of the General Annexes[21] to the EC Work Programme shall apply mutatis mutandis for the actions covered by this Work Plan.

ELIGIBILITY CRITERIA

Part C of the General Annexes to the EC Work Programme shall apply mutatis mutandis for the actions covered by this Work Plan.

[20] Pursuant to the Commission Delegated Regulation (EU) No 622/2014 of 14 February 2014 establishing a derogation from Regulation (EU) No 1290/2013 of the European Parliament and of the Council laying down the rules for participation and dissemination in 'Horizon 2020 — the Framework Programme for Research and Innovation (2014-2020)' with regard to the Innovative Medicines Initiative 2 Joint Undertaking

[21] http://ec.europa.eu/research/participants/data/ref/h2020/wp/2014_2015/annexes/h2020-wp1415-annex-ga_en.pdf

TYPES OF ACTION: SPECIFIC PROVISIONS AND FUNDING RATES

Part D of the General Annexes to the EC Work Programme shall apply mutatis mutandis for the actions covered by this Work Plan.

TECHNOLOGY READINESS LEVELS (TRL)

Part G of the General Annexes to the EC Work Programme shall apply mutatis mutandis for the actions covered by this Work Plan.

EVALUATION

Part H of the General Annexes to the EC Work Programme shall apply *mutatis mutandis* for the actions covered by this Work Plan with the following exceptions: the proposals are evaluated against the specific IMI2 Evaluation Criteria (Excellence, Impact and Quality and efficiency of the implementation)[22] which include scoring and thresholds. If a proposal fails to achieve the threshold for a criterion, the other criteria will not be assessed and the evaluation of the proposal will be discontinued.

The proposals will be evaluated according to the evaluation procedure as defined in this annual work plan and in the relevant call text. The full evaluation procedure is described in the IMI2 Manual for submission, evaluation and grant award.[23].
Where appropriate and duly justified, IMI 2 JU calls for proposals may follow a single or a two-stage process.

Under the single-stage process, all evaluated proposals will be ranked in one single list. Best-ranked proposals, in the framework of the available budget, will be invited to prepare a Grant Agreement.

Under the two-stage evaluation procedure, the applicant consortium of the highest ranked short 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 short proposals (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.

As part of the panel deliberations, the IMI2 JU may organise hearings with the applicants to:

- clarify the proposals and help the panel establish their final assessment and scores or
- improve the experts' understanding of the proposal.

[22] http://www.imi.europa.eu/content/documents#calls_for_proposals_-_imi_2_programme
[23] http://www.imi.europa.eu/sites/default/files/uploads/documents/IMI2_Call1/Manual_for_submission_evaluation_grant%20award_2014.06.26.pdf

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
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.

BUDGET FLEXIBILITY

Part I of the General Annexes to the EC Work Programme shall apply mutatis mutandis for the actions covered by this Work Plan.

FINANCIAL SUPPORT TO THIRD PARTIES

Part K of the General Annexes to the EC Work Programme shall apply mutatis mutandis for the actions covered by this Work Plan.

Applicants intending to submit a proposal in response to the IMI2 JU Calls should also read the topic text, the IMI2 JU Manual for submission, evaluation and other relevant documents[24] (e.g IMI2 Model Grant Agreement) grant award.

SUBMISSION TOOL

Unless otherwise stipulated in the relevant Call Conditions of the specific Call, the IMI electronic submission tool **SOFIA** (Submission OF Information Application) is to be used for submitting a proposal in response to a topic of the IMI2 Call; no other means of submission will be accepted. Updates of the proposals may be submitted online until the Call submission deadline. Proposals need to be formally submitted in the tool indicated in the Call text to trigger the admissibility and eligibility checks, and the peer review evaluation.
Access to the IMI electronic submission tool SOFIA first requires a request to access to the tool.

OTHERS

For proposals including clinical trials/studies/investigations, a specific template to help applicants to provide essential information on clinical studies in a standardised format 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.

Ethical issues should be duly addressed in each submitted proposals to ensure that the proposed activities comply with ethical principles and relevant national, Union and international legislation. Any proposal that contravenes ethical principles or which does not fulfil the conditions set out in the H2020 Rules for Participation, or in the IMI2 Call for proposals shall not be selected. [25]In order to ensure excellence in Data and Knowledge Management consortia will be requested to:

[24] http://www.imi.europa.eu/content/documents#calls_for_proposals_-_imi_2_programme
[25] Article 19 of Horizon 2020 Framework Programme, and Articles 13 and 14 of the Horizon 2020 Rules for Participation

1) Disseminate scientific publications and research data on the basis of open access. Collection, processing and generation of research data is to follow documented data management procedures (see "Guidelines on Open Access to Scientific Publications and Research Data in Horizon 2020" and "Guidelines on Data Management in Horizon 2020 "). In order to ensure adherence to the legislation concerning protection of personal data, controlled access digital repositories and data governance will need to be considered.

2) Use well-established data format and content standards in order to ensure interoperability to quality standards. Preferably existing standards should be adopted. Should no such standards exist, consideration should be given to adapt or develop novel standards in collaboration with a data standards organization (e.g. CDISC).

3) In order to make the resources included and generated by the IMI Actions discoverable for metrics and re-use, consortia will be required to disseminate a description of resources[26] according to well-established metadata standards such as the Dublin Core (ISO15836).

Proposals shall contain a draft plan for the exploitation and dissemination of the results.

[26] Examples of Resources are (a collection of) biosamples, datasets, images, publications etc.

ANNEX III - Indicators of Results and Impact as specified in the Legislative Financial Statement of IMI2 JU for monitoring implementation of the initiative[27]

Scientific and technological progress		
	Indicator	**Target**
Monitoring achievement of objectives of the JU	**Monitoring the achievement of specific objectives** (section 3.2 of the Impact Assessment Report)	Specific metrics and targets are listed in Annex IV
	Number of open innovation networks established	3 open innovation network between different industry sectors, and 2 clinical trial networks
	Number of strategic agenda setting beyond JU	Strategic agenda setting in 3 research areas defined by the specific objectives in section 3.2;
	Number of partnerships established	Partnerships in 16 research areas defined by the specific objectives in section 3.2
Monitoring implementation of the strategic research agenda	Number of data points analysed for reaching at unbiased molecular taxonomy of disease	5 million data points
	Number of diseases classified	4 diseases area
	Number of trials analysed for learning from negative results	125 trials
	Level of taking account of health and demographic change and wellbeing policy goals	Strategic research agenda needs to address points 1.1.2, 1.2.2, parts of 1.2.3 and parts of 1.3.1 of partial general approach of Horizon 2020
Monitoring JU operations		
Selection of projects and allocation of funding	Time-to-grant	270 days
	Time-to-pay	30 days
	Level of adherence to time schedule	Budget committed and calls launched accordingly
	Level of SME participation and benefits	From the beginning, 20% of IMI2 funding goes to SMEs, benefit to SMEs monitored as from 2nd year: at least 70% of SME respondents stating that they benefit from the expertise of industry and/or academic partners; 80% of SMEs stating that objectives could not have been met without IMI2 support.

[27] http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52013SC0245&from=EN

Efficiency of research programme	Number of publications	On average 20 publications per €10 million funding
	Impact factor of journals where articles are published	Average impact factor 10% above EU average
	Impact of publications	Citations 20% above average for EU publications
	Number of patents	On average 2 patent applications per €10 million

Monitoring the achievement of specific objectives	**2020Target**
1. Increase success rate in clinical trials in diseases identified from the 'Priority Medicines for Europe and the World Report' that has been prepared by the WHO.	Increased by 30%
1.1 Validate novel drug targets (i.e. clinical proof of concept demonstrated in a phase 2b clinical trial).	12
1.2 Improve from 70 to 80% the predictive capacity of early stage (non-human) safety testing models	≥ 70%
1.3 Establish new clinical trial networks in areas of high unmet need.	2 new networks
2. Reduce the time to reach clinical proof of concept in immunological, respiratory, neurological (including neurodegenerative) diseases.	Reduce to 5 years (from the current 7)
2.1 Reclassifying major disease groups, thereby allowing a significantly better diagnosis and simplifying the conduct of clinical trials	Reclassifying four major disease groups: immunological, respiratory, neurological, neurodegenerative
3. To develop new therapies for diseases for which there is a high unmet need and limited market incentives: antimicrobial resistance (two new classes in the past 30 years) or Alzheimer's disease (only two treatments of limited efficacy have been developed until now)	At least two new therapies
4. Develop diagnostic and treatment biomarkers for diseases clearly linked to clinical relevance, approved by regulators.	4 diseases
5. In the area of vaccines: develop a transparent and comprehensive infrastructure model to gather data on disease incidence and medico- and socio-economic burden of major infectious diseases.	Infrastructure model to gather data
5.1 In the area of vaccines: develop tested novel biomarkers to predict vaccine efficacy and safety early in the process to improve multiple candidates screening leading to a 50% reduction in the failure rate in phase III clinical trials	2 markers each
5.2 In the area of vaccines: develop novel adjuvants for human use, which will allow increasing the body's immune response to the vaccine, boosting in particular reaction in specific target groups, such as the elderly and non-responders	2 novel adjuvants
5.3 In the area of vaccines: identify novel predictive models for efficacy, and for safety	At least two novel predictive models for efficacy and two novel predictive models for safety, for two major infectious diseases and for two types of cancer or chronic disorders (e.g. autoimmune diseases)
5.4 Contribute to strengthening the link between human and veterinary vaccine research.	
6. 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.	

ANNEX IV - Standard H2020 Performance Indicators (Annex I and II of the Council Decision 2013/743/EU of 3 December 2013 establishing the specific programme implementing Horizon 2020 - the Framework Programme for Research and Innovation (2014-2020)[28]

Indicator	Definition/Responding to question	Type of data required	Data to be provided by	Baseline at the start of H2020 (latest available)	End of 2020 Target
SME - Share of participating SMEs introducing innovations new to the company or the market (covering the period of the project plus three years);	Number and % of participating SMEs that have introduced innovations to the company or to the market;	Number of SMEs that have introduced innovations;	H2020 beneficiaries through project reporting	n.a. [new approach under H2020]	50%
SME - Growth and job creation in participating SMEs	Turnover of company, number of employees	Turnover of company, number of employees;	H2020 beneficiaries through project reporting	n.a. [new approach under H2020]	To be confirmed: 3% per year more than SMEs covered in Eurostat's Structural Business Statistics
Societal Challenges - Publications in peer-reviewed high impact journals in the area of the different Societal Challenges	The percentage of papers published in the top 10% impact ranked journals by subject category.	Publications from relevant funded projects (DOI: Digital Object Identifiers); Journal impact benchmark (ranking) data to be collected by commercially available bibliometric databases.	H2020 beneficiaries through project reporting; Responsible Directorate/Service (via access to appropriate bibliometric databases)	n.a. [new approach under H2020]	On average, 20 publications per €10 million funding (for all societal challenges)
Societal Challenges - Patent applications and patents awarded in the area of the different Societal Challenges	Number of patent applications by theme; Number of awarded patents by theme	Patent application number	H2020 beneficiaries through project reporting; Responsible Directorate/Service (via worldwide search engines such as ESPACENET, WOPI)	n.a. [new approach under H2020]	On average, 2 per €10 million funding (2014 - 2020) RTD A6
Societal Challenges - Number of prototypes and testing activities	Number of prototypes, testing (feasibility/demo) activities, clinical trials	Reports on prototypes, and testing activities, clinical trials	H2020 beneficiaries through project reporting	n.a. [new approach under H2020]	To be developed on the basis of first Horizon 2020 results

[28] http://ec.europa.eu/research/participants/data/ref/h2020/legal_basis/sp/h2020-sp_en.pdf
This Annex III of the IMI2 JU Annual Work Plan 2015 presents a selection of the most relevant performance indicators for IMI2 JU.

Societal Challenges - Number of joint public-private publications	Number and share of joint public-private publications out of all relevant publications.	Properly flagged publications data (DOI) from relevant funded projects	H2020 beneficiaries through project reporting; Responsible Directorate/Service (via DOI and manual data input-flags)	n.a. [new approach under H2020]	To be developed on the basis of first Horizon 2020 results
New products processes, instruments, methods, technologies launched into the market	Number of projects with new innovative products, processes, instruments, methods, technologies	Project count and drop down list allowing to choose the type processes, products, instruments, methods, technologies	H2020 beneficiaries through project reporting		
Total number of participations by EU-28 Member State		Nationality of H2020 applicants & beneficiaries	H2020 applicants & beneficiaries at the submission and grant agreement signature stage		
Total amount of EU financial contribution by EU-28 Member State (EUR millions)		Nationality of H2020 beneficiaries and corresponding EU financial contribution	H2020 beneficiaries at grant agreement signature stage		
Share of EU financial contribution going to SMEs (Enabling & industrial tech and Part III of Horizon 2020)		H2020 beneficiaries flagged as SME; EU contribution to H2020 beneficiaries	H2020 beneficiaries at grant agreement signature stage		
Percentage of women participants in H2020 projects		Gender of participants in H2020 projects	H2020 Beneficiaries through project reporting		
Percentage of women project coordinators in H2020		Gender of MSC fellows, ERC principle investigators and scientific coordinators in other H2020 activities	H2020 beneficiaries at the grant agreement signature stage		
Percentage of women in EC advisory groups, expert groups, evaluation panels, individual experts, etc.		Gender of memberships in advisory groups, panels, etc.	H2020 beneficiaries at the grant agreement signature stage		
Share of third-country participants in Horizon 2020		Nationality of H2020 beneficiaries	H2020 beneficiaries at the grant agreement signature stage		
Percentage of EU financial contribution attributed to third country participants		Nationality of H2020 beneficiaries and corresponding EU financial contribution	H2020 beneficiaries at the grant agreement signature stage		
Share of EU financial contribution that is sustainability-related in Horizon 2020 (EUR), calculated on the basis of the " RIO markers" methodology developed by OECD		Budget figures by topic for top-down activities. For "bottom-up" topics: budget allocated to retained proposals.	For "top-down" topics: Responsible Directorate/Service (Call coordinator (ex-ante tracking)		

			• For "bottom-up" topics: Project Officers (ex-post tracking) -at grant agreement signature stage the PO will be requiered to flag on SYGMA		
Share of projects and EU financial contribution allocated to innovation actions in H2020		Proposals and projects properly flagged ; Topics properly flagged in the WP; follow-up at grant level	Project Officer - at grant agreement signature stage the PO will be required to flag on SYGMA; Responsible Directorate/Service (WP coordinator) - via tool CCM2		
Within the innovation actions, share of EU financial contribution focussed on demonstration and first-of-a-kind activities		Topics properly flagged in the WP; follow-up at grant level	Responsible Directorate/Service (WP coordinator) - via tool CCM2		
Share of EU financial contribution that is ICT Research & Innovation related in Horizon 2020 (EUR), calculated on the basis of the " RIO markers" methodology developed by OECD: • Expenditure for topics/projects where ICT R&I is the principal (primary) objective to be counted as 100% ICT related; • Expenditure for topics/projects where ICT R&I is a significant (secondary), but not predominant objective to be counted as 40% ICT related; • Expenditure for topics/projects not targeted to ICT R&I objectives to be counted as 0% ICT related. Note: ICT Innovation is defined as "ICT and ICT-enabled new products, services or processes within and outside the ICT sector".		· For "top-down" topics: budget figures by topic; • For "bottom-up" topics: budget allocated to retained proposals. Note: *"Top-down" topics are topics for which markers can be allocated on the basis of the Work Programme. "Bottom-up" topics are topics for which it is not possible to allocate ICT R&I marker on a topic basis.*	· For "top-down" topics: Responsible Directorate/Service (Call coordinator (*ex-ante* tracking) • For "bottom-up" topics: Project Officers (ex-post tracking) - at grant agreement signature stage the PO will be required to flag on SYGMA		
Percentage of H2020 beneficiaries from the private for profit sector		H2020 beneficiaries classified by type of activity and legal status	H2020 beneficiaries at grant agreement signature stage		
Share of EU financial contribution going to private for profit entities (Enabling & industrial tech and Part III of Horizon 2020)		H2020 beneficiaries classified by type of activity; corresponding EU contribution	H2020 beneficiaries at at grant agreement signature stage		
EU financial contribution for PPP-P2Ps		EU contribution to PPP-P2Ps	Responsible Directorate/Service		
PPPs leverage: total amount of funds leveraged through Art. 187 initiatives, including additional activities, divided by the EU contribution		Total funding made by private actors involved in PPPs	Art.187 Joint Undertaking Services		

Dissemination and outreach activities other than peer-reviewed publications - [Conferences, workshops, press releases, flyers, exhibitions, trainings, social media]		A drop down list allows to choose the type of dissemination activity. Number of events and funding amount	H2020 Beneficiaries through project reporting		
Proposal evaluators by country		Nationality of proposal evaluators	Responsible Directorate/Service in charge with the management of proposal evaluation		
Proposal evaluators by organisations' type of activity		Type of activity of evaluators' organisations	Responsible Directorate/Service in charge with the management of proposal evaluation		