Annual Activity Report 2016

In accordance with Article 17 of the Statutes of IMI2 JU annexed to Council Regulation (EU) No 557/2014 of 6 May 2014 and with Article 20 of the Financial Rules of IMI2 JU.

The Annual Activity Report will be made publicly available following approval by the IMI Governing Board.

Annex 1 to the Decision of the IMI2 Governing Board no. IMI2-GB-DEC-2017-10 approved by the Governing Board of the Innovative Medicines Initiative 2 Joint Undertaking on 27.06.2017

Document reference: IMI2/OUT/2016-04031

Contents

Factsheet – IMI at a glance

Name	**Innovative Medicines Initiative 2 Joint Undertaking (IMI2 JU)**
Objectives	According to Article 2 of the Council Regulation establishing IMI2, the IMI2 Joint Undertaking shall have the following objectives: a) to support, in accordance with Article 25 of Regulation (EU) No 1291/2013, the development and implementation of pre-competitive research and of innovation activities of strategic importance to the Union's competitiveness and industrial leadership or to address specific societal challenges in particular as described in parts II and III of Annex I to Decision 2013/743/EU, and in particular the challenge to improve European citizens' health and well-being; b) to contribute to the objectives of the Joint Technology Initiative on Innovative Medicines, in particular to: i. increase the success rate in clinical trials of priority medicines identified by the World Health Organisation; ii. where possible, reduce the time to reach clinical proof of concept in medicine development, such as for cancer, immunological, respiratory, neurological and neurodegenerative diseases; iii. develop new therapies for diseases for which there is a high unmet need, such as Alzheimer's disease and limited market incentives, such as antimicrobial resistance; iv. develop diagnostic and treatment biomarkers for diseases clearly linked to clinical relevance and approved by regulators; v. reduce the failure rate of vaccine candidates in phase III clinical trials through new biomarkers for initial efficacy and safety checks; vi. improve the current drug development process by providing support for the development of tools, standards and approaches to assess efficacy, safety and quality of regulated health products.
Founding legal act	Council Regulation (EU) No 557/2014 of 6 May 2014 establishing the Innovative Medicines Initiative 2 Joint Undertaking
Executive Director	Pierre Meulien
Governing Board	Representatives of the European Federation of Pharmaceutical Industries and Associations (EFPIA) Marc de Garidel – Chairman of Ipsen Group, member of the EFPIA Board and Vice-President of EFPIA Chair, IMI Governing Board Richard Bergström – Director General of EFPIA Salah-Dine Chibout – Global Head Discovery and Investigational Safety at Novartis, Chairman of the EFPIA Innovative Medicines Strategy Priority Working Group Carlo Incerti – Head of Global Medical Affairs at Sanofi Genzyme, member of the EFPIA Board Paul Stoffels – Chief Scientific Officer at Johnson & Johnson, Worldwide Chairman of Janssen Pharmaceutical Companies of Johnson & Johnson Representatives of the European Commission (EC) Ruxandra Draghia-Akli – Deputy Director-General responsible for Research Programmes within the Directorate-General for Research and Innovation, European Commission Deputy Chair, IMI Governing Board Arnd Hoeveler – Head of Unit responsible for Innovative tools, technologies and concepts in health research within the Directorate-General for Research and Innovation,

		European Commission
	Irene Norstedt	Head of Unit responsible for Innovative and Personalised Medicine within the Directorate-General for Research and Innovation, European Commission
	Carlo Pettinelli	Director responsible for Consumer, Environmental and Health Technologies within the Directorate-General for Internal Market, Industry, Entrepreneurship and SMEs, European Commission
	Andrzej Jan Rys	Director responsible for Health systems, medical products and innovation within the Directorate-General for Health and Food Safety, European Commission
Other bodies	States Representatives Group (SRG): 28 European Union (EU) Member States and 15 Associated Countries to the Horizon 2020 Framework Programme Scientific Committee: 11 members including ad hoc members Stakeholder Forum: 554 registrations in 2016 Strategic Governing Groups: 7	
Staff	Total posts: 52 (38 Temporary Agents, 14 Contract Agents) Posts filled: 41 (34 Temporary Agents, 7 Contract Agents)	
2016 budget	Commitment appropriations: EUR 307 052 760 Payment appropriations: EUR 263 423 490	
2016 budget implementation	Commitment appropriations: EUR 288 872 480 *(94.08 %)* Payment appropriations: EUR 183 338 540 *(69.60 %)*	
Grants	14 grants signed in 2016 for a total value of EUR 135 153 198	
Strategic Research Agenda	The focus of the IMI2 JU Strategic Research Agenda (SRA) is on delivering 'the right prevention and treatment for the right patient at the right time'. No amendment in 2016.	
Call implementation in 2016	Calls launched: 2 Proposals submitted under two-stage Calls: ▪ Short proposals submitted: 60 ▪ Eligible proposals submitted: 60 ▪ Full proposals submitted: 17 Proposals submitted under single-stage Calls: ▪ Full proposals submitted: 4 ▪ Eligible proposals submitted: 4 Total proposals selected for funding: 19 Global project portfolio as of end 2016 (signed grant agreements only): 84 projects (59 under IMI1 and 25 under IMI2)	
Participation, including SMEs	Beneficiaries receiving funds in IMI1 and IMI2 projects represent a range of different types of organisations, including universities, research organisations, small and medium-sized enterprises (SMEs) and patient organisations. For IMI2, SME participations account for 11.78 % of EU beneficiaries and receive 10.33 % of EU funding. For IMI1, SMEs participations account for 15.96 % of EU beneficiaries and receive 13.25 % of EU funding.	

Note: This factsheet reflects the situation as of 31 December 2016.

Foreword

In 2016, IMI continued to consolidate its reputation as a pioneer in open innovation. Throughout the year, our projects continued to deliver exciting results that address very real, practical issues in medical research and drug development. Through the Calls and projects launched during the year, we are bringing new partners into the IMI community, including major philanthropic organisations and charities, as well as companies from the diagnostic, imaging and other sectors.

We have launched projects and Call topics that are in line with some of the major drivers of change in medical research today, namely the rise of digital technologies, and the greater involvement of patients in research and drug development.

Our May 2016 report on the socio-economic impacts of the first IMI projects to finish confirms that the projects leverage funding and are delivering on IMI's goal of helping to make concrete improvements to the medicines development process. More importantly, the relationships forged during the projects persist even after the project has ended, and the successes of the projects showcase Europe as an attractive place to carry out pharmaceutical research.

We are also systematically holding meetings with the leaders of projects that have finished, to hear from them what they consider to be the most important project results, and how IMI helped to move their respective fields forwards. The results of these meetings, which are summarised in this report and published on the IMI website, also offer important insights on issues such as the sustainability of and access to results. Personally, I have found these meetings to be hugely inspiring; the scientists working on our projects are true leaders in their fields and the project results clearly demonstrate IMI's added value.

In late 2016, independent experts started to work on an evaluation of IMI, and their report will be published in 2017. At IMI, we hope that their findings and recommendations will help us to improve the way we work so that we can continue to deliver excellent collaborative projects that will make a real difference to the way medicines are developed in Europe and beyond.

IMI owes its success to the many people who collaborate on and contribute to our work: our contacts at the European Commission and EFPIA, the members of our Governing Board, Scientific Committee, and States Representatives Group, the Strategic Governing Groups, and the many stakeholders who have given their input on our activities and plans via events and consultations throughout the year. We have also benefitted from the insights of Members of the European Parliament and various auditors.

I would also like to acknowledge the hard work of the thousands of scientists working on our projects; the results of their efforts form the backbone of this Annual Activity Report. Finally, I would like to thank my highly efficient and motivated team at the IMI Programme Office, whose members work hard to ensure the success of this ambitious and much-needed programme.

Pierre Meulien

IMI Executive Director

Executive summary

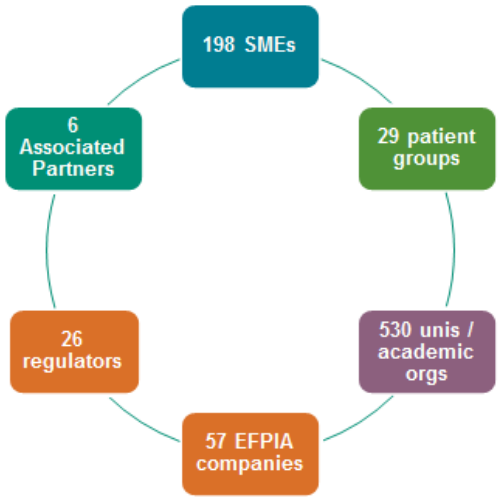
IMI puts open innovation into practice

The Innovative Medicines Initiative (IMI) is built on the principle of open innovation, which means creating a dynamic, networked, multi-stakeholder, collaborative innovation ecosystem. IMI puts open innovation into practice by building ambitious projects that bring together academics, large pharmaceutical companies, small and medium-sized enterprises (SMEs), patient groups, and medicines regulators to join forces and share resources, ideas and expertise to tackle some of the biggest challenges in medical research and drug development. Our open innovation approach allows us to achieve results and make a difference faster and at an unprecedented scale.

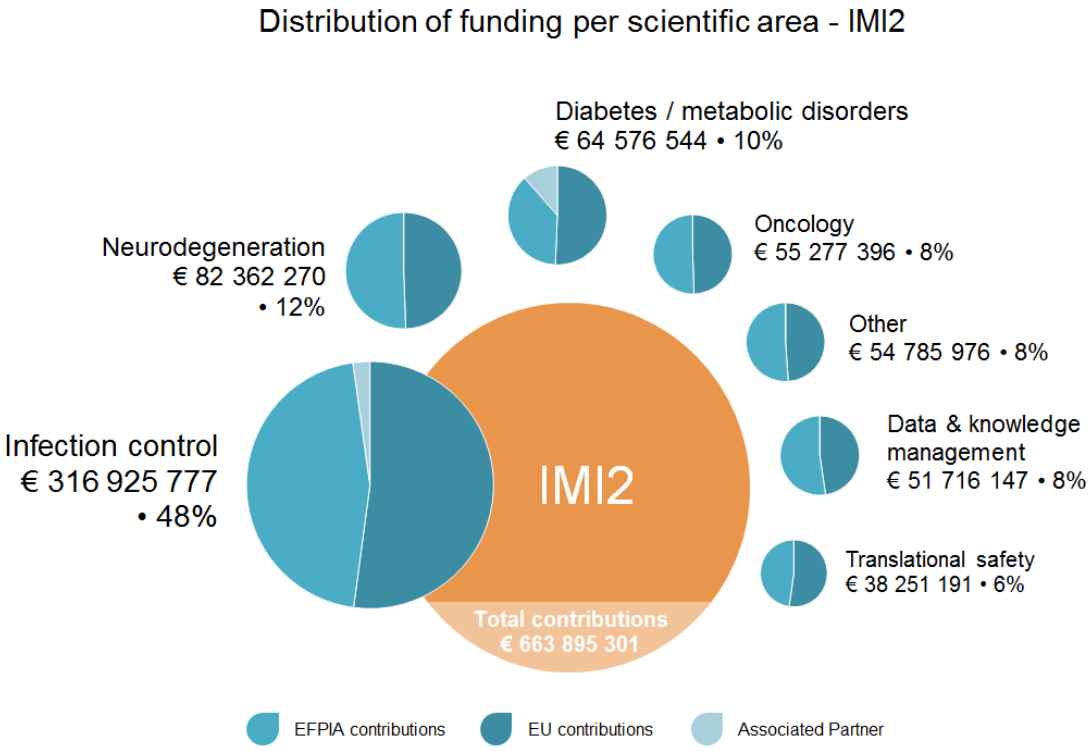
Today, the IMI community brings together 11 500 scientists and experts from across Europe and beyond working in 84 projects.

What's more, the IMI community is growing, as 46 % of the participants in IMI2 projects were not involved in IMI1.

The graph to the right presents a snapshot of the IMI community today.



IMI projects also cover a wide range of disease and research areas. The graph below shows the breakdown by scientific area of IMI2 projects, including the contributions from the EU, EFPIA companies, and Associated Partners.



Large collaborative projects with diverse stakeholders tend to take people outside their comfort zone; ways of working are open to challenge, old habits (such as not sharing results with 'the competition') have to be unlearnt, and prejudices have to be set aside. However, our experience at IMI shows by acting as a neutral broker, IMI helps project partners to overcome these challenges, and our projects are now delivering results that could not have been achieved without the public-private partnership model.

For example, through the **European Lead Factory**, public and private organisations have pooled their resources to create a 460 000-strong collection of compounds that universities, SMEs and others can screen for molecules that could prove useful for their own drug development programmes. By the end of 2016, the project had run over 100 screens, helping to accelerated drug development in areas like cancer, antimicrobial resistance, and dengue fever.

Our **PREDECT** project has developed novel tools that will make it easier for researchers to study cancer in the laboratory. One tool, which focuses on a common form of breast cancer, has been hailed by other researchers as 'a potential game-changer for breast cancer research' that could trigger new approaches to treatment of breast cancer in the near future.

IMI projects are also putting in place networks to make it easier to carry out large-scale, pan-European clinical trials and studies in areas where there is a high unmet medical need, most notably antimicrobial resistance (the **COMBACTE** family of projects now boasts a pan-European network of over 800 clinical sites that) and Alzheimer's disease (**EPAD**, which in 2016 recruited the first patients for a major study on dementia).

In 2016, we commissioned a group of independent experts to analyse the **socio-economic impacts** of the results of nine of the first IMI projects to finish. Between them, they have a total budget of €217.6 million, and cover areas such as diabetes, medicines safety, schizophrenia and depression, education and training, chronic pain, and severe asthma. The analysis revealed that:

- IMI projects are delivering on IMI's goal of helping to make concrete improvements to the medicines development process;
- IMI projects are creating long-lasting collaborative networks;
- IMI leverages additional funding for medicines research and development;
- IMI is making Europe an attractive place to carry out pharmaceutical research.

Importantly the report notes that **many of the projects' achievements would not have been possible without IMI.** The report also includes a number of recommendations on how we can maximise the socio-economic impacts of our projects. We have analysed these and we are now integrating them into a new framework for key performance indicators for IMI that will be finalised in 2017.

Meanwhile, we remain committed to pushing the boundaries of open innovation by bringing new stakeholders into the medical research and development (R&D) ecosystem we are creating.

The need to do this is recognised in the legislation establishing the IMI2 programme, which creates the status of **'Associated Partner'** to make it easier for a wider range of organisations to contribute to IMI. In 2016, IMI's Associated Partner family grew substantially.

- Diabetes charity **JDRF** and philanthropic foundation the **Leona M. and**

IMI in 2016 at a glance

New projects

In **2016**, IMI signed **14** Grant Agreements to launch new projects with a combined budget of **EUR 269 million** coming from EU, EFPIA, and Associated Partners…

Neurological disorders & digital health
RADAR-CNS

Dementia
ADAPTED
AMYPAD
MOPEAD
PHAGO

Diabetes
BEAT-DKD
RHAPSODY

Infectious diseases
RESCEU

Big Data for Better Outcomes
HARMONY (haematological cancers)
ROADMAP (Alzheimer's disease),

Vaccines
PERISCOPE
VAC2VAC

Patient involvement
PREFER

Medicines safety
TransQST

Harry B. Helmsley Charitable Trust became IMI Associated Partners back in 2014. In 2016, both organisations increased their contributions to IMI by joining the new IMI2 – Call 10 topic on diabetes, which also features a new Associated Partner in the form of **T1D Exchange**.

- The **Bill & Melinda Gates Foundation** is an Associated Partner via the PERISCOPE project, which started in early 2016 and aims to improve vaccines for pertussis (whooping cough).
- **Autism Speaks** and the **Simons Foundation Autism Research Initiative (SFARI)** became Associated Partners through the IMI2 – Call 10 topic on autism spectrum disorders.

These organisations are based in the United States. Their involvement in IMI demonstrates IMI's role in making Europe an attractive place to carry out medical research and drug development. In the longer term, these links contribute to IMI's strategy to promote the internationalisation of its projects and create a global community with Europe at its heart.

Reaching out to other sectors

As of the end of 2016, 14 companies from outside the pharmaceutical sector had also got involved in IMI via EFPIA membership and committed a total of EUR 18.2 million to new IMI projects.

In this way, IMI has expanded its stakeholder base to include companies with expertise in animal health, imaging, software, diagnostics, medical technology, and data management, for example.

Catching the digital wave

Digital technologies play an increasingly important role in research and healthcare, and this is reflected in the following projects launched in 2016 which have a combined budget of EUR 71 million. The projects also demonstrate IMI's increased openness towards the digital technology sector.

The **RADAR-CNS** project, which got underway in April, aims to develop new ways of measuring major depressive disorder, epilepsy and multiple sclerosis (MS) using wearable devices and smartphone technology. For all three disorders, patients often experience periods where their symptoms are manageable, followed by periods of deterioration and acute illness (relapse). Data from mobile devices can give a full picture of a person's condition at a level of detail which was previously impossible. This offers the potential to detect changes in behaviour, sleep, or mood before the individual themselves is aware of it. This could help them to predict – or even avoid – a relapse.

2016 also saw the launch of the first two projects in IMI's **Big Data for Better Outcomes (BD4BO)** programme, which aims to facilitate the use of diverse data sources to deliver results that reflect health outcomes of treatments that are meaningful for patients, clinicians, regulators, researchers, healthcare decision-makers, and others.

HARMONY will capture, integrate, analyse and harmonise anonymous patient data from numerous high-quality sources to unlock valuable knowledge on haematological malignancies (blood cancers such as leukaemia, myeloma, and lymphoma). These diseases account for about one third of cancer cases in children and about one third of cancer deaths.

ROADMAP aims to deliver a series of methods and tools that will allow the scalable, transferable integration of data on patient outcomes in the real world.

IMI in 2016 at a glance

New Call topics

In **2016**, IMI launched **2 Calls** for proposals with a total of **14 topics** and a budget of **EUR 228 million** from the EU & **EUR 237 million** from EFPIA & Associated Partners

Antimicrobial resistance

Rheumatic diseases

Data quality

Medicines safety

Liver disease

Vaccines

Diabetes

Pain

Big data & prostate cancer

Paediatric clinical trials

Biomanufacturing

Genes & disease

Patient perspectives in medicines lifecycle

Autism spectrum disorders

The tools will be developed and tested through pilot projects and will lay the foundations for a Europe-wide platform on real world evidence in Alzheimer's disease. The project will also deliver tools for patient engagement and address the ethical, legal and social implications of adopting a real world evidence approach to Alzheimer's disease.

Partnering with patients

Patients increasingly want and expect to be involved in research that will ultimately affect them. At the same time, there is growing recognition that patients' contribution research can help to make it more effective. Therefore, at IMI we champion a patient-centric approach, encouraging all the projects that we fund to work in partnership with patients wherever possible.

In 2016, IMI's landmark project in this area, **EUPATI**, held its closing conference. A highlight of the event was the graduation ceremony for the over 90 patients and patient advocates who have passed the EUPATI Expert Course, which provided training in medicines research and development to allow them to contribute more to medical research and drug development. A survey of course participants reveals that they are already putting their new-found skills to use by taking on active roles advising regulatory agencies and pharmaceutical companies, for example. The need for this project is also demonstrated by the fact that the project leaders managed to secure funding to run a third round of the course after the IMI funding period has finished. The project also lives on in the multilingual online toolbox packed with educational material for patients on medicines research and development.

The year also saw the launch of a major new IMI project in this area – **PREFER**. PREFER aims to assess when and how patient preferences on benefits and risks should be incorporated into decisions on medicinal products. While there is broad agreement that patient preferences are very valuable, there is little guidance on conducting and using such studies. The goal of PREFER is to provide a set of systematic methodologies and recommendations to assess, engage and include patient perspectives during the development, approval, and post-approval of new therapies. PREFER brings together experts from academic research institutions, pharmaceutical companies, patient organisations, a health technology assessment body, and SMEs. In addition the consortium has set up stakeholder advisory groups to work closely with patients, regulators, health technology assessment (HTA) bodies and payers, to ensure that recommendations are evidence based, relevant and useful.

Finally, at the end of 2016 we included a topic on patient perspectives in research in **IMI2 – Call 10**. The goal of this topic is to provide a framework and guidance for all stakeholders on the best ways to meaningfully engage patients at different stages of the medicines lifecycle.

Governance at IMI

IMI is a public-private partnership between the European Union and the European pharmaceutical industry. This is reflected in the IMI Governing Board, IMI's highest decision-making body, which is made up of five representatives of the European Commission and five representatives of the pharmaceutical industry. IMI also has a strong Scientific Committee; in 2016 we bid farewell to the members whose mandate had come to an end and welcomed seven new members who bring to IMI a wealth of expertise in fields such as neurology, public health, immunology, infectious diseases, and cancer, to name just a few. We also continued to work closely with the States Representatives Group. Between them, these bodies have helped us to maintain IMI's neutral role in the development of our projects; provided a channel for input from stakeholders; and also enabled us to stay abreast of the latest developments in the medical research and drug development fields.

1 Implementation of the Annual Work Plan 2016

1.1 Key objectives in 2016

IMI's key objectives in 2016 were based on the overall IMI2 objectives. IMI's progress on these objectives, and control of related risks, is summarised below. More details can be found in the rest of this report[1].

Objective: Efficient management of Calls for proposals preparation, evaluation and grant award processes

In 2016, IMI's streamlined approach to the management of the entire Call process, and the proactive control of potential risks identified through the annual risk assessment exercise risks (related in particular to the topic definition process and delays in financial planning), allowed it to successfully:

- **launch 2 Calls for proposals** with a total IMI/EU contribution of over EUR 230 million, matching an equivalent commitment from EFPIA companies and Associated Partners;
- **run 7 evaluations** relating to 5 Calls for proposals;
- **sign 14 Grant Agreements** allowing the launch of projects in areas as diverse as dementia, diabetes, vaccines, and medicines safety, as well as the first projects in IMI's Big Data for Better Outcomes programme.

Objective: Close monitoring of ongoing projects' achievements, in particular the efficient use of resources and the quality of scientific outputs, as well as contributing to the analysis and dissemination of results and outputs

IMI has always closely monitored its projects' results via project reports, interim reviews, and the Thomson Reuters analyses of project publications, for example. In 2016, four things helped the IMI programme Office to achieve more in this important area.

- **Report on socio-economic impacts of IMI projects**
  Commissioned by IMI and written by a panel of independent experts, this report focused on the outputs and impacts of the first nine IMI projects to finish. The analysis revealed that IMI projects are making concrete improvements to pharmaceutical R&D, creating new knowledge and tools, and making Europe an attractive place to carry out research. Most importantly, many project achievements would not have been possible without IMI.
- **Meetings with projects that have finished**
  In 2016, IMI started to organise meetings with the coordinators of projects that had recently finished, with the goal of identifying and discussing the most significant project results and their impact, as well as the legacy of the projects in the longer term. In addition, the meetings aid in the identification of best practice that could be shared with other projects.
- **Recruitment of a writer / editor**
  The recruitment of a writer / editor has allowed IMI to devote more time and effort to gathering news on project successes, and transforming them into success stories for different IMI communication channels including the newsletter, website, social media, etc.
- **Revision and improvement of the operating procedure for assessment and acceptance of periodic and final reports**
  Improvements of this operating procedure will make it easier and faster for the IMI Programme Office to better document the scientific and financial assessment of the activities carried out by projects as well as the eligibility of costs claimed and the overall legality and regularity of transactions. Further to the relevant legislation, this guidance also takes into consideration lessons learnt from previous years as well as the comments expressed by the European Court of Auditors (ECA) in their annual report as well as the Internal

[1] See in particular Section 4.5 on risk management.

Audit Service's (IAS) recommendations on project monitoring, ex-ante controls, and reporting of operational performance.

Objective: Reaching out to new stakeholders towards broadening the network of collaboration in the healthcare family

IMI's successes are due to the involvement in its projects of a wide range of stakeholders from around Europe and beyond. Some come into IMI as Associated Partners or by becoming members of EFPIA. Others, such as patients and SMEs, are more likely to join projects as funding beneficiaries.

- **New Associated Partners**
  In 2016, IMI welcomed three new Associated Partners in the form of Autism Speaks, the Simons Foundation Autism Research Initiative (SFARI), and T1DExchange. In addition, existing Associated Partners JDRF and the Leona M. and Harry B. Helmsley Charitable Trust extended the scope of their involvement in IMI by joining a new consortium.
- **Bringing in new sectors via EFPIA**
  EFPIA's 'Partners in Research' membership category also offers companies outside the pharmaceutical sector to contribute to IMI as EFPIA members. As of the end of 2016, 14 EFPIA Partners in Research[2] with expertise in fields such as diagnostics, medical technology, imaging and data analysis had committed € 18.2 million to new IMI Call topics.
- **IMI and patients**
  IMI also continued to engage with patients, most notably through the organisation of a workshop dedicated to patients that gathered together around 70 patients and their representatives. The event highlighted both patients' interest in IMI and their expectations of how they feel they can and should contribute to it. IMI also produced a new booklet on patient engagement in IMI.

Objective: Optimal use of the internal resources of IMI2 JU Programme Office, supported by efficient IT systems

- **Office re-organisation & new recruitments**
  In 2016, IMI optimised its organisational structure by hiring a Head of Institutional Relations and Communication and a Head of Scientific Operations. The Governing Board also approved a new Staff Establishment Plan that will see the number of Programme Office staff rise to 52. This increase will help IMI to handle its growing workload, and mitigates the risk related to the efficient management of the operational budget and IMI's capacity to adapt its organisation to the evolving needs of its members and stakeholders.
- **Move to the Horizon 2020 IT tools**
  Another milestone in 2016 was the move, for IMI2 – Call 10, to the Horizon 2020 portal for the submission of short proposals. This also represents an important effort in terms of risk mitigation for the office.

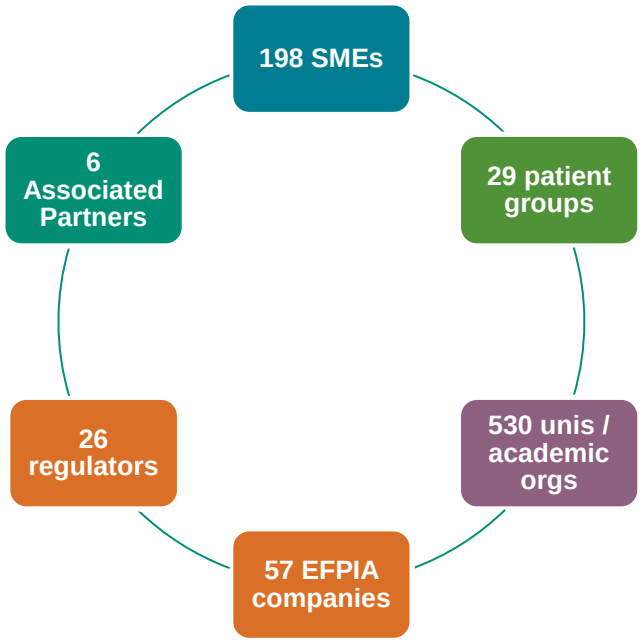
[2] The full list of EFPIA Partners in Research can be found online at www.efpia.eu/about-us/membership/.

1.2 Research and innovation activities

IMI is built on the principle of open innovation. Since IMI's creation, our projects have brought together academics, large pharmaceutical companies, small and medium-sized enterprises (SMEs), mid-sized companies, patient groups, and medicines regulators[3] to work together and share resources, ideas and expertise in ambitious projects designed to tackle shared challenges in medical research and drug development. Our open innovation approach allows us to achieve results and make a difference faster and at an unprecedented scale and speed.

Today, the IMI community brings together 11 500 scientists and experts from across Europe and beyond working in 84 projects. What's more, the IMI community is growing, as 50 % of the participants in IMI2 projects were not involved in IMI1.

The graph below shows the breakdown of the IMI community by organisation type. Note that while most EFPIA companies are in the pharmaceutical sector, there are also members from fields such as diagnostics, imaging, medical technology, etc.



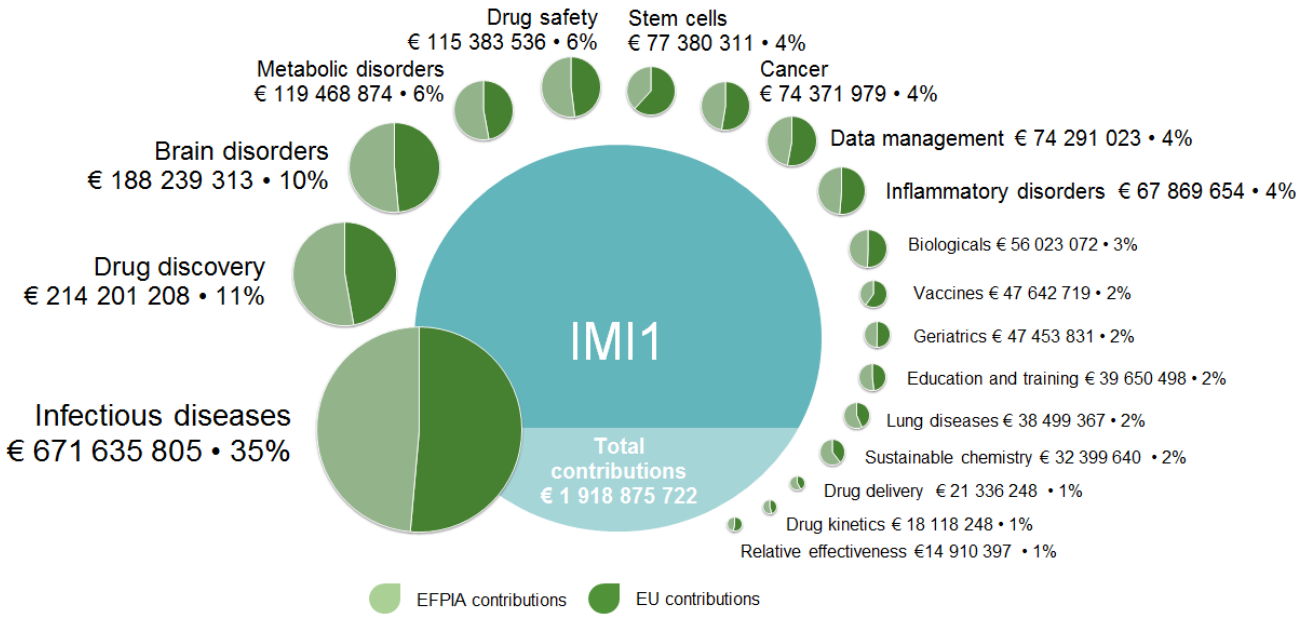
IMI's projects cover a wide range of subjects. Some focus on specific diseases and health issues that will be all too familiar to many Europeans, including neurological conditions (Alzheimer's disease, schizophrenia, depression, chronic pain, and autism), diabetes, lung disease, cancer, Ebola, inflammation & infection, tuberculosis, and obesity.

Others focus on broader challenges in drug development like drug and vaccine safety, knowledge management, the sustainability of chemical drug production, the use of stem cells for drug discovery, drug behaviour in the body, the creation of a European platform to discover novel medicines, and antimicrobial resistance. In addition to research projects, IMI supports education and training projects.

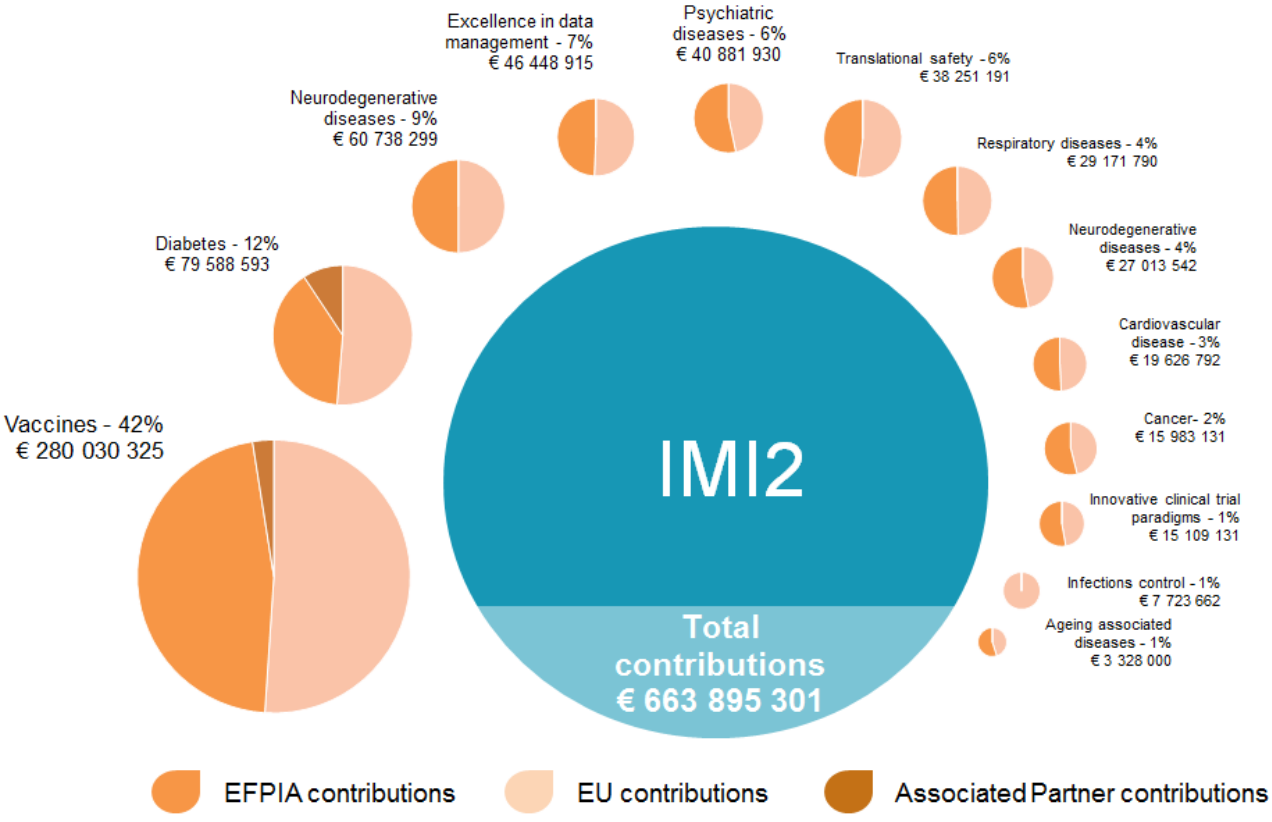
The graphs below show the breakdown of IMI funding by research / disease area and, for each area, the breakdown of funding coming from the EU and EFPIA and (in the case of IMI2 projects) Associated Partners.

[3] Details of organisations eligible to receive EU funding through IMI2 can be found in the delegated regulation (EU) No 622/2014 of 14 February 2014.

Distribution of funding per scientific area - IMI1



Distribution of funding per scientific area - IMI2



IMI project outputs

The overarching goal of IMI1 was 'significantly improving the efficiency and effectiveness of the drug development process with the long-term aim that the pharmaceutical sector produce more effective and safer innovative medicines'. For IMI2, the goals are more specific and are:

- increase the success rate in clinical trials of priority medicines identified by the World Health Organisation;
- where possible, reduce the time to reach clinical proof of concept in medicine development, such as for cancer, immunological, respiratory, neurological and neurodegenerative diseases;
- develop new therapies for diseases for which there is a high unmet need, such as Alzheimer's disease and limited market incentives, such as antimicrobial resistance;
- 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;
- 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.

The following sections provide a snapshot of the successes generated by IMI1 and IMI2 projects in 2016. A detailed list of project achievements for the year can be found in Annex 3 of this report. In both this section and the annex, results are classified according to the following categories that reflect specific issues and stages in drug development which have to be addressed if IMI is to achieve its goals:

- Identification and validation of new drug targets and novel hit and lead discovery
- Establishment of robust validated models and tools for drug discovery and development
- Development of biomarkers and tools predictive of clinical outcomes (efficacy and safety)
- Clinical trials - improved design and process
- Big data solutions to leverage knowledge / implementation of data standards
- Impact on regulatory framework
- Implementation of project results inside industry
- Education and training for new generation of R&D scientists

As both this section and the annex show, IMI projects are delivering a wealth of new knowledge, approaches, tools, methods and technology to help improve the drug development process and achieve IMI's goals in many ways. Furthermore, these results are being taken up and used by the project partners in their everyday activities.

1.2.1 Collaborative research and development related outputs from IMI1 projects

Identification and validation of new drug targets and novel hit and lead discovery

Today, many diseases are still described on the basis of their symptoms. However, while two patients may share a diagnosis, the causes may be different. Many IMI projects are studying the underlying causes of disease, such as genes that are mutated or molecular pathways that have gone wrong. Information on these 'drug targets' is the starting point for a more personalised or stratified approach to treatment. Researchers can screen vast banks of compounds to identify 'hits' – molecules that could interact with the drug targets and stop them from causing disease. These 'hits' are then further studied and refined to create 'leads', molecules which could eventually become drugs if further tests prove that they are safe and effective.

The European Lead Factory – boosting early stage drug discovery in Europe

A key tool in the earlier stages of drug development is a technique called High Throughput Screening (HTS), in which researchers screen large collections of chemical compounds in the hunt for molecules that could be potential drugs or be used in drug development in other ways. Through the European Lead Factory (ELF), 7 companies have pooled 330 000 compounds from their own compound collections to create a single Joint European Compound Library (JECL). By the end of 2016, public partners had contributed a further 130 000 compounds to this unique resource, and it is on track to hit its target size of 500 000 on schedule. The project

also boasts a state-of-the-art screening centre, and between them, the compound library and screening centre represent a unique resource for researchers in Europe and is allowing scientists in both the public and private sectors to speed up their drug development programmes in a wide range of disease areas. So far, ELF has run over 100 screens generating a total of 3 408 hits for public and private target owners. The programme's award-winning intellectual property (IP) system effectively protects the interests of the compound owners, whether they come from the public or private sector, while providing users with information on their 'hits' that allows them to take their research forward.

In 2016, the project decided to waive certain fees for non-profit drug discovery programmes on diseases on the World Health Organization list of neglected tropical diseases (NTDs). The diseases on the list, which include sleeping sickness, rabies, leprosy, and dengue fever, are found in 149 (mainly tropical and sub-tropical) countries and affect one billion people worldwide. The project has already run screens in areas such as dengue fever, sleeping sickness, and leishmaniasis. Another highlight in 2016 was the creation of the first spin-out company based on ELF results. Dr Margit Mahlapuu of the University of Gothenburg in Sweden used the ELF to identify a set of molecules that could be effective at treating certain complications in type 2 diabetes. She has now set up a spin-out company, ScandiCure, with the goal of turning these molecules into a first-in-class anti-diabetic drug.

ENABLE-ing antibiotic discovery

Antimicrobial resistance (AMR) kills at least 25 000 people every year in the EU, and with AMR on the rise, we urgently need new antibiotics. However, developing new antibiotics is extremely difficult and requires a wide range of expertise, including in the early stages of drug development; once a hit has been identified, a lot more work is needed to turn it into a lead.

Guiding academics, SMEs and larger companies along this tricky path is IMI's ENABLE project, which has created a 'drug discovery engine' for researchers with promising early-stage antibiotic discovery programmes. Through ENABLE, researchers work with a diverse range of experts in microbiology, pharmacology and chemistry to help advance their molecule through the drug development process until it is an attractive candidate for clinical testing. Programme owners retain full ownership of their molecules to ensure optimum future commercial development.

SMEs are key players in ENABLE. As of the end of 2016, there were 15 SMEs participating in the project, and SMEs were behind 7 of the 10 new antibiotic discovery programmes submitted to ENABLE during the year. One company that joined ENABLE in 2016 is Spero Therapeutics, which focuses on drugs that could interfere with the activity of DHFR, an enzyme that is used by bacteria in the synthesis of DNA. A US-based company, Spero opened a European office to pursue its activities in ENABLE and to facilitate collaborations with leading European scientists in the AMR field.

ELF and ENABLE link up to advance antibiotic development

The synergies between IMI's ELF and ENABLE projects were made clear in 2016 thanks to a case study involving the University of Oxford. Professor Chris Schofield had identified a potential target in certain bacteria that are currently resistant to a major class of antibiotics. A screen run by the ELF identified some small molecules that could interact with the target. The Oxford and ELF teams worked together to improve the hits, resulting in highly potent compounds with a lot of potential for further development. Professor Schofield then successfully applied to ENABLE for their help in this, and he and his team are now collaborating with ENABLE partners in pharma, small companies and universities from across Europe to optimise this early stage hit and hopefully take it to the more advanced stages of drug development and even early clinical trials.

Other project highlights in 2016

- AETIONOMY identified 180 putative disease mechanisms for Alzheimer's and Parkinson's diseases, of which 6 have been selected for validation.
- DIRECT discovered that the human gut microbiome impacts the serum metabolome and associates with insulin resistance.
- EMIF demonstrated that harmful saturated, ceramide-enriched liver lipidome is a marker of non-alcoholic fatty liver disease (NAFLD).
- ULTRA-DD, together with the Structural Genomic Consortium (SGC) launched the chemical probes portal (www.chemicalprobes.org) to make high quality data available to the chemical biology community.
- ZAPI identified key immunogens against new potential zoonotic diseases.

A more extensive, detailed list of project results in this area can be found in Annex 3 of this report.

Establishment of robust validated models and tools for drug discovery and development

Throughout the earlier stages of drug development, researchers deploy a range of tests and tools to determine whether a potential drug will actually be effective and safe in humans. As they cannot test drugs directly in humans at this stage, researchers rely heavily on 'models' of the disease they are studying. These models can be samples of cells or tissues (these are known as *'in vitro'* models), animals with the disease (*'in vivo'* models), or computer-based virtual models of the disease (*'in silico'* models). However, all too often, these models do not accurately mimic the disease under investigation and so fail to accurately predict how a potential drug will behave in humans. Many IMI projects are therefore working to both assess existing tools, to see which work and which do not, and develop new, better tools.

EBiSC launches European Stem Cell Bank

Most of the cells in our body can only divide to produce other cells of the same type – for example, skin cells can only make other skin cells, and blood cells can only make other blood cells. In contrast, embryonic stem cells are 'pluripotent', i.e. able to give rise to all the different kinds of cell that make up the human body. However, back in 2006 researchers found a way to reprogramme ordinary adult cells to create so-called induced pluripotent stem (iPS) cells. Like embryonic stem cells, iPS cells are able to generate any kind of cell; as such, they offer researchers a good supply of different kinds of human cell that can be used in research and drug development.

For example, iPS cells can be used to study disease biology, identify markers of disease and potential drug targets, and test drug safety and efficacy. In addition, iPS cells help to reduce the use of animals in research.

There are now hundreds of human iPS cell lines and some cell banks around the world. However, the quality of these lines varies enormously (some may not even be pluripotent), and few lines are accompanied by sufficient clinical and other data to ensure that researchers are using the right cell for their needs. Finally, access to these cell lines is often tightly restricted. For this reason, demand for high quality, well characterised iPS cells vastly outstrips supply.

IMI's EBiSC project was set up to stablish a centralised facility where academics, biotech companies, and big pharmaceutical companies can store and access high-quality, well-characterised iPS cells covering a range of disease areas as well as cells from healthy donors.

In early 2016, the EBiSC team launched its online catalogue of induced pluripotent stem cells (iPSCs) which are available to academic and commercial scientists alike for use in research. The cell lines in the EBiSC catalogue were made and deposited by both EBiSC project partners and external organisations. They include cells taken from people with neurodegenerative, heart, and eye diseases as well as from healthy donors. Since the launch of the catalogue, further cell lines have been added; for example, the University of Edinburgh contributed 28 cell lines from patients with bipolar disorder.

By standardising procedures and ensuring the quality of the cell lines and associated data, EBiSC will help academic and clinical researchers shed new light on the biology of diverse diseases. For the pharmaceutical efficiency, the cell lines will represent an important tool for carrying out early stage drug testing. For patients, the project represents an important step in ensuring that iPS cells realise their potential as a tool to improve and speed up the development of better and safer treatments.

Capturing cancer's complexity – PREDECT delivers 'game changer' for research

The goal of the PREDECT project is to improve the animal and laboratory models used in cancer research. In 2016, the team delivered a breakthrough for breast cancer research when they developed the first animal model of a common form of breast cancer that faithfully replicates the human disease. The model opens up new avenues for studying breast cancer and developing and evaluating treatments. Some three quarters of breast cancer cases feature tumours that have a receptor for the hormone oestrogen. Efforts to study these ER+ cancers have been hampered by the fact that animals (like mice) used to study the disease do not accurately replicate how the disease behaves in human patients. Now, PREDECT researchers have created a

mouse model that mimics human ER+ cancer better than any other existing model and so will make it easier for researchers to study things like the action of hormones and molecular responses to treatments. The model is described in the prestigious journal Cancer Cell, and an accompanying editorial describes it as 'a potential game-changer for breast cancer research'.

PREDECT has also made great strides to improve in vitro models of cancer, in which cancer cells are analysed in petri dishes, for example. These models are typically two-dimensional, and as they are relatively cheap and easy to use, they are still widely used in research. However, they do not accurately replicate real tumours in the body, and this hinders the ability of researchers to study cancer in detail and develop new treatments. PREDECT researchers have developed and analysed a number of more complex, three-dimensional models of prostate, breast and lung cancer that may more accurately mimic the behaviour of tumours in the body. Nevertheless, according the project partners, there is no single perfect model that fits all purposes. To help scientists pick the right model for the right situation, the project team has written a paper in the journal Scientific Reports. The article sets out the strengths and weaknesses of the different models and provides detailed protocols for their use as well as advice on when and how to use them. The team hopes that the robust protocols for the set-up and analysis of 3D cultures, as well as the cross-comparison of the platforms presented in the paper, should help scientists both in academia and industry to better incorporate these complex models in the drug discovery pipeline.

Other project highlights in 2016

- COMPACT developed a toolbox of assays to monitor cytosolic delivery of biopharmaceuticals.
- DDMoRe made 105 models available via http://repository.ddmore.eu/models.
- eTOX's main project output, the eTOXsys database, consists of over 7 000 animal toxicity reports and approximately 80 computer models.
- EU-AIMS reprogrammed and genome-edited 8 patient derived induced pluripotent stem cell (iPSC) lines.
- K4DD has developed 26 different assays for 12 soluble targets, and 34 assays for 10 different G-protein-coupled receptors (GPCRs).
- OrBiTo completed a landmark study of existing physiologically based pharmacokinetic (PBPK) modelling tools to determine the most appropriate parameters for *in silico* prediction of drug absorption and plasma concentrations as a result of drug uptake.
- StemBANCC recruited 466 participants, including health people and people from disease cohorts, for the production of iPSCs to produce models of human diseases.

A more extensive, detailed list of project results in this area can be found in Annex 3 of this report.

Development of biomarkers and tools predictive of clinical outcomes (efficacy and safety)

How do you know which patients are on the path to recovery and which not? How can you identify patients who may be at greater risk of developing complications? How do you know which medicine will be safe and effective for which patients? Answering these questions is a key part of drug development, and requires an understanding of which biological markers ('biomarkers') could provide clues to help researchers answer these questions. Ideally, these biomarkers should be easily obtainable, for example through a simple blood test, scan, or patient-reported outcome (PRO). Ultimately, more reliable predictive tests will help to eliminate ineffective or unsafe compounds earlier in the development process, thereby avoiding unnecessary patient exposure and stopping investments in programmes that will ultimately prove unsuccessful.

ABIRISK discovers risks that drive immune response to biopharmaceuticals

A growing number of medicines are based on biological molecules such as proteins and antibodies. Known as biopharmaceuticals, these novel drugs have resulted in new, more effective treatments for a number of serious conditions, including multiple sclerosis (MS) and rheumatoid arthritis. Yet occasionally these medicines trigger an immune reaction in some patients. When this happens, the immune system produces anti-drug antibodies (ADAs) which neutralise the drug; this can reduce the effectiveness of the biopharmaceutical and lead to severe side effects. Now scientists from IMI's ABIRISK project have discovered that the patient's age and gender and even the time of the year that a drug is taken can increase the risk of an immune reaction.

The team studied data from more than 20 000 multiple sclerosis patients who were tested for ADAs in routine clinical testing or research studies in four countries: Sweden, Austria, Denmark and Germany. They found that males and older adults are at a higher risk of developing an immune response when receiving the biopharmaceutical called IFNβ. In patients from Sweden and Germany, starting therapy in April also coincided with a higher likelihood of developing an immune response, indicating that seasonal factors might also play a role. When it comes to a biopharmaceutical called Natalizumab, researchers discovered that females and older people are at a higher risk.

According to the scientists in the study, the findings could be used to develop more personalised monitoring programmes and interventions for patients who are at a higher risk. For example, if the seasonal factor behind the higher risk is due to lower vitamin D levels, vitamin D supplementation at the start of therapy could be used to decrease the risk of the immune response.

EU-AIMS offers early clues on autism

Autism spectrum disorder (ASD) refers to a diverse group of development disorders that are characterised by difficulties in social interaction and communication, and the presence of unusual repetitive behaviours. It affects one child in 110, with boys at greater risk of developing ASD than girls. ASD is a lifelong condition, and for reasons which are not fully understood, the prevalence of ASD is rising. There is currently no treatment designed specifically for ASD.

As the range and severity of symptoms is so broad, identifying young children who are at risk of developing ASD is difficult. Part of IMI's EU-AIMS project is devoted to identifying signs of autism in babies. For example, they have found that early markers of autism identified in babies in previous studies are only associated with later autism symptoms in boys, but not girls. The findings have important implications for prospective studies in terms of directly testing for the moderating effect of sex on emerging autistic traits.

In a preliminary study, the EU-AIMS team also examined more than 20 infants for their light reflexes. They found that infants at risk for autism had hypersensitive pupillary light reflexes, meaning that their pupils have a faster and stronger response to flashes of light. This result, if replicated in a larger cohort, may indicate an early behavioural risk marker for ASD.

This is important because if we can identify ASD earlier, we can ensure children and their families are able to access support from the beginning.

Other project highlights in 2016

- BTCURE discovered that antibodies which can be detected in the blood of some people years before developing rheumatoid arthritis, contribute to the development of the disease.
- DIRECT identified 23 antibodies that are associated with measures of insulin secretion or insulin sensitivity.
- FLUCOP put in place a toolbox to aid in the standardisation of assays to assess human flu vaccines.
- iABC completed a collection of 1 018 cystic fibrosis (and bronchiectasis) pathogens and completed susceptibility testing of these against 9 antibiotics.
- PreDiCT-TB fine-tuned a method that offers a faster way to diagnose tuberculosis (TB) and could improve the speed and effectiveness of preclinical and clinical trials.
- QUIC-CONCEPT elaborated an imaging biomarker roadmap for cancer studies including 14 recommendations to accelerate the clinical translation of imagine biomarkers.
- RAPP-ID completed two prototypes of platforms for point of care testing, a step towards the development of diagnostic tests for use in the clinical setting.
- SUMMIT identified a panel of six biomarkers with improved prediction of type 2 diabetic cardiovascular disease.

A more extensive, detailed list of project results in this area can be found in Annex 3 of this report.

Clinical trials - improved design and process

During clinical trials, medicines are tested for the first time in humans, firstly in healthy volunteers (to check that the drug is safe) and then in patients (to check that it works and to determine the best dose). Clinical trials can take years to run and are incredibly expensive. In addition, the results of clinical trials cannot always be extrapolated to the real world, as patients enrolled in a trial may not be fully representative of the wider patient community. IMI projects are investigating ways of improving the way clinical trials are run, so that they can generate reliable results, faster.

New Drugs for Bad Bugs – tackling the scourge of antimicrobial resistance

Antimicrobial resistance (AMR) represents a serious and growing threat to human and animal health worldwide. It already kills 700 000 people worldwide every year, and that figure could rise to 10 million by 2050. We urgently need new antibiotics, capable of destroying drug-resistant bacteria, yet the drug development pipeline is drying up. The reasons for this are manifold. One major challenge for drug developers is the extremely high cost of running clinical trials on new antibiotics. Put simply, it is hard to find enough patients with the resistant bacteria under investigation to demonstrate that a new antibiotic is at least as good as other, comparable antibiotic drugs.

To address this problem, IMI's COMBACTE family of projects is setting up a pan-European network of hospitals and associated laboratories. So far, the hospital network, dubbed CLIN-Net, counts over 800 hospitals in more than 340 cities in over 35 countries in Europe. The project is working to ensure that the sites are fully trained according to Good Clinical Practice (GCP) guidelines. The COMBACTE team is also setting up two other networks: STAT-Net (which brings together statistics experts to optimise trial design) and EPI-Net (which links up and harmonises different systems of disease surveillance). Between them, these networks will help to significantly facilitate and speed up clinical trials of new antibiotics in the future.

The COMBACTE projects are already running a number of clinical trials of promising antibiotics via the networks. For example, there are two studies of antibiotics designed to prevent Staphylococcus aureus pneumonia in intensive care patients who need a machine to help them breathe: SAATELLITE, a phase 2 trial of MEDI4893; and EVADE, a phase 2 trial of MED13902. By the end of 2016, over 100 patients had been randomised in the SAATELLITE study, while EVADE enrolled its first patients in 2016.

Writing in the journal Clinical Infectious Diseases, the scientists explain the benefits of running these trials through COMBACTE: '[COMBACTE] merges expertise and capabilities from basic science and clinical research experts in the field of infectious disease and critical care, thereby optimizing the interaction of experts. Accordingly, instead of the traditional study designed by a sponsor, with limited scientific input through advisory boards, both SAATELLITE and EVADE have been built by a working group within the consortium, including not only the clinical experts and the Sponsor (MedImmune), but also microbiologists to take advantage of this innovative public–private partnership to address several important microbiological, clinical, immunological, biological, and biomarker questions.'

The network also facilitates the running of studies designed to evaluate the incidence of specific infections in Europe, or to assess the risk factors for certain infections. For example, in 2016, the first patients were enrolled in the ANTICIPATE study, which aims to determine the incidence of Clostridium difficile infection in hospitalised patients who are on antibiotics. The project also continued to recruit patients for ASPIRE-ICU, a study on the incidence of pneumonia caused by *Staphylococcus aureus* and *Pseudomonas aeruginosa* in patients in intensive care. The knowledge gathered through these studies will contribute to efforts to develop new antibiotics and aid in decision making on both research and healthcare priorities.

EPAD – revolutionising clinical trials for Alzheimer's treatments

Dementia already affects over 47 million people globally, and as populations age, this figure is set to rise to over 131 million by 2050. The disease places a huge and growing burden on health and social care systems and on the families and carers of those affected. Yet despite decades of research, there is still neither treatment nor cure for the disease.

One important way of tackling dementia could lie in treating people while they are in the very earliest stages of the disease, when they may have little or nothing in the way of symptoms. IMI's EPAD project's long-term goal is to set up a pan-European platform for clinical trials of novel treatments designed to prevent the onset of dementia. By using a pioneering 'adaptive' clinical trial model, the project will be able to test multiple

treatments at the same time, and analyse the results continuously. The adaptive trial model also allows a more rapid assessment of treatments and the identification of groups of patients that respond best to them. Ultimately, this adaptive model should deliver more reliable results faster and at lower cost.

In 2016, the project started recruiting volunteers for a cohort of people who could eventually be called on to take part in clinical trials run through the EPAD platform. The very first volunteer was Julie Duffus from Scotland; she was inspired to take part by her parents, both of whom had dementia. By the end of the year, the project had recruited almost 100 people from a number of centres across Europe. The project aims to recruit a total of 6 000 people from across Europe to take part in the project. Participants will have regular health checks including blood tests and brain scans. Researchers will also track their thinking skills over time using tests of mental agility.

The team hopes to use the information gathered to develop tests for early signs of Alzheimer's disease that may indicate when a person is at risk of dementia, but before symptoms appear. They will then invite these people to take part in clinical trials aimed at testing interventions that could delay, or even prevent, the onset of dementia.

Other project highlights in 2016

- AETIONOMY recruited 165 people for the Parkinson's disease part of a clinical study.
- COMBACTE-CARE has so far recruited 200 patients in over 20 countries for the EURECA study on multidrug-resistant Gram-negative infections.
- COMBACTE-MAGNET completed recruitment for the RESCUING study on complicated urinary tract infections; the project is now analysing 1 009 evaluable cases collected from 20 sites in 8 countries.
- EU-AIMS enrolled 341 and 155 children and high and low risk respectively of ASD. The projects Longitudinal European Autism Project (LEAP) completed recruitment, exceeding its target of 727 participants.
- GetReal published case study reports on 5 disease areas on the use of real-world evidence to demonstrate the effectiveness of new drugs.

A more extensive, detailed list of project results in this area can be found in Annex 3 of this report.

Big data solutions to leverage knowledge / implementation of data standards

Vast amounts of data are generated daily by researchers and in healthcare. If this data can be linked up and analysed, new information and insights can be gathered to further our understanding of diseases and help in the development of new treatments. However, combining data from lots of different sources brings technical challenges (if file formats and terminology are different) as well as legal and ethical challenges (depending on what permissions were asked of people, like patients, behind the data). IMI projects are devising innovative ways of overcoming these challenges in a number of ways.

Open PHACTS – rapid access to consolidated information

A lot of useful information on drugs, drug targets and drug development can be found in diverse databases that are publicly available online. However, looking for information in these databases one by one is a long and laborious task. IMI's Open PHACTS project created an online, open access platform that uses semantic web technology to allow scientists to easily access and process data from multiple sources to rapidly solve real-world drug discovery problems. Studies showed that the platform could dramatically cut the time taken to carry out certain searches. The project has regularly improved on and added to the platform, for example by including access to additional databases and by creating a 'virtual machine' version of the platform. This allows companies to integrate their own data into the platform inside their firewalls, without having to worry about confidential information getting into the public domain.

The IMI-funded project ended in 2016, and the project's legacy passed to the Open PHACTS Foundation, which the project created to ensure the sustainability of the work carried out by the consortium. The foundation is already a member of two Horizon 2020 projects, demonstrating its expertise in data interoperability.

At the end of the project, the partners reflected on the success of the initiative in an article on the project website: 'Overall the development of the Open PHACTS Discovery Platform has been a remarkable success, demonstrating just what can be achieved when the private and public sectors work together,' they wrote. 'Although Open PHACTS began as somewhat of an "arranged marriage", over the last five years the project has fostered and supported a community that has become much closer to a real family. We managed to bridge not only the cultural divides among different nationalities, but also the divide between scientists and engineers – which some would argue is much bigger!'

EHR4CR – drawing on electronic health records for clinical research

Electronic health records (EHRs) contain information that has immense potential for research use. However, different EHR systems and concerns about privacy and security mean that accessing and making use of this information is now always is. IMI's EHR4CR project has developed a robust, scalable platform that can draw on de-identified data from hospital EHR systems in different countries in Europe, while respecting all relevant ethical, regulatory, and data protection policies. Crucially, the project secured acceptance from the patients, the public and the research and health service communities.

The platform allows those running clinical trials to predict how many patients may be eligible for a clinical trial, assess the feasibility of the study, and locate the most relevant hospital sites. EHR4CR showed that such a platform can significantly improve the efficiency of designing and conducting clinical trials, reducing time and costs, reducing administrative burdens, optimising protocol feasibility assessments, accelerating patient recruitment, making study conduct more efficient, and enabling the participation of European hospitals in more clinical trials and thereby potentially increasing research income. The platform has been implemented in 11 hospital sites.

The project created the European Institute for Innovation through Health Data (i~HD) as a not-for-profit organisation to carry on the project's work and to develop and promote best practices in the governance, quality, semantic interoperability and uses of health data, including its reuse for research. An important role of i~HD is to provide independent governance oversight of clinical research platforms and their expanding networks of hospitals. i~HD held its inaugural conference in March 2016. It is also one of 30 organisations in Europe appointed by the European Commission to its strategic consultation and think tank organisation: the eHealth Stakeholder Group. This Group, representing the interests of just about every kind of stakeholder involved in health, healthcare and health ICT, is regularly updated and consulted on the strategy and initiatives led by DG CONNECT and DG SANTE.

Other project highlights in 2016

- Largest existing database of AMR spanning 22 years and 68 countries allowed completion of two systematic reviews on spread and impact and informed design of 2 models of the spread of AMR.
- EMIF harmonised 6 cohorts that are now available in tranSMART, and included the first 124 cognitively normal subjects in the preclinical Alzheimer's disease cohort study.
- eTOX's OntoBrowser allows curators to map terms from multiple systems to preferred ontology terms.
- eTRIKS is currently engaging 40 projects and exploring opportunities with a further 8.
- EUROPAIN created the largest available clinical database of volunteers and neuropathic pain patients, with 3 500 individuals.
- iABC established a data coordinating centre to support the European Bronchiectasis Registry.
- Open PHACTS released an updated version of the project's application programming interface (API), thereby allowing researchers free access to a large, rich pharmacology data set.
- WEB-RADR developed and applied English, French and Spanish dictionaries to map colloquial phrases commonly used in social media to 500 MedDRA preferred terms.

A more extensive, detailed list of project results in this area can be found in Annex 3 of this report.

Impact on regulatory framework

Before medicines can be used in patients, they must be approved by regulatory authorities, such as the European Medicines Agency (EMA). Regulatory authorities assess data on the benefits and risks of a new medicine that is gathered during drug development. Many IMI projects are developing innovative tools and methods of assessing the safety and effectiveness of medicines, and are liaising closely with regulatory authorities to be sure that results based on these are accepted as reliable and valid.

WEB-RADR apps make reporting side-effects easier

When people taking a medicine experience a side-effect (often known as an adverse drug reaction or ADR), the regulatory authorities want to know about it so that they can assess the safety of medicines in the long term and, if needed amend the advice given to patients for example. For a long time, reporting an ADR involved filling in a paper form or, in more recent years, an online form.

Now IMI's WEB-RADR project has brought ADR reporting into the 21st century by developing apps that allow patients, carers and healthcare professionals to report suspected ADRs via a simple app on their smartphones. Through the app, users can not only report ADRs, but find out about reported side effects of any medicine, and opt to receive alerts about specific drugs.

A UK version of the app was launched in 2015, and Dutch and Croatian versions followed in 2016. All three national versions of the app are available for both iOS and Android phones. The project team is now developing a generic app toolbox that other countries can use and adapt for their own reporting systems.

SAFE-T gains support of regulatory agencies for safety tests

It is estimated that 197 000 deaths per year in the EU are caused by adverse drug reactions and that the total cost to society in the EU is EUR 79 million. Among the side effects most challenging to drug developers and prescribers alike are drug-induced injuries to the kidney, liver and vascular system. Current tests designed to detect these problems before drugs make it to the patient do not always predict side effects. There is therefore an urgent need for new and better tools in this area.

IMI's SAFE-T project has made enormous progress in this important area, by developing and improving tools for the prediction, detection, and monitoring of drug-induced injuries to the kidney, liver, and vascular system, using markers in patients' blood and/or urine.

Most importantly, the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA) and have both issued 'letters of support' on some of these biological markers. The letters of support indicate that the new biomarkers have the potential for use in drug development, and that additional exploration and data generation is warranted. As such, the letters are designed to encourage scientists to collect additional data from nonclinical and exploratory clinical trials.

Project coordinator Michael Merz of Novartis is optimistic about the long-term impacts of the project, stating 'We have generated a lot of data on new biomarkers – molecules that we can measure in the blood or urine – that allow us to detect drug side-effects earlier and more accurately than has been feasible in the past. In addition to helping detect drug-related injuries, these biomarkers will also help improve diagnosis and monitoring in chronic disease patients. They will help clinicians make better decisions on specific treatment alternatives and other things, such as when to stop treatment. I think there will be lots of benefits to patients across a large variety of different diseases.'

Other project highlights in 2016

- ADVANCE finalised its code of conduct for benefit-risk monitoring of vaccines.
- EUROPAIN input was integrated into the new EMA guideline for the development of new treatments for pain.
- SPRINTT found that frailty has an incremental effect on ambulatory health expenditures of an additional EUR 570 for pre-frail people and EU 1 270 for frail people.

A more extensive, detailed list of project results in this area can be found in Annex 3 of this report.

Implementation of project results inside industry

The ultimate goal of IMI is to make a very practical, concrete difference to the way new medicines are developed, by delivering tools, knowledge and methods to make the process faster and more efficient. With this in mind, the ultimate test of the significance of a project result is whether or not it has been taken up and used by the project partners, particularly those in industry. With the first IMI projects now closing, it is clear that many results have indeed been taken up by project participants.

U-BIOPRED breathes new life into severe asthma research

About 300 million people worldwide suffer from asthma, and some 250 000 deaths annually are attributed to the disease. The vast majority of asthma patients are able to control their symptoms with corticosteroids. However, for patients with severe asthma, currently available drugs simply don't work and as a result they require frequent hospital admissions. Although they represent just 3-8% of asthma patients, severe asthma patients account for half of all asthma-related healthcare costs.

The U-BIOPRED project was the biggest and most complex research project undertaken to understand severe asthma to date. It aimed to speed up the development of better treatments for patients with severe asthma by understanding the disease in more depth. More specifically, its main goal was to identify different subtypes or 'handprints' of severe asthma by adding complex biological markers to clinical characteristics, so that new treatments can better target the disease in different patients.

Thanks to close collaboration between academics, industry and patients, the project succeeded in identifying four to five subtypes of severe asthma among adult patients (depending on the clinical and biological markers used), a discovery which is already paving the way for the development of more effective treatments. Initial results also show that there might be several, slightly different subtypes of asthma in children, but that analysis is still on-going. The project is therefore helping to redefine the classification of disease for severe asthma.

The project also resulted in the development of a range of tools and resources relevant to severe asthma research.

The knowledge and data from U-BIOPRED is already being used extensively by the pharmaceutical companies to address a number of key bottlenecks in drug discovery which will bring immense benefits to patients. For example, as U-BIOPRED has mapped the biological processes of severe asthma in patients, companies now have a clearer view on which biological processes should be targeted with future drugs.

Furthermore, thanks to the U-BIOPRED data, companies can now predict whether some of the drugs which they have in the pipeline will be effective for severe asthma patients.

Finally, the project will help to get the right drugs to the right patients. There are already some new drugs for asthma and severe asthma which work in some patients and not in others. By using the handprints as part of clinical trials, companies and caretakers can now start predicting whether or not a certain drug will be effective in individual patients. In the long run, this will be very beneficial for patients because they won't be unnecessarily treated by drugs which don't work for their asthma subtype.

eTRIKS inspires a spin-off for scientific data analysis

IMI projects not only deliver great results, but sometimes also inspire the creation of spin-off projects, providing indirect economic benefits. Proof of that is ITTM (Information Technology for Translational Medicine, S.A.), a Luxembourg company, which was built on the knowledge and expertise gained during the eTRIKS project.

While working on eTRIKS, researchers from the University of Luxembourg realised that there is really high demand for cleaning, filtering, hosting and standardising data in the pharmaceutical sector. Those services were outside the scope of the eTRIKS project which mainly focuses on providing an open source platform for knowledge management. So, the Luxembourg partners involved in the project started a new company, ITTM. 'The expertise we gained during eTRIKS regarding curation and standardisation of data are the building blocks of ITTM's service offers,' said Reinhard Schneider, Head of the Bioinformatics Core facility at the University of Luxembourg's Centre for Systems Biomedicine. 'In addition we were lucky to get the POST

group of Luxembourg as a strategic investor. They own big, very secure data centres, which give ITTM a very professional hosting infrastructure.'

Other project highlights in 2016

In total, 17 projects had results implemented inside industry in 2017.

- CHEM21 developed a rapid, simple way to synthesise the medicine flucytosine; the technology involved has been patented and is being developed further within industry.
- eTOX's toxicology database and models have been implemented in all 13 industry partners.
- In the European Lead Factory, 17 out of 49 screens run by EFPIA partners have triggered further work.
- K4DD results are being integrated in companies' drug discovery pipelines, with some implementing kinetic aspects in the hit finding phase and others in the lead optimisation phase.
- OncoTrack's animal and cell culture models are being used for drug screening by EFPIA partners.
- PREDECT's bioreactor-based 3D tumour cell models have been implemented in 4 organisations.
- TRANSLOCATION's assays are being used by industry partners.
- ULTRA-DD results have spurred at least one pharmaceutical company to launch an effort to generate compounds suitable for trials in glioblastoma.

A more extensive, detailed list of project results in this area can be found in Annex 3 of this report.

Education and training for new generation of R&D scientists

If Europe is to stay at the forefront of medical research and drug development, it needs a highly-skilled workforce with a broad understanding of the viewpoints of the different stakeholders involved in the process. IMI's education and training projects have now trained large numbers of new and existing professionals from across Europe and from different sectors, giving them the skills and knowledge to advance in their careers.

Patient power! EUPATI trainees get to work

Patients increasingly want and expect to be involved in all aspects of medical research and drug development. There is also greater recognition of the value patients bring to research, in terms of their knowledge of their disease/condition, and input and ideas on issues like setting research priorities, study design and communication. However, for patients to be able to contribute effectively to research projects, they need to understand how medicines are developed and get to grips with the jargon used. IMI's EUPATI project was set up to train patients and their representatives in medicines development so that they can effectively contribute to projects, programmes and initiatives as experts.

The project's legacy is embodied most visibly in the almost 100 patients and advocates who took the year-long EUPATI 'expert level' course. The course covered six areas: the medicines development process; personalised medicine; drug safety and risk/benefit assessments; health economics and health technology assessment; clinical trials; and patients' roles and responsibilities in medicines development. The second edition of course finished in autumn 2016, early indicators are that the graduates are already using their skills and knowledge in committees, projects and initiatives across Europe and beyond. For example, they are now more likely to be involved in leadership roles in patient groups, and are much more likely to be providing advice to various stakeholders in medicines development, such as pharmaceutical companies and regulators. The value of the course is also demonstrated by the fact that the project has obtained resources to continue running the course even once the IMI-funded project has finished.

The project has also developed an online educational toolbox with extensive resources in several languages that will help patients worldwide to learn about medicines development and how patients can contribute to it. The toolbox was launched at the beginning of 2016 and by the end of the year had attracted 18 000 users.

EU2P – training new and existing professionals in pharmacovigilance and pharmacoepidemiology

Since its launch in 2009, IMI's education and training project EU2P has developed an impressive suite of courses in pharmacovigilance and pharmacoepidemiology, ranging from full-blown Master and PhD programmes to short courses and, as of 2016, bite-sized online courses. The courses are delivered online,

and feedback from course participants is positive. The project has achieved a global reach; 47% of students now come from outside the EU and 15% come from developing countries.

Although the IMI-funded project ended in 2016, nine project partners (five academic and four pharmaceutical companies) signed a Memorandum of Understanding to continue working together to deliver the Masters, Certificate and short courses.

Other project highlights in 2016

- CHEM21 launched an online training platform on green and sustainable methodologies for the synthesis of pharmaceuticals.
- DDMoRe ran 8 tutorials on building and uploading models.
- EBiSC ran two courses on iPS cells.
- The European Lead Factory trained over 75 post-docs in industry methods and approaches.
- EMTRAIN's on-course resource centre now has around 7 700 entries with 3 627 masters programmes, 3 787 continuing professional development courses, and 1 157 PhD programmes. Use of on-course now exceeds 1 500 visits per week.
- EU2P awarded 9 students the joint Master of Science in Pharmacovigilance and Pharmacoepidemiology and 55 students the joint EU2P certificate.
- SafeSciMET completed the final 7 courses to complete the project's third course cycle. In total 230 people from 34 countries participated in the third course cycle, including attendees from industry (52%), academia (37%) and regulatory agencies (9%).

A more extensive, detailed list of project results in this area can be found in Annex 3 of this report.

1.2.2 Collaborative research and development related outputs from IMI2 projects

The first IMI2 projects started around the beginning of 2015 and reported for the first time in 2016. Although it is still early days for these projects, their initial results show that they are indeed making progress. The greatest progress has been made in IMI's Ebola projects, which were the first IMI2 projects to get underway.

Ebola+ projects: preparing for the next outbreak

The eight projects in IMI's Ebola+ programme started in late 2014 and early 2015, when the outbreak in western Africa was still going strong. The projects necessarily had to get up and running quickly. In addition, as the outbreak evolved, they had sometimes had to change their plans to adapt to the new situation.

During an Ebola outbreak, healthcare workers need to be able to safely and rapidly diagnose patients. This is challenging as blood and other bodily fluids are highly infectious. IMI's EbolaMoDRAD project developed a way to inactivate the Ebola virus in blood samples so they can be safely processed in the field or easily transported to other centres without the need for high containment facilities. Meanwhile the MOFINA project successfully tested a device designed to test for the Ebola virus and related diseases in three European reference labs. It has also passed initial field studies in Sierra Leone. The device is now ready for product registration and the data obtained from lab and field tests is being submitted to the regulatory authorities.

IMI projects are also running clinical trials of two Ebola vaccine regimens. Of particular interest here is the work of the EBODAC project, which was set up to develop a communication strategy and tools to promote the acceptance and uptake of new Ebola vaccines. Here the project faced two major challenges: fear, mistrust and resistance directed towards the Ebola response which also permeates vaccine trials and risks affecting the acceptance of an approved vaccine without adequate trust-building; and difficulties in correctly identifying people, in settings where people do not always have a form of identification, and where fear and distrust around Ebola have sometimes led people to go into hiding.

By working closely with local groups and community leaders and using public meetings, house visits, drama and radio, EBODAC engaged with almost 10 000 people in Kambia, a remote area of Sierra Leone. The project used biometric identification (iris scans and fingerprints) for nearly 900 volunteers to ensure that trial participants received both vaccines in the regimen. The project also used mobile message to help 419 participants from rural areas to vaccinate on time. The project hopes that its experiences in Kambia will also prove useful in other regions and for other disease outbreaks.

The projects are also providing an important role in education and training of the local population in western Africa. For example, the EBODAC trained over 100 local staff in clinical trials, community engagement, data entry, use of biometric identification and other technological tools, while EBOVAC2 provided training on blood sample handling and other techniques.

Other IMI2 project highlights in 2016

- ADAPT-SMART published a discussion paper on engagement criteria for MAPPs (medicines adaptive pathways to patients).
- EBOMAN extends its aseptic fill and finish capability by around 300% and reinforces its ability to support early phase biologic supply needs for clinical trials.
- EBOVAC1 published data from a trial in the UK (87 participants) showing that the Janssen prime-boost Ebola vaccine regimen is safe, well tolerated, and induces durable immune responses. In total, 1 653 people have been enrolled in the EBOVAC1 and EBOVAC2 trials in Europe and Africa.
- INNODIA discovered novel beta cell targets of early autoimmune attack in diabetes.
- VSV-EBOVAC identified a series of new biomarkers of vaccination with VSV-ZEBOV.

A more extensive, detailed list of project results in this area can be found in Annex 3 of this report.

1.2.3 Assessing the impacts of IMI project outputs

In 2016, IMI commissioned a detailed analysis of the socio-economic impacts of its first projects, and started to organise meetings with the first projects to finish with a view to capturing their most significant results and impacts. All of these have helped to reveal the sheer diversity of results delivered by IMI's projects and, most importantly, their impact on the project participants in particular and drug development more broadly.

Major report reveals socio-economic impact of Innovative Medicines Initiative projects

IMI commissioned a panel of independent, high-level experts from the fields of health economics and research and innovation policy to analyse in detail the outputs and impacts of the first nine IMI projects to finish. Their report, published in May 2016, demonstrates that IMI projects are making concrete improvements to pharmaceutical R&D, for example by leveraging funding; creating new knowledge and tools; and making Europe an attractive place to carry out research. Importantly the report notes that many of the projects' achievements would not have been possible without IMI. Key messages from the report include:

IMI projects are delivering on IMI's goal of helping to make concrete improvements to the medicines development process

Broadly, most of the impacts identified by the experts fall into the category of improvements to the medicines R&D processes. As such, the report demonstrates that IMI is delivering on its goal, set out in the legislation creating IMI, of 'significantly improving the efficiency and effectiveness of the drug development process'.

Here one very clear impact is the vast amounts of new knowledge generated by the projects, which between them have already published 546 scientific papers, with more in the pipeline. The projects have also developed and tested many new tools for studying diseases and developing new drugs. Furthermore, in some cases, new tools and resources developed by IMI projects have been commercialised, often by small and medium-sized enterprises (SMEs). In the long term, the knowledge and tools arising from these projects should help to speed up drug development, improve clinical trial design, cut costs, reduce the need for animal testing, and cut failure rates in drug development.

IMI projects are creating long-lasting collaborative networks

The report also highlights IMI's role in creating long-lasting, collaborative networks. For many of the projects studied, the groups involved had never worked together before embarking on the IMI project together. Collaborating allowed the partners to share ideas, knowledge and experiences as well as risks. The benefits of these collaborations are evidenced by the fact that in several cases, the partners are continuing to collaborate even though the IMI project is over.

IMI leverages additional funding for medicines research and development

Through IMI, the European Commission invested a total of €82.3 million in the 9 projects studied. On top of this, EFPIA companies committed €104.8 million to the projects and a further €30.5 million came from other sources. This means that every euro invested in IMI by European taxpayers leveraged an additional €1.64.

IMI is making Europe an attractive place to carry out pharmaceutical research

The report also notes that the projects have helped to raise the profile and reputation of Europe as a location for medical and pharmaceutical research.

The report includes a number of recommendations on how IMI can maximise the socio-economic impacts of its projects. IMI is analysing the recommendations and determining how best to implement them.

Meetings with projects highlight projects' legacies and impacts

In 2016, IMI started organising meetings with the coordinators and other key partners of projects that have come to a close. The meetings provide an opportunity for the consortium to highlight to the IMI office the most significant results and discuss the impact and legacy of the project in the longer term. IMI uses the information presented during the meeting to update the project's factsheet on the IMI website, and the communication team publishes interviews with the project coordinator(s). The project representatives are also invited to discuss any lessons learned and best practices that could be useful to the IMI office, other projects, or EFPIA and the European Commission. Points raised by many projects include:

- involve core stakeholders (patients, regulators) early on;
- ensure good communication within the project;
- set up good governance structures (but be flexible with them if needed);
- manage data proactively;
- allow sufficient resources for project coordination and management (and make sure the project manager is up to the task);
- maintain a strong focus on achieving the project objectives – this will help the project to deal with changes and challenges that are inevitable in a multi-year, multi-partner project;
- don't wait until the end of the project to start thinking about sustainability.

The following projects had meetings with IMI in 2016. Summaries of the projects' impacts are described below; more information can be found in the project factsheets and interviews with the coordinators on the IMI website.

U-BIOPRED

Severe asthma patients were poorly understood until now and no effective treatment is available for them. IMI's U-BIOPRED project made a groundbreaking step forward in understanding this disease by uncovering a number of subtypes of severe asthma. The discovery is already helping researchers from universities, pharmaceutical companies and patient groups in their search for new, more effective treatments. Thanks to U-BIOPRED, it will soon be easier to select the right patients for the right drug, bringing concrete socio-economic benefits.

- Project factsheet
- 'Without IMI this would have never happened' – an interview with U-BIOPRED's Peter Sterk

PROactive

Although lack of physical activity is one of the most common predictors of mortality in patients with chronic obstructive pulmonary disease (COPD), there are no validated tools to measure the impact of the disease on how patients experience physical activity. The PROactive project developed new, innovative patient reported outcome tools to capture both the experienced amount of physical activity and the difficulties during activity, opening the way for the development of more effective treatments. The project also developed innovative ways to enhance physical activity, both as it is objectively measured and as it is experienced by patients. Furthermore, the project succeeded in placing physical activity higher on the agenda of clinicians, patient organisations and researchers, and patients are already reaping the benefits.

- Project factsheet
- PROactive draws to a close, delivers on its promises – an interview with the project coordinators

SAFE-T

One of the key challenges in drug development is improving patient safety: many drug side effects are not adequately predictable and are detected too late, when the risk for serious outcomes is high. The scientists of the SAFE-T project developed improved tools for prediction, detection, and monitoring of drug-induced injuries to the kidney, liver, and vascular system, using markers in patients' blood and/or urine. Application of SAFE-T biomarkers will make drugs safer, reduce the number of drugs that have to be abandoned in late stages of development, and improve diagnosis and management of acute and chronic diseases relevant to public health not only in Europe, but globally.

- Project factsheet
- ‘There will be lots of benefits to patients’ – an interview with the SAFE-T project coordinators

SUMMIT

Diabetes is becoming a worldwide epidemic and there is a high therapeutic need for new treatments for diabetes complications, such as chronic kidney disease and cardiovascular disease. SUMMIT developed new biomarkers, imaging techniques and animal models which will make future preclinical and clinical trials more reliable and efficient, speeding up the development of new drugs. The project also raised the profile of European researchers, enabling them to become globally recognised as leaders in the field. Finally, the project resulted in several patent applications and the creation of a start-up, bringing concrete socio-economic benefits.

- Project factsheet
- ‘We took the lead over US-based projects’ – an interview with the SUMMIT project coordinators

MARCAR

One of the key questions scientists ask during early drug development is: could a potential drug cause cancer? MARCAR project scientists set out to discover early biological indicators which could help detect some of the more indirect ways in which drugs cause tumour formation. During the project, they discovered several potential biological indicators and a wealth of knowledge which could make drugs safer and decrease the time it takes for innovative drugs to reach patients. Additionally, one of the imaging techniques developed during the project has the potential to significantly reduce the number of animals used in the early stages of drug development.

- Project factsheet
- ‘It was a really fantastic experience’ – an interview with the MARCAR project coordinator

EUROPAIN

Only 30 % of patients with chronic pain receive effective treatment and when it comes to neuropathic pain, which results from nerve fibres being damaged, dysfunctional or injured, this figure is even lower. By creating unprecedented levels of cooperation among industry, academia and SMEs, EUROPAIN transformed the neuropathic pain field in a number of ways. Firstly, it generated the knowledge and tools which will make conducting pre-clinical and clinical trials more reliable and effective. Secondly, it came up with a new way of classifying patients which could lead to the development of more personalised medicines. Thirdly, the project made its mark on the European regulatory guidelines and a number of its outputs are already being used by the pharmaceutical industry. In the long-term, patients could reap many benefits by gaining access to more affordable, personalised treatments.

- Project factsheet
- ‘More successful than what we thought possible’ – an interview with the EUROPAIN project coordinator

1.2.4 Collaboration among consortia and with external bodies

IMI Alzheimer's Platform and the Human Brain Project (HBP)

A workshop was organised on 7-8 June 2016 in Geneva, Switzerland, bringing together teams from HBP's Medical Informatics and Neuroinformatics Platforms, and representatives from three projects of the IMI Alzheimer's Platform: EMIF, AETIONOMY and EPAD. The aim of this technical workshop was to enable sharing and learning between the HBP and IMI projects with regards to platforms technologies and data.

The Global CEO initiative for Alzheimer's disease (GAP)

The collaboration between IMI's EPAD project and GAP progressed in 2016 and the two consortia met during the Alzheimer's Association International Conference, held on 22-28 July in Toronto, Canada to further advance discussion on alignment of protocols and sharing learning on ways to access large numbers of participants who are well-characterised and ready to enter a longitudinal cohort study, and on processes for certifying networks of sites that use streamlined procedures with a standing staff.

Foundation for the National Institutes of Health (FNIH) Biomarker Consortium and National Institute for Mental Health (NIMH)

Collaboration has continued throughout 2016 between IMI's EU-AIMS project, the FNIH Autism Biomarkers Consortium for Clinical Trials (ABC-CT), and NIMH, with further alignment on development of biomarkers as well as coordination among public and private sector partners.

As a further development of the collaboration between IMI and the NIMH, the latter decided to contribute to the project to be created via the autism topic launched as part of IMI2 – Call 10 in December 2016 via a Memorandum of Understanding that will be signed between the project and NIMH, to fully align the NIMH and IMI activities.

In July 2016 at the Alzheimer's Association International Conference in Toronto, the leadership of the IMI SGG Neurodegeneration met with the leadership of the FNIH Accelerating Medicines Partnership (AMP) to continue discussions and share their vision for future research priorities and discuss how to best align.

Critical Path Institute (C-Path)

IMI became an observer on the Coordinating Committee in the Critical Path Institute's Pediatric Trials Consortium (PTC). As IMI was preparing a topic related to the creation of a pan-EU paediatric clinical trials network that became part of IMI2 – Call 10 launched in December 2016, this participation was important to share information in particular on the progress of PTC. Ultimately, collaboration and alignment between the C-Path initiative and the resulting IMI project is expected to foster the goal of developing a global paediatric clinical trials network.

In addition, IMI diabetes project INNODIA has entered into collaboration with C-Path by signing a Confidential Disclosure Agreement (CDA). C-Path is fostering US-based public-private-partnerships in currently 12 consortia dealing with different disease areas and regulatory topics. INNODIA and C-Path plan to collaborate in the area of type 1 diabetes.

ULTRA-DD and patient organisations

ULTRA-DD has established formal collaborations with several patient organisations, including Myeloma UK and The Brain Tumour Charity. The patient organisations have committed to sponsoring postdoctoral researchers whose scientific outputs will contribute directly to the project. The sponsorship of about €1.5 million for the next two years will be done through the Structural Genomics Consortium (SGC), one of the partners in ULTRA-DD. With this step, these organisations will become directly involved in the scientific aspects of the project, helping to speed up the development of medicines for diseases which they are most interested in.

ULTRA-DD and other funders

Some members of the ULTRA-DD project hold grants with the Medical Research Council (MRC) and Biotechnology and Biological Sciences Research Council (BBSRC) involving numerous collaborators. As part of these grants, we collaborate with companies outside the ULTRA-DD partners, e.g. Boehringer Ingelheim. Collaboration with Promega on bromodomain profiling; Science for Life Lab in Stockholm for antibody production; University of California at San Francisco (UCSF) and Karolinska for chemical probe profiling; collaboration with a number of partners and academic entities for target selection and prioritisation; collaboration with Diamond Light Source (Oxford).

Workshop: Transatlantic collaboration on clinical trials related to antimicrobial resistance

A workshop, 'Transatlantic collaboration on clinical trials related to antimicrobial resistance', was held in Stockholm, Sweden in January 2016 to discuss opportunities for collaboration and challenges for the efficient conduct of high-quality clinical trials related to antimicrobial resistance. The workshop was organised by IMI in collaboration with the National Institute of Health/National Institute of Allergy and Infectious Diseases (NIH/NIAID), the European Commission (EC), the Joint Programming Initiative on Antimicrobial Resistance (JPIAMR), and the IMI project COMBACTE. At the workshop, very committed and lively discussions took place between the different stakeholders from Europe, the US, and Canada, including academic clinical investigators, large pharmaceutical companies, small- and medium-sized companies, and relevant funding organisations. This workshop was an important opportunity for recognising similar lessons learned and difficulties experienced by the ND4BB clinical networks and US initiatives. It also set the grounds for the US Antibacterial Resistance Leadership Group (ARLG) and the ND4BB clinical investigator network CLIN-NET to exchange and align for increased collaboration, as well as for further exploration of a joint clinical trial network. Since the workshop, continuous exchange between existing EU and US networks for the conduct of clinical trials related to antimicrobial resistance has taken place, resulting in alignment between EU and US capabilities and an increase in sharing of experiences in conducting multidrug resistance trials. Specifically, a test case is ongoing on how alignment of EU and US clinical trial structures could help meet patient enrolment goals. Through IMI's CLIN-NET and LAB-NET, suitable clinical sites are being identified to participate in one of the ongoing NIH/NIAID targeted clinical trials on multidrug resistance.

Workshop: Driving infectious diseases diagnostics toward the sustainable development and use of antibiotics

Because of the major health threat of antimicrobial resistance, we need a paradigm shift in the way we deliver healthcare: novel ways to prevent infections, real-time tracking of resistance trends, innovative actionable diagnostics, and reduced inappropriate antibiotic prescribing. Personalised medicine in infectious diseases, based on novel, rapid and reliable diagnostic strategies would help achieve this paradigm shift by identifying those patients who really need antibiotics, and by helping to select the narrow-spectrum antibiotic of choice. A workshop, organised by IMI in collaboration with BioMerieux and EFPIA in December 2016, brought together for the very first time the major diagnostics companies in Europe with an interest in AMR, including (in alphabetical order) Alere, BD, Biocartis, BioMerieux, Bio-Rad, Cepheid, Janssen Diagnostics, Philips, Roche, and Thermo Fisher, as well as representatives from the Bill & Melinda Gates Foundation the Wellcome Trust. The group explored whether there was scope to collaborate and as a result of the workshop was able to formulate a joint mission statement for a potential IMI project to 'demonstrate the value of diagnostics for the optimal use of antimicrobials and healthcare resources in a standardised care environment, thereby reducing inappropriate antibiotic utilisation and AMR rates'. As a next step, a consultation workshop with stakeholders more broadly is envisaged.

Cross Project Meeting: EBOLA+ (IMI2 – Call 2)

In February 2016, the IMI Programme Office organised a one-day cross-project meeting bringing together the eight IMI projects funded under the Ebola+ programme. The meeting was also attended by the newly formed Ethics Board supporting all Ebola+ projects. The meeting helped foster exchanges between the projects and identify common challenges. It also helped to more clearly identify the scope of a Joint Information Centre.

1.3 Stakeholder engagement

1.3.1 SME involvement

In total, there are 198 SMEs involved in IMI projects. As a proportion of participations, SMEs account for 11.78 % of EU beneficiaries and receive 10.33 % of EU funding for the IMI2 programme. For IMI1, SMEs participations account for 15.96 % of EU beneficiaries and receive 13.25 % of EU funding.

In 2016, the IMI SME engagement strategy was reviewed and updated based on consultations with a broad range of stakeholders. The first elements were implemented which included highlighting opportunities for SMEs in IMI2 - Call 10 topic texts and promoting these opportunities through a number of communication channels such a dedicated SME webpage, through the IMI2 States Representatives Group, and through interactions with Europe-wide umbrella organisations. In 2017, these activities will be continued, and the remaining elements of the SME strategy will be implemented.

In addition to the direct involvement of SMEs as IMI beneficiaries, several IMI projects support the activities of SMEs. For example, the European Lead Factory and ENABLE provide open platforms that allow SMEs to progress interesting drug targets and candidate molecules. Since the start of the project, 39 of the 60 applications to enter ENABLE with a programme have come from SMEs, and there are now 15 SMEs participating directly in ENABLE. Other projects with particularly strong SME involvement include EMIF, TRANSLOCATION, CANCER-ID, EBiSC, and DDMoRe.

1.3.2 Patient involvement

IMI recognises that patients can make a vital contribution to shaping research, making it more effective and more oriented to patient needs. Therefore, IMI's goal has been to champion a patient-centric approach, encouraging all the projects that it funds to work in partnership with patients wherever possible. Patients play an essential role when designing and implementing the IMI SRA, alongside researchers from public and private sectors, including the pharmaceutical industry, biotech companies, academia and regulators. This is why IMI's intention is to embed patients and their advocates at all levels: agenda setting for research in medical innovation, project planning, implementation, evaluation processes, and content. Therefore the Programme Office continuously engages with patients and promotes patient involvement in its projects and activities. In particular, our goal is to facilitate patient involvement throughout the programme as well as to deliver a number of projects designed to develop and improve the processes and tools for patient/healthcare consumer engagement in research, development and healthcare.

Thus far, patients are involved and/or represented in 75 % of relevant IMI projects as consortium partners, members of advisory boards, ethical advisory boards, or on a consultancy basis for topics of relevance.

In April 2016, IMI organised a Patient Engagement Strategy Workshop, during which a number of experienced stakeholders shared their experience to help IMI identify appropriate levels and mechanisms of involvement of patients in IMI and its projects. Another important topic was the strategy for optimising and coordinating patient engagement practice in different projects and turning the patient-centric goals of the IMI Strategic Research Agenda into reality. Lastly, ideas for possible future research projects for IMI were discussed on enabling patient involvement in the medicines lifecycle, including collaboration opportunities with similar and complementary initiatives in various countries and regions. During the workshop, it was further emphasised that patient involvement is critical and should be encouraged, facilitated and embedded in IMI at all levels. It was also pointed out that IMI needs a robust IMI patient engagement strategy to ensure that patient engagement is universally understood, recognised and effectively upheld where appropriate.

1.3.3 Interactions and involvement with regulatory authorities

As the scientific knowledge derived from the IMI projects has the potential to support the evolution of the regulatory environment, IMI has maintained a close collaboration with regulators, mainly the EMA and FDA, since its creation. In 2016, IMI strengthened its ties with regulators, most notably by streamlining processes for optimising the scientific engagement of EMA in IMI activities.

Regulators also participated in consultative workshops organised by IMI on strategic research areas to shape the future of IMI's programme, namely preparedness for emerging diseases, digital health, and oncology, as well as in workshops to discuss more specific proposals for topics under consideration (creation of the pan-European paediatric clinical trials network; safe use of medicines during pregnancy and lactation).

IMI met with the Heads of Medicines Agencies at their 83rd meeting in Rotterdam, the Netherlands, and contributed to the EMA workshop of 14-15 November on identifying opportunities for 'big data' in medicines development and regulatory science.

IMI continued to encourage consortia to take advantage of possible ways to engage in early dialogue with regulators and raised awareness among consortia of existing services offered by EMA. This year a number of projects benefited from these services, in particular through briefing meetings for input on the project plan, and EMA's 'qualification advice of novel methodologies for drug development' which resulted in the EMA issuing Letters of Support to the project SAFE-T on biomarkers for drug-induced renal injury and drug-induced liver injury (DILI).

Regular teleconferences throughout the year with the EMA and FDA provided an opportunity to exchange information on activities relevant for IMI, discuss topics and projects under development, and to follow up on progress on action points agreed at the IMI regulatory science summit held at the end of 2014.

Dialogue with other healthcare decision makers such as health technology assessment bodies and payers has been further enhanced, through informal meetings, with a view to developing framework for interactions, taking into consideration experience from the IMI project ADAPT-SMART.

1.3.4 Outreach to new stakeholders

To be successful, IMI must engage with a wider range of stakeholders than before, including with companies from outside the pharmaceutical sector. These are primarily involved in IMI through EFPIA's 'Partners in Research' membership category. As of the end of 2016, 14 EFPIA Partners in Research[4] with expertise in fields such as diagnostics, medical technology, imaging and data analysis had committed € 18.2 million to new IMI Call topics.

The IMI Associated Partner status is another route for organisations to take part in IMI. In 2016, three new Associated Partners joined IMI – Autism Speaks, the Simons Foundation Autism Research Initiative (SFARI), and T1DExchange. In addition, JDRF and the Leona M. and Harry B. Helmsley Charitable Trust, which have been Associated Partners since the beginning of IMI2, extended the scope of their involvement in IMI by joining a new consortium.

[4] The full list of EFPIA Partners in Research can be found online at www.efpia.eu/about-us/membership/.

1.4 Calls for proposals and grant information

1.4.1 Launch and management of IMI2 Calls in 2016

In 2016, two Calls for proposals were launched (IMI2 - Calls 9 and 10) and six Calls were at various stages of the evaluation and granting process (IMI2 - Calls 3, 5, 6, 7, 8 and 9). The evaluation stages for IMI2 - Call 3 had been completed in 2015 but grant preparation and Grant Agreement signature were completed in 2016, except for 1 grant that was signed in 2015.

An overview of these activities is displayed in the chart on the next page, along with a mapping of how the scientific priorities identified in the Annual Work Plan 2016 (AWP2016) were addressed through Calls launched in 2016.

The key points in the submission and evaluation process are highlighted as following:

- Cx Topics Text GB DEC – Call x Topics Text Governing Board Decision
- Cx –Call Launch
- SP SUBM – Short Proposal Submission deadline
- SP Evaluation – Short Proposal Evaluation
- SP GB DEC – Short Proposal Governing Board Decision
- FP SUBM – Full Proposal Submission deadline
- FP Evaluation – Full Proposal Evaluation
- FP GB DEC – Full Proposal Governing Board Decision
- GAP – Grant Agreement Preparation
- GA – Grant Agreement

The chart also provides information on the consultation period of the IMI advisory bodies (the States Representatives Group – the SRG, and the Scientific Committee – the SC), as well as of the European Commission (EC). There were no redress procedures after evaluation in 2016.

Chart showing overview of Call processes in 2016

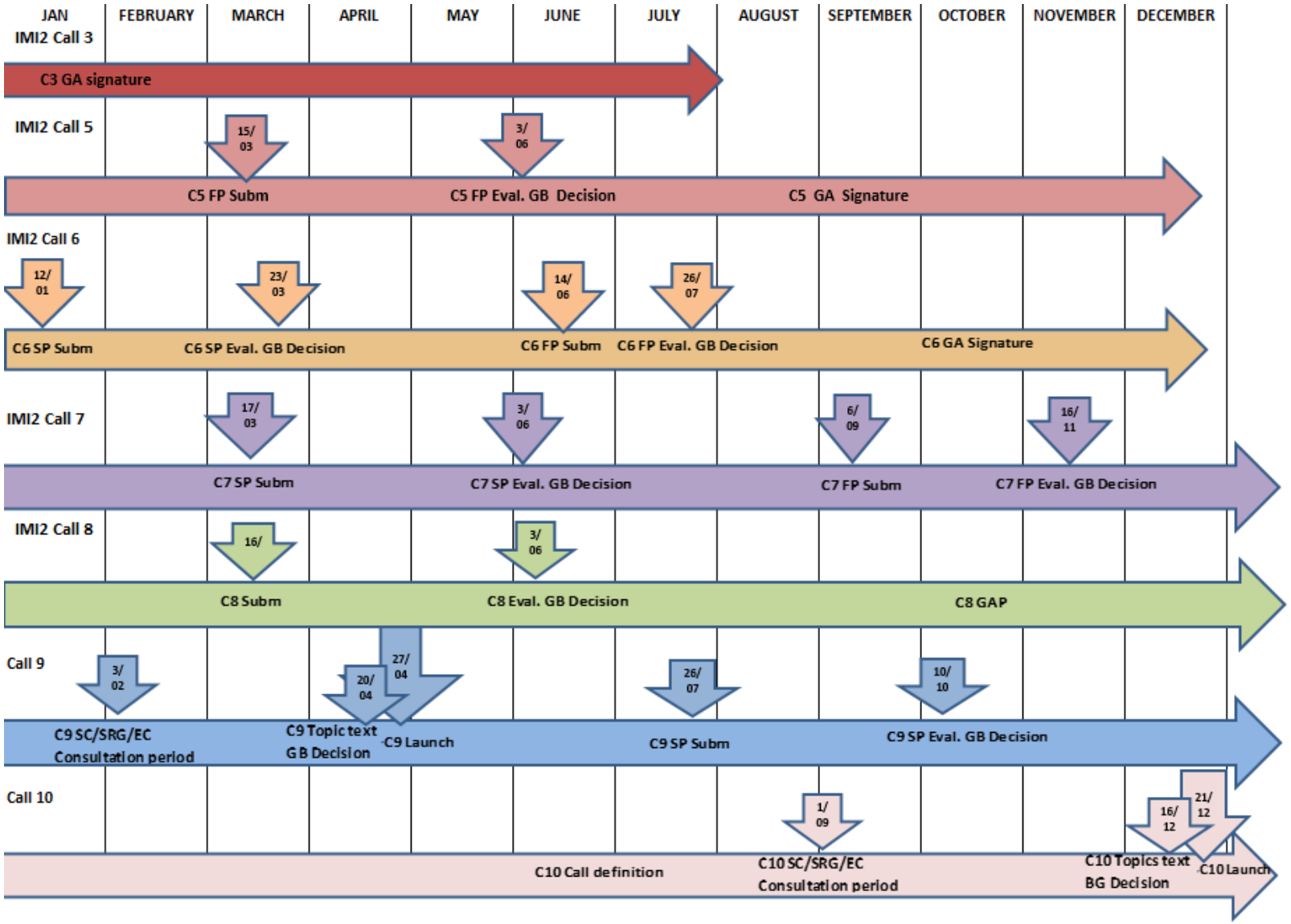


Table summarising key information related to IMI Call launches, submission deadlines and Grant Agreements signed in 2016[5]

Call	Topic title	Call process	Launch date	Deadline for sub-mission of SPs	Number of SPs received	Number of particip-ants in eligible SPs, FPs	Number of SPs selected to prepare a FP	Number of FPs selected for funding	Number of GAs signed in 2016
IMI2 - Call 3	▪ Remote assessment of disease and relapse-CNS ▪ Assessing risk and progression of prediabetes and type 2 diabetes to enable disease modification ▪ Linking clinical neuropsychiatry and quantitative neurobiology ▪ The consistency approach to quality control in vaccine manufacture ▪ Pertussis vaccination research ▪ Patient advocacy knowledge repository to enable patient focused medicine development	two-stage	17/12/2014	24/03/2015	38	470	6	5	4
IMI2 - Call 5	▪ Patient perspective elicitation on benefits and risks of medicinal products, from development through the entire life cycle, to inform the decision-making process by regulators and health technology assessment bodies ▪ Diabetic kidney disease biomarkers (DKD-BM) ▪ Inflammation and AD: modulating microglia function – focussing on TREM2 and CD33 ▪ Understanding the role of amyloid biomarkers in the current and future diagnosis and management of	two-stage	9/07/2015	13/10/2015	25	279	6	6	6

[5] Note: all topics are research and innovation actions (RIAs), with the exception of one coordination and support action (CSA) in IMI2 – Call 7, which is marked as such in the table.

Call	Topic title	Call process	Launch date	Deadline for sub-mission of SPs	Number of SPs received	Number of particip-ants in eligible SPs, FPs	Number of SPs selected to prepare a FP	Number of FPs selected for funding	Number of GAs signed in 2016
	patients across the spectrum of cognitive impairment (from pre-dementia to dementia) ▪ Evolving models of patient engagement and access for earlier identification of Alzheimer's disease: Phased expansion study ▪ ApoE biology to validated Alzheimer's disease targets								
IMI2 - Call 6	▪ Development of quantitative system toxicology (QST) approaches to improve the understanding of the safety of new medicines ▪ Establishing impact of RSV infection, resultant disease and public health approach to reducing the consequences ▪ Real world outcomes across the AD spectrum (ROADS) to better care ▪ Development of an outcomes-focused data platform to empower policy makers and clinicians to optimize care for patients with hematologic malignancies	two-stage	6/10/2015	12/01/2016	11	153	4	4	4
IMI2 - Call 7	▪ Validation of translational imaging methods in drug safety assessment (TRISTAN) ▪ Identification of druggable targets modulating misfolded proteins in Alzheimer's and Parkinson's diseases ▪ Pathological neuron-glia interactions in neuropathic pain ▪ Dry age-related macular	two-stage	18/12/2015	17/03/2016	32	317	7	7	open

Call	Topic title	Call process	Launch date	Deadline for sub-mission of SPs	Number of SPs received	Number of particip-ants in eligible SPs, FPs	Number of SPs selected to prepare a FP	Number of FPs selected for funding	Number of GAs signed in 2016
	degeneration: development of novel clinical end points for clinical trials with a regulatory and patient access intention ▪ A comprehensive 'paediatric preclinical POC Platform' to enable clinical molecule development for children with cancer Topics under the Big Data for Better Outcomes programme: ▪ Coordination and Support Action (CSA) for the Big Data for Better Outcomes programme ▪ Increase access and use of high quality data to improve clinical outcomes in heart failure (HF), atrial fibrillation (AF), and acute coronary syndrome (ACS) patients								
IMI2 Call 8 Ebola +	▪ Ebola and other filoviral haemorrhagic fevers (Ebola+) programme: future outbreaks (two year Call with multiple cut-off dates)	single-stage	18/12/2015	First cut-off date: 16/03/2016	4	62	2	2	open
IMI2 Call 8 Ebola +	▪ Ebola and other filoviral haemorrhagic fevers (Ebola+) programme: future outbreaks (two year Call with multiple cut-off dates)	single-stage	18/12/2015	Second cut-off date: 15/09/2016	0	0	0	0	0
IMI2 Call 9	Addressing the clinical burden of *Clostridium difficile* infection (CDI): Evaluation of the burden, current practices and set-up of a European research platform (Part of the IMI New Drugs for Bad Bugs (ND4BB) programme)	two-stage	27/04/2016	26/07/2016	17	253	6	open	open

Call	Topic title	Call process	Launch date	Deadline for sub-mission of SPs	Number of SPs received	Number of particip-ants in eligible SPs, FPs	Number of SPs selected to prepare a FP	Number of FPs selected for funding	Number of GAs signed in 2016
	▪ Development of immune tolerance therapies for the treatment of rheumatic diseases ▪ Data quality in preclinical research and development ▪ Next generation of electronic translational safety – NexGETS ▪ Identification and validation of biomarkers for non-alcoholic steatohepatitis (NASH) and across the spectrum of non-alcoholic fatty liver disease (NAFLD) ▪ Joint influenza vaccine effectiveness studies								
IMI2 Call 10	▪ Understanding hypoglycaemia: the underlying mechanisms and addressing clinical determinants as well as consequences for people with diabetes by combining databases from clinical trials ▪ How Big Data could support better diagnosis and treatment outcomes for Prostate Cancer Part of the IMI2 Big Data for Better Outcomes Programme (BD4BO) ▪ Improving the care of patients suffering from acute or chronic pain ▪ Creation of a pan-European paediatric clinical trials network ▪ Biomanufacturing 2020: Development of innovative high throughput analytical tools and methods to characterize cell culture fluid during development and commercial cell culture processes	two-stage	21/12/2016	28/03/2017	open	open	open	open	open

Call	Topic title	Call process	Launch date	Deadline for sub-mission of SPs	Number of SPs received	Number of particip-ants in eligible SPs, FPs	Number of SPs selected to prepare a FP	Number of FPs selected for funding	Number of GAs signed in 2016
	▪ Unlocking the solute carrier gene-family for effective new therapies (unlock SLCs) ▪ Patient perspectives in medicines lifecycle ▪ Personalised medicine approaches in autism spectrum disorders								

Table summarising IMI2 Calls for proposals launched in 2016, highlighting the priorities of Annual Work Plan 2016 implemented, the date of Call launch and budget available per Call

Call number	Call type	Number of topics	Annual Work Plan 2016 Priorities implemented	Launch date	Budget		
					EU (in EUR)	EFPIA (in EUR)	Associated Partners (in EUR)
IMI2 Call 9	Two stage	6	▪ Diabetes/metabolic disorder ▪ Immunology ▪ Infection control including vaccines ▪ Translational safety ▪ Neurodegeneration and other Neuroscience Priorities	27 March 2016	54 328 000	63 328 000	none
IMI2 Call 10	Two stage	8	▪ Diabetes/metabolic disorders ▪ Neurodegeneration and other Neuroscience Priorities ▪ Data and Knowledge Management ▪ Other enablers of innovation	21 Dec 2016	173 890 000	118 184 000	55 956 000

Further details are available in Annex 6 ‘Scoreboard of H2020 common KPIs’

Evaluation experts

In 2016, IMI used 148 experts from 33 countries in the evaluation of IMI2 - Calls 5,6,7,8 and 9. Most (88.5 %) came from EU and H2020 associated countries. Over two thirds (102) came from academia and research institutes. Other sectors represented are: consultations (20), private sector (non-EFPIA) (19), governmental and non-governmental organisations (4) and regulators (3).

For each Call in 2016, the breakdown of evaluators is as follows:

Call	Total no. experts	Science evaluation	Ethical screening	Observers	Gender: Female	Gender: Male
IMI2 - Call 5: stage 2	43	38	3	2	19	24
IMI2 - Call 6: stage 1	25	24		1	9	16
IMI2 - Call 6: stage 2	21	18	2	1	8	13
IMI2 - Call 7: stage 1	43	41		2	16	27
IMI2 - Call 7: stage 2	39	34	3	2	14	25
IMI2 - Call 8: 1st cut-off date*	10	7	2	1	5	5
IMI2 - Call 9: stage 1	38	36		2	18	20

*For IMI2 Call 8 - second cut-off date, no application was received.

IMI2 – Call 3

Progress in 2016: Signature of GAs for 4 projects

In 2016, the GAs of four projects resulting from IMI2 – Call 3 (H2020-JTI-IMI2-2015-03-two-stage): were signed RADAR-CNS, RHAPSODY, VAC2VAC, and PERISCOPE (the PRISM consortium had signed its grant agreement on 18 December 2015 and one FP was found to be of insufficient quality to be retained for funding).

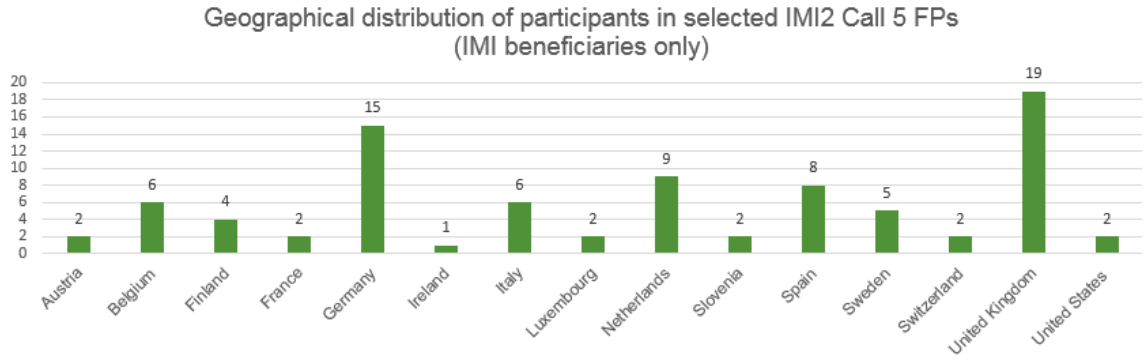
IMI2 – Call 5

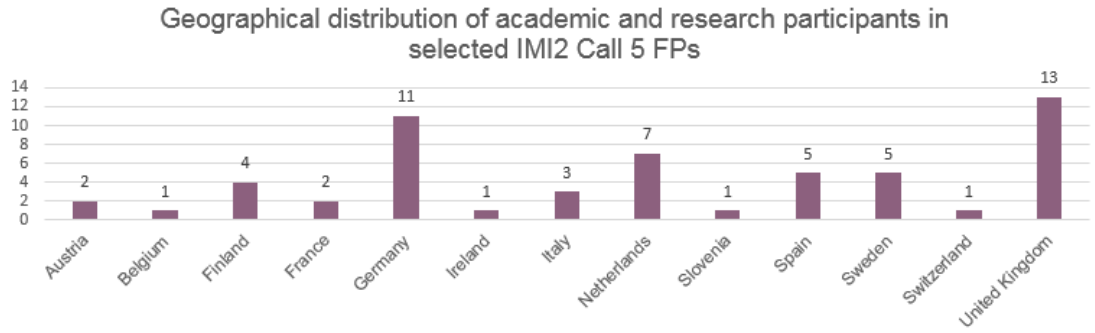
Progress in 2016: From FP submission and evaluation to GA preparation and signature for 6 projects

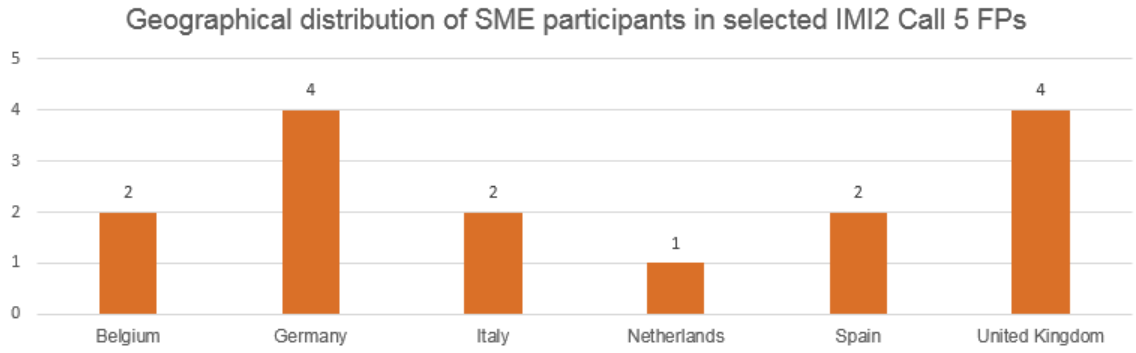
IMI2 – Call 5 (H2020-JTI-IMI2-2015-05-two-stage) was launched on 9 July 2015. The stage 1 evaluation of SPs was successfully concluded and the Governing Board adopted the results of the evaluation on 18 December 2015. The consortia of successful SPs were invited to submit FPs with a submission deadline of 15 March 2016.

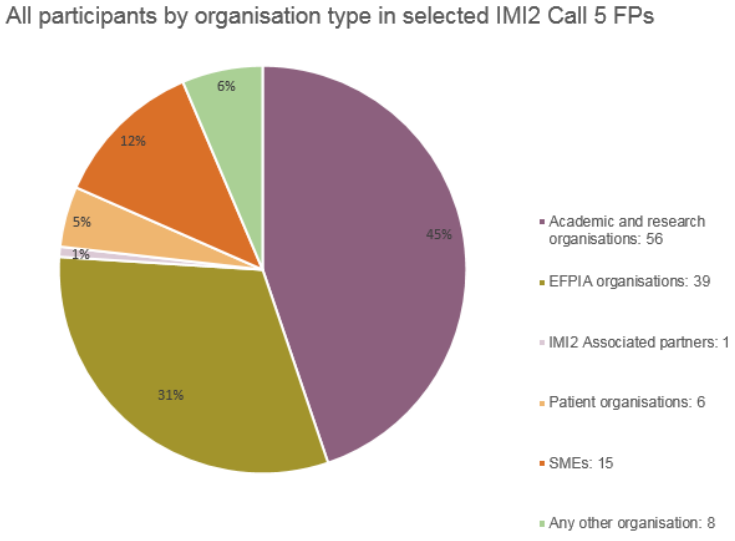
All six FPs successfully completed the stage 2 in-house evaluation and the Governing Board adopted the outcome on 3 June 2016. The GAs of all six projects - PREFER, BEAT-DKD, PHAGO, AMYPAD, MOPEAD, and ADAPTED - were signed in the second part of 2016.

IMI2 - Call 5: Full proposal participant details









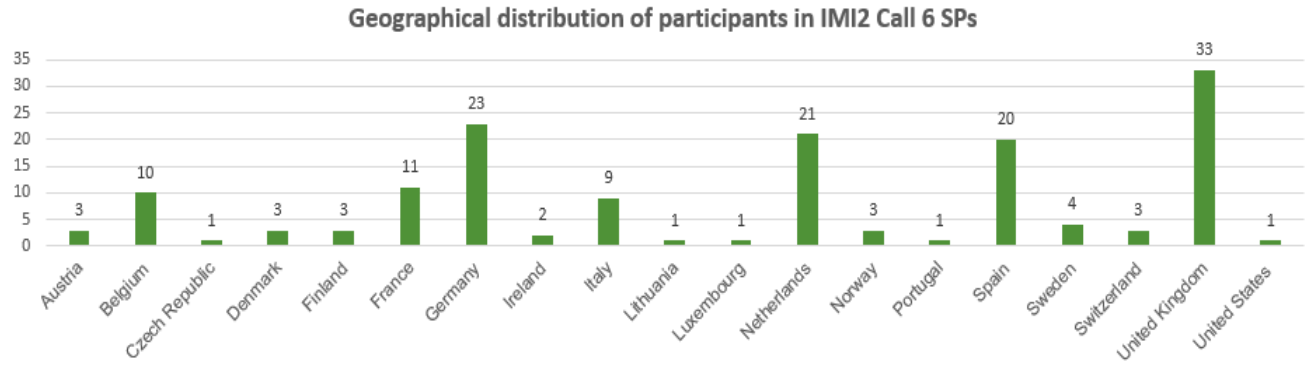
IMI2 – Call 6

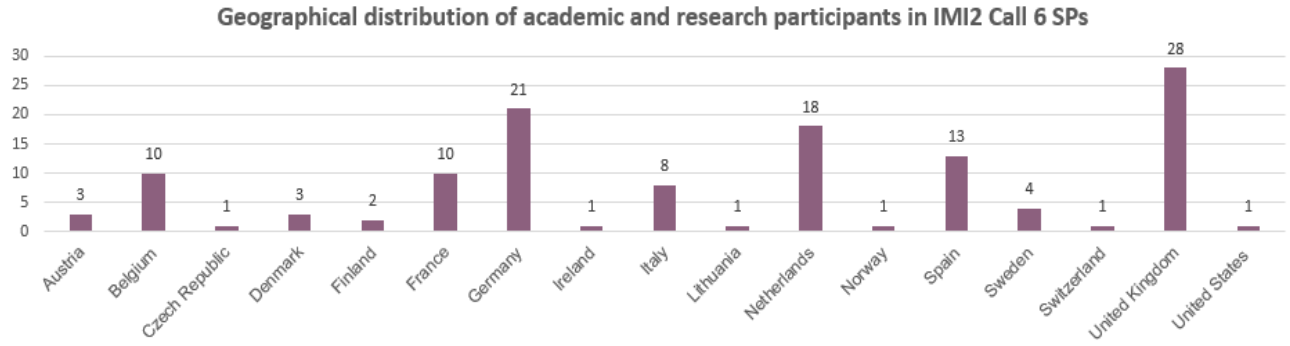
Progress in 2016: From SP submission and evaluation to FP submission and evaluation to GA preparation and signature for 4 projects

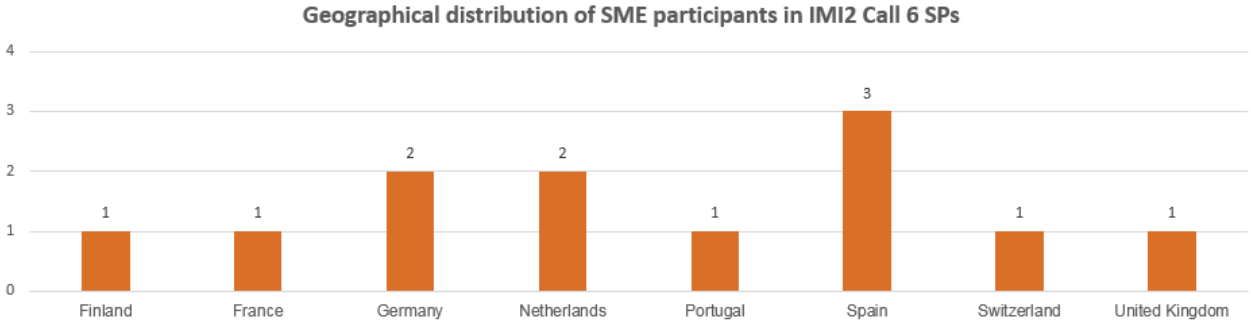
IMI2 – Call 6 (H2020-JTI-IMI2-2015-06-two-stage) was launched on 6 October 2015, with a submission deadline for SPs of 12 January 2016. The stage 1 evaluation was completed successfully and the IMI2 JU Governing Board adopted the outcome on 23 March 2016. The four first-ranked SPs were invited to prepare FPs together with the pre-established EFPIA consortia with a deadline for submission of 14 June 2016.

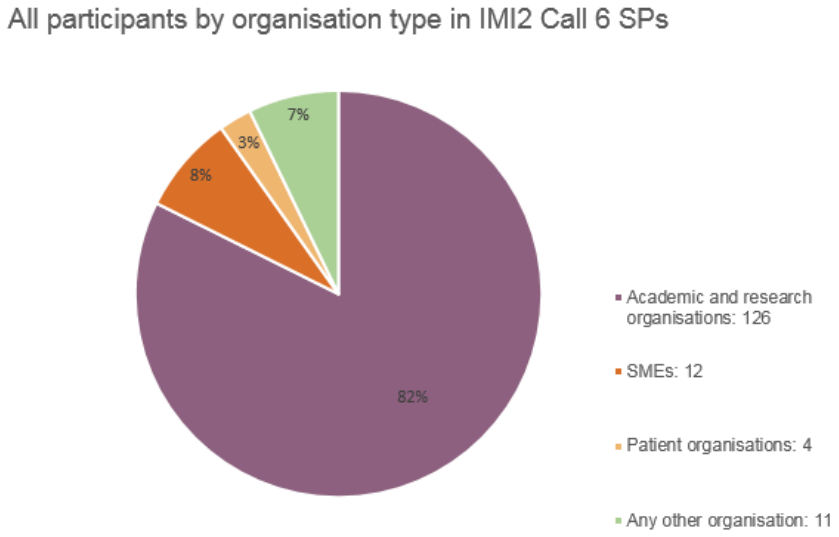
The stage 2 in-house evaluation was successfully concluded, and the evaluation results were adopted by the IMI Governing Board on 26 July 2016. The GAs for all four projects – RESCEU, TransQST, ROADMAP, and HARMONY, were concluded by the end of 2016.

IMI2 - Call 6: Short proposal participant details

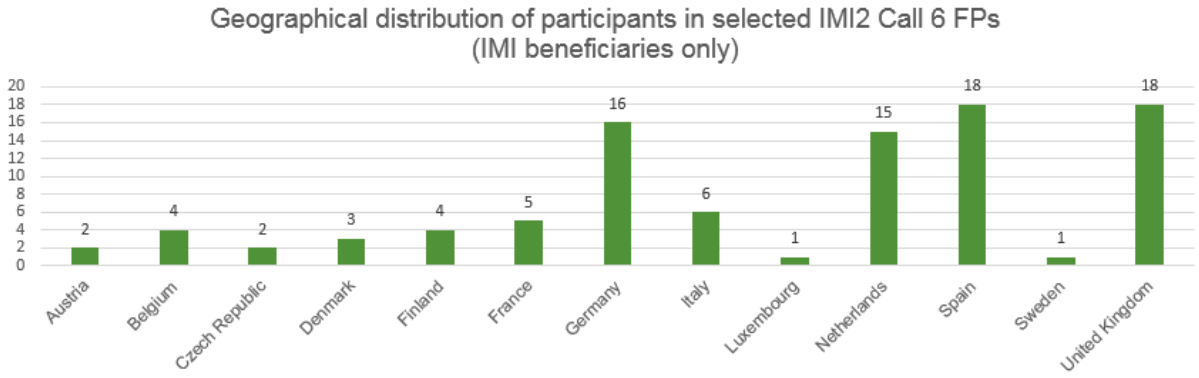


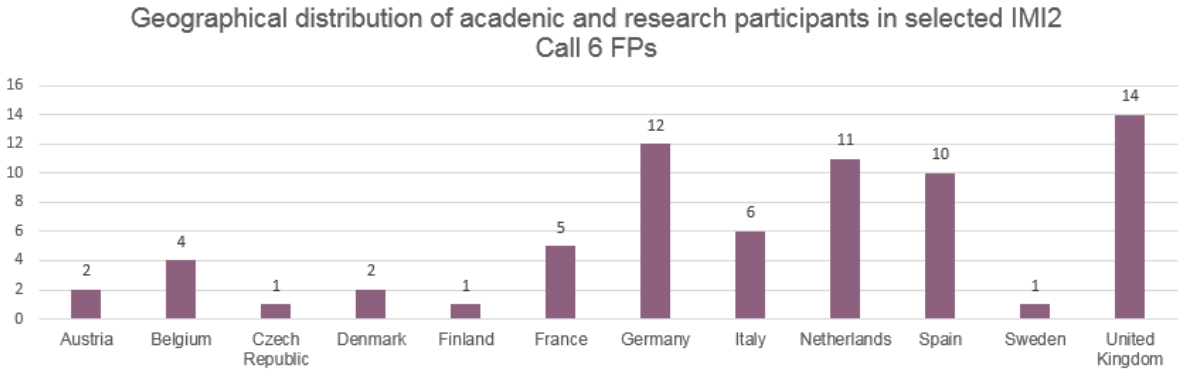


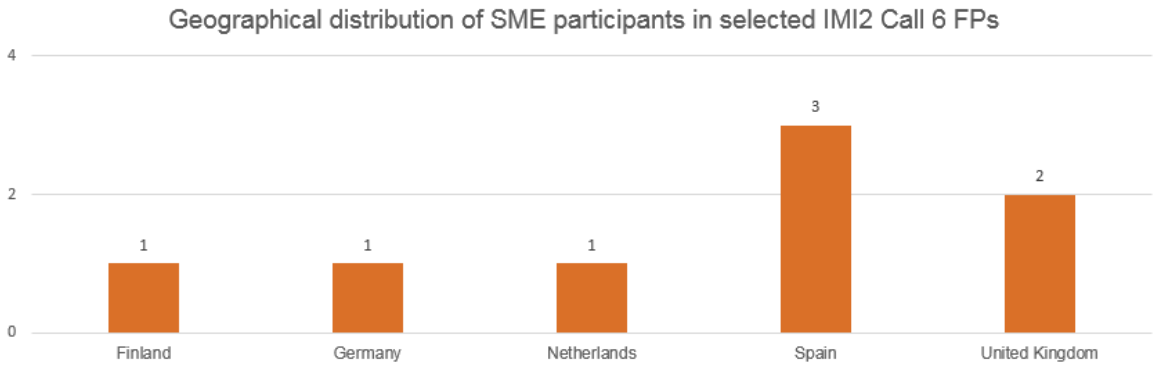


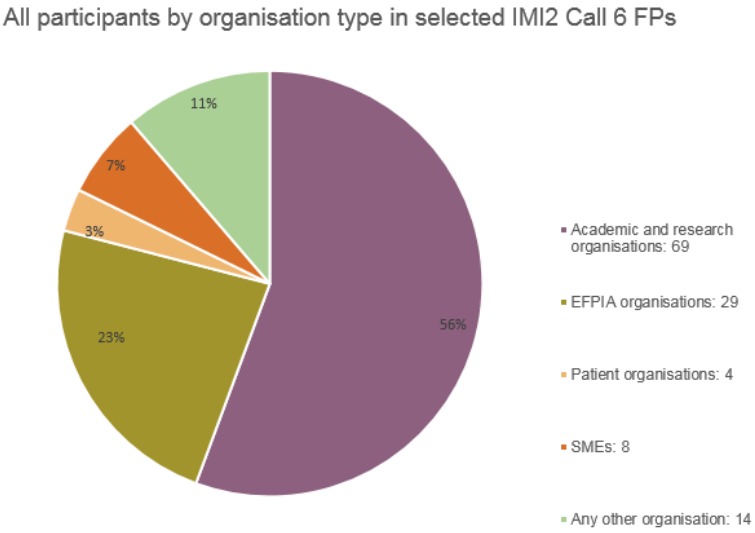


IMI2 - Call 6: Full proposal participant details









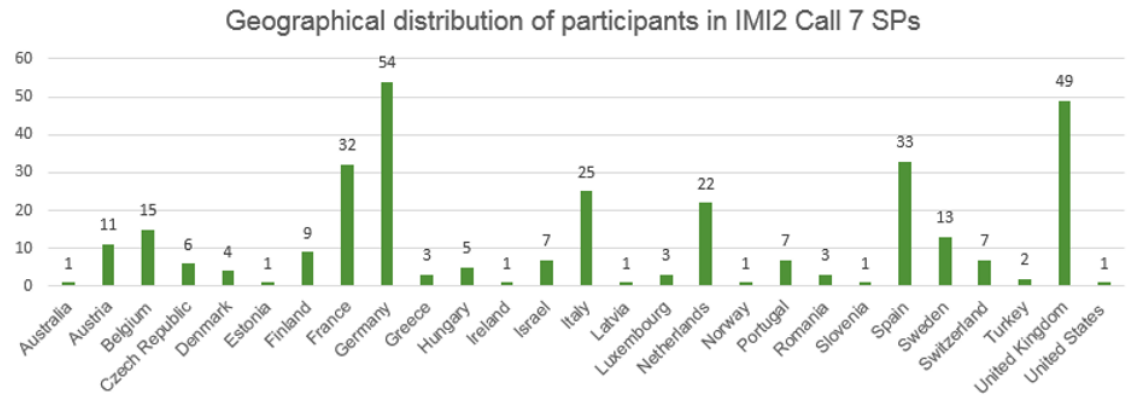
IMI2 - Call 7

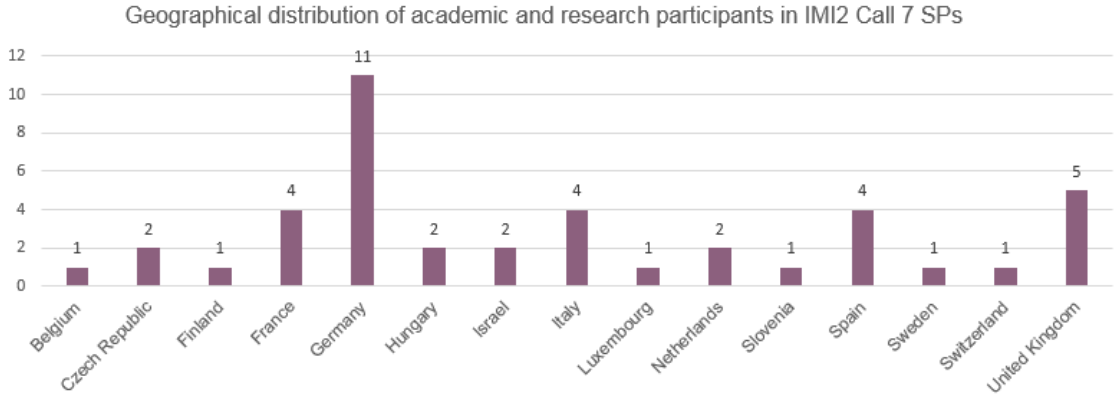
Progress in 2016: From SP submission and evaluation to FP submission and evaluation to GA preparation for 6 projects

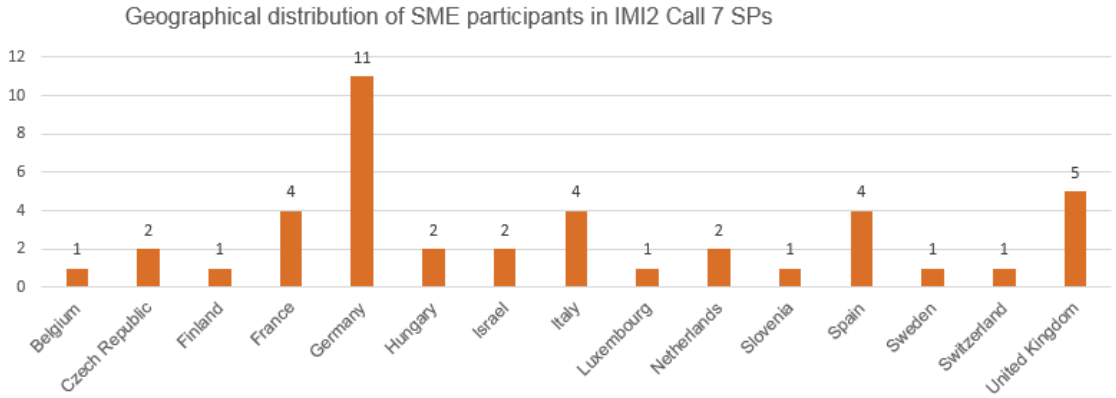
IMI2 - Call 7 (H2020-JTI-IMI2-2015-07-two-stage) was launched on 18 December 2015, with an SP submission deadline of 17 March 2016. The submission of SPs and the stage 1 evaluation was completed successfully according to IMI rules and procedures and the Governing Board adopted the outcome on 3 June 2016. The first-ranked SP in each of the seven topics was invited to prepare an FP together with the pre-established EFPIA consortia with a deadline for submission of 6 September 2016.

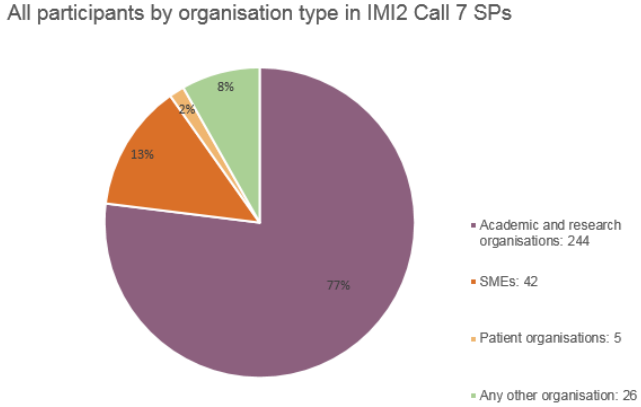
The stage 2 in-house evaluation was successfully concluded and the IMI Governing Board adopted the outcome on 16 November 2016. The applicants were invited to start the GAP and the GAs will be signed in 2017.

IMI2 - Call 7: Short proposal participant details

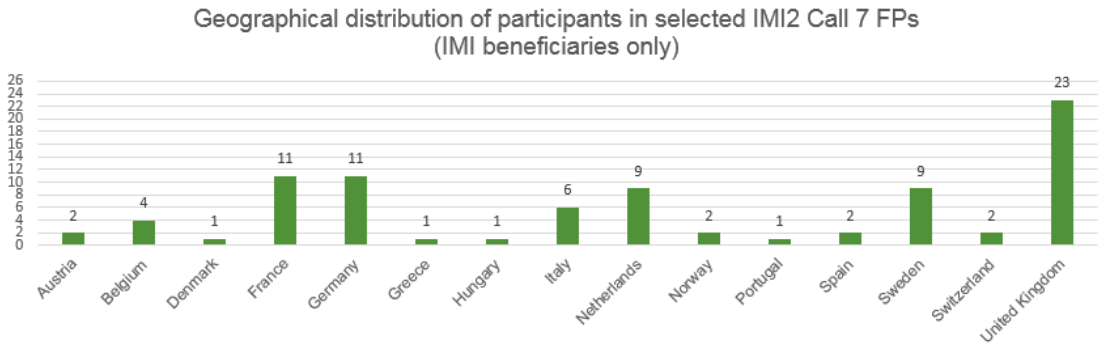


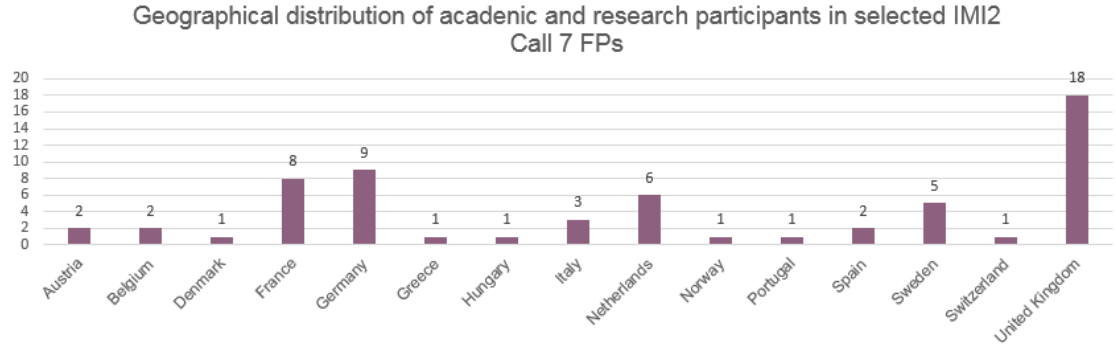


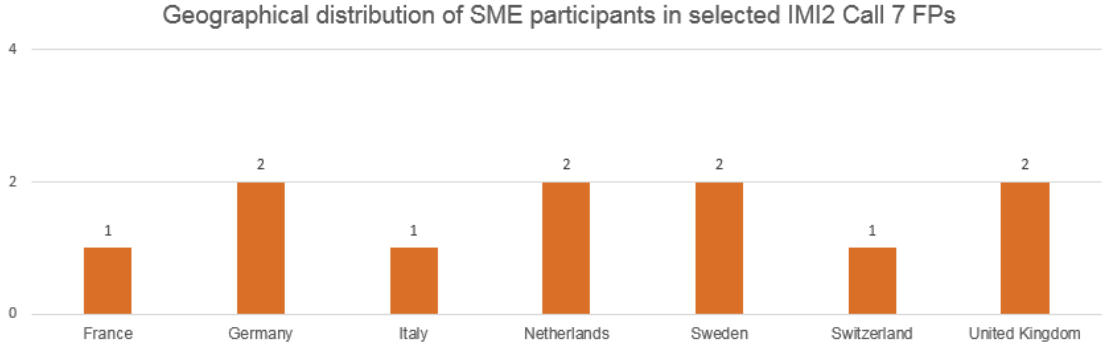


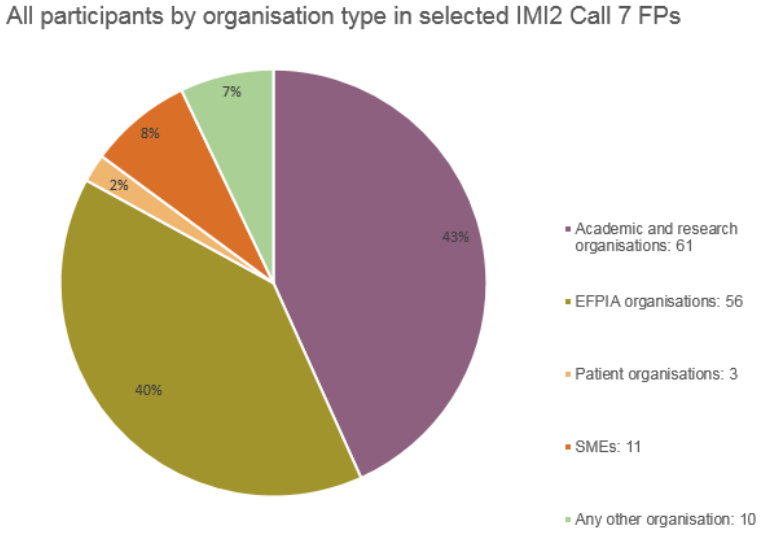


IMI2 - Call 7: Full proposal participant details









IMI2 - Call 8

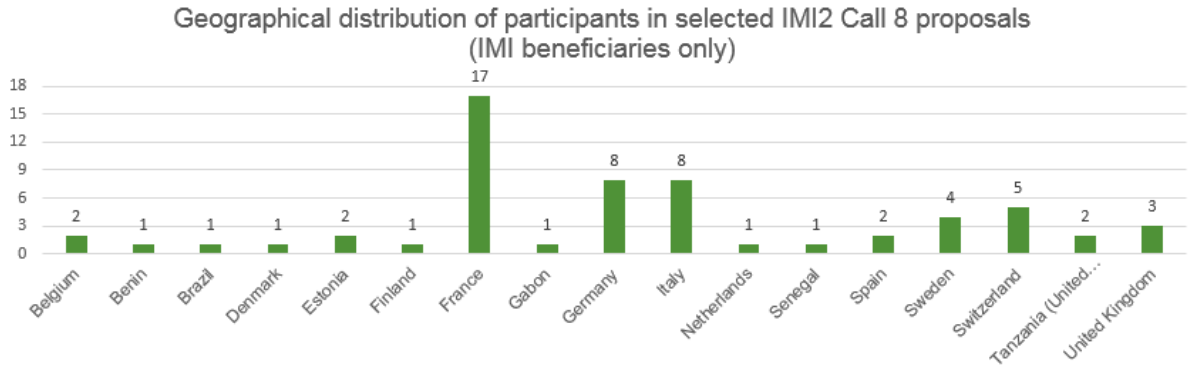
Progress in 2016: From FP submission and evaluation to GA preparation for 2 projects

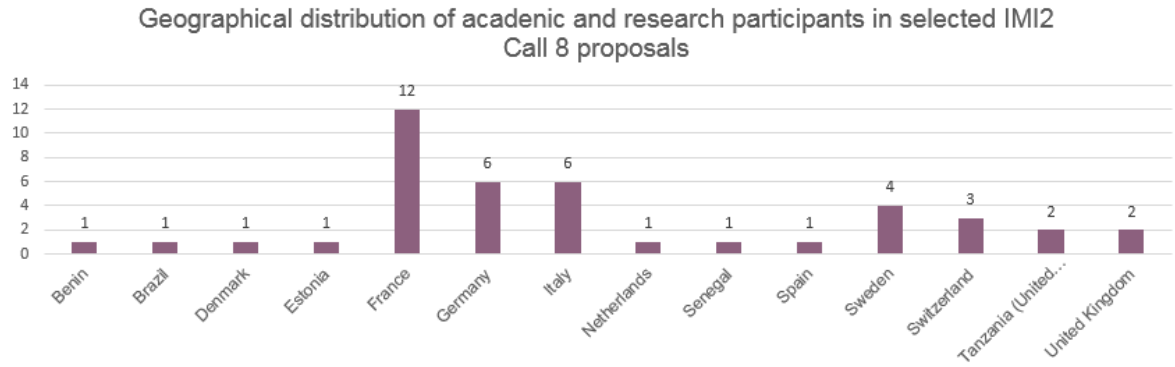
IMI2 - Call 8 (H2020-JTI-IMI2-2015-08-single-stage) on Ebola and other filoviral haemorrhagic fevers (Ebola+) programme: future outbreaks consist of a single topic with multiple cut-off dates. The call was launched on 18 December 2015 with deadlines for submission of FPs of 16 March 2016, 15 September 2016, 16 March 2017, 14 September 2017 and 15 March 2018.

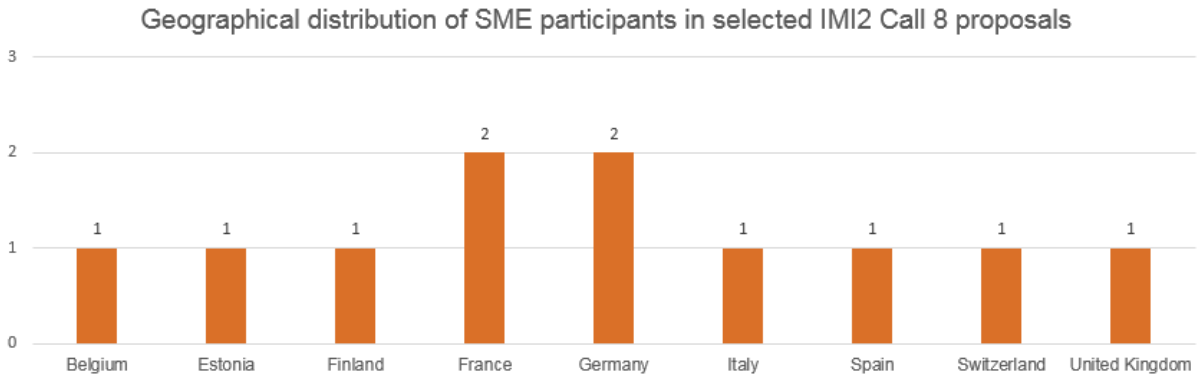
The evaluation process of the first cut-off date was concluded successfully according to IMI rules and procedures. Two of the four proposals submitted passed the relevant thresholds and were recommended for funding. The IMI Governing Board adopted the outcome of the evaluation process on 3 June 2016. The successful applicants were invited to start the GAP.

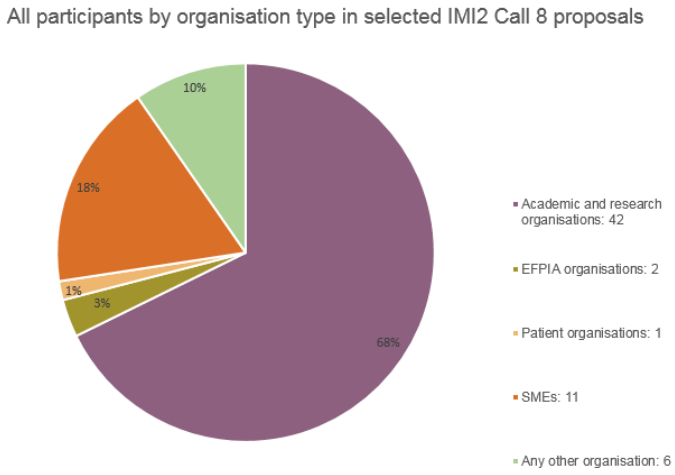
No proposals were received in response to the Call prior to the second cut-off date of 15 September 2016.

IMI2 - Call 8: Participant details







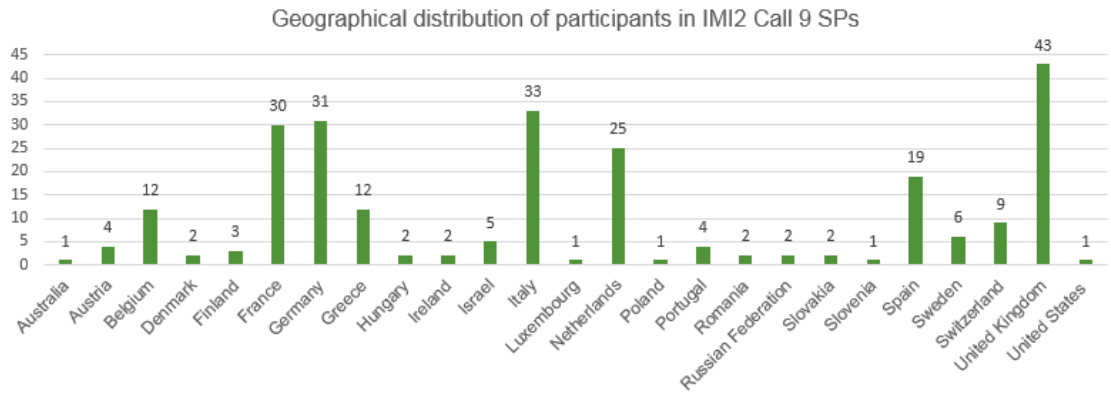


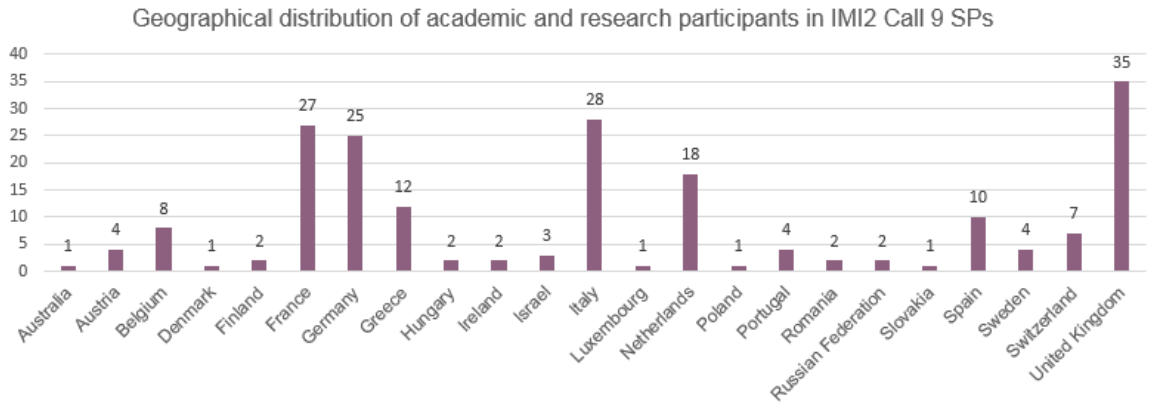
IMI2 - Call 9

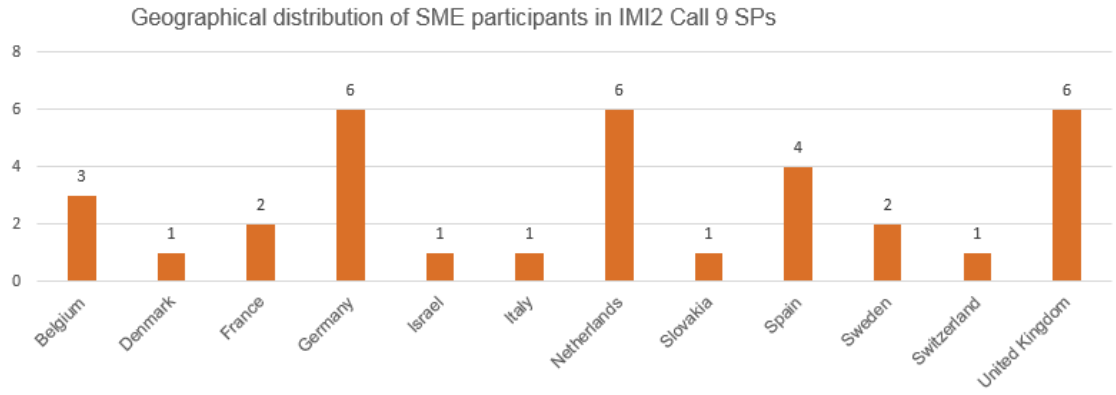
Progress in 2016: From Call launch and SP submission and evaluation to FP preparation

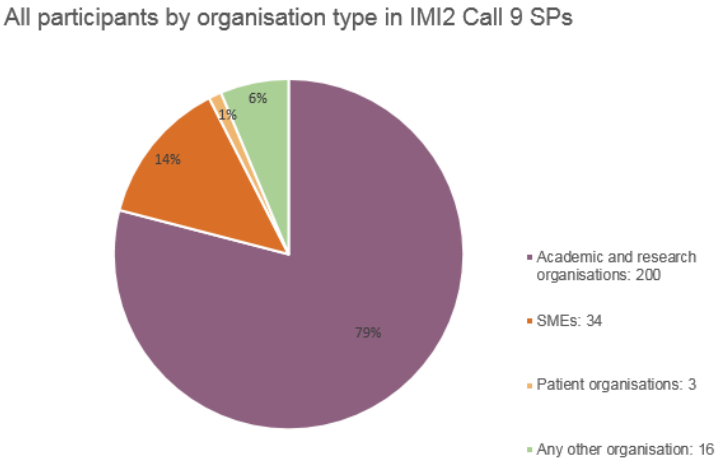
IMI2 - Call 9 (H2020-JTI-IMI2-2016-09-two-stage) was launched on 27 April 2016, with an SP submission deadline of 26 July 2016. The submission of SPs and the stage 1 evaluation was completed successfully according to IMI rules and procedures. The IMI2 JU Governing Board adopted the outcome on 10 October 2016, and the first-ranked SP in each of the six topics was invited to prepare an FP together with the pre-established EFPIA consortia with a deadline of 10 January 2017.

IMI2 - Call 9: Short proposal participant details









IMI2 - Call 10

Progress in 2016: Call launch

IMI2 - Call 10 (H2020-JTI-IMI2-2016-10-two-stage) was launched on 21 December 2016 with a deadline for submission of SPs of 28 March 2017.

Table summarising the number of beneficiaries and budgets for projects with GAs signed in 2016

IMI2 Call	Project acronym	No. IMI2 JU beneficiaries	No. EFPIA companies	No. IMI2 JU Associated Partners	IMI2 JU funding to academic &research (EUR)	IMI2 JU funding to SMEs (EUR)	IMI2 JU funding to patient orgs (EUR)	Others (EUR)	Total IMI2 JU contribution (EUR)	EFPIA in-kind contribution (EUR)	IMI2 JU Associated partners (EUR)	Total budget (EUR)
					(1)	(2)	(3)	(4)	1+2+3+4 = (5)	(6)	(7)	(=5+6+7)
3	RADAR-CNS	22	5	0	9 560 000	1 010 000	0	430 000	11 000 000	13 322 379	0	24 322 379
3	RHAPSODY	24	4	0	7 606 289	418 968	0	104 743	8 130 000	6 882 049	0	15 012 049
3	VAC2VAC	14	5	0	6 594 240	0	0	1 255 760	7 850 000	8 128 429	0	15 978 429
3	PERISCOPE	22	2	0	20 293 652	706 348	0	0	14 000 000	7 125 114	7 000 000	28 125 114
5	PREFER	17	16	0	3 839 968	522 437	368 250	1 269 345	6 000 000	6 000 000	0	12 000 000
5	BEAT-DKD	27	6	1	14 743 937	342 000	0	0	15 085 937	11 687 100	1 851 000	28 624 037
5	PHAGO	11	8	0	7 354 250	1 483 750	0	0	8 838 000	9 092 496	0	17 930 496
5	AMYPAD	12	3	0	10 240 500	1 558 886	200 500	0	11 999 886	12 233 950	0	24 233 836
5	MOPEAD	12	2	0	1 320 333	235 421	117 466	369 780	2 043 000	1 967 251	0	4 010 251
5	ADAPTED	10	3	0	2 612 320	897 680	0	0	3 510 000	3 286 740	0	6 796 740
6	TransQST	13	8	0	5 911 750	1 061 500	0	1 026 750	8 000 000	7 802 874	0	15 802 874
6	RESCEU	12	6	0	11 803 875	1 093 750	504 375	1 096 125	14 498 125	14 673 665	0	29 171 790
6	ROADMAP	15	7	0	3 102 000	305 750	176 000	414 500	3 998 250	3 768 726	0	7 766 976
6	HARMONY	45	7	0	7 646 335	849 016	500 000	11 204 649	20 200 000	19 094 265	0	39 294 265

Note: some projects may also receive funding from other sources that is not recorded here. For example, organisations that are not eligible to receive IMI funding may receive funding from other sources to support their participation in the project.

1.4.2 Interim reviews for IMI projects

In 2016, IMI conducted 10 reviews of projects from IMI1 - Calls 4, 7, 8, 9 and IMI2 - Calls 2 and 3, as shown in the table below.

IMI project acronym	Call #	Full project name	Interim review
EBODAC	IMI2 - Call 2	Communication strategy and tools for optimizing the impact of Ebola vaccination deployment	01/02/2016
EBOVAC1	IMI2 - Call 2	Development of a prophylactic Ebola vaccine using an heterologous prime-boost regimen	01/02/2016
EBOVAC2	IMI2 - Call 2	Development of a prophylactic Ebola vaccine using an heterologous prime-boost regimen: phase II	03/02/2016
EBOMAN	IMI2 - Call 2	Manufacturing and development for rapid access Ebola vaccine	03/02/2016
EMIF	IMI1 - Call 4	European Medical Information Framework	15/04/2016
PRECISESADS	IMI1 - Call 8	Molecular reclassification to find clinically useful biomarkers for systemic autoimmune diseases	19/05/2016
ADVANCE	IMI1 - Call 7	Accelerated development of vaccine benefit-risk collaboration in Europe	31/05/2016
DRIVE AB	IMI1 - Call 9	Driving re-investment in R&D and responsible antibiotic use	31/05/2016
PRISM	IMI2 - Call 3	Psychiatric Ratings using Intermediate Stratified Markers: providing quantitative biological measures to facilitate the discovery and development of new treatments for social and cognitive deficits in AD, SZ, and MD	07/09/2016
SPRINTT	IMI1 - Call 9	Sarcopenia and physical frailty in older people: multi-component treatment strategies	17/11/2016

The expert reviewer panel consisted of at least three experts, one from each group: the IMI Scientific Committee, the full project proposal evaluation panel, and selected from suggestions by the consortium.

The only exception was the case of the PRISM milestone review where, due to the limited scope of the review, only two experts (one from the full project proposal evaluation panel, and one selected from suggestions by the consortium) were appointed.

Overall, the reviewers were satisfied with the progress made by the projects. The consortia had completed the majority of the milestones set and are now on track for the final, critical steps of the projects, such as clinical and validation studies. A review report prepared by the experts was shared with the consortia. In most cases, the reviewers made recommendations designed to ensure the delivery of tangible achievements by the end of the funding period. Where recommendations were made, the consortia responded by proposing appropriate actions and/or amending the work planned for the remainder of the project. Further information per project is presented below.

Ebola+ projects EBOVAC1, EBOVAC2, EBODAC, EBOMAN

The Ebola+ programme was the result of a fast-track Call for proposals (IMI2 - Call 2) launched in response to the 2014 Ebola epidemic, and the projects selected for funding, including EBOVAC1, EBOVAC2, EBODAC, and EBOMAN, started at the height of a major public health emergency. Subsequently, the planning and activities had to constantly be adapted to the changing environment, as new cases of Ebola infections declined. Each of the four projects had a M12 review included in their Description of Action, to allow for an independent assessment of the proposed adjustments in the work plan and to ensure that the changes proposed to adapt to the changing environment are in line with the original objectives of the projects.

EBODAC

The experts recognised that EBODAC's objectives and the socio-anthropological elements it investigates are still relevant despite the adaptations to the clinical trial designs that were required. The support system EBODAC has developed for the conduct of clinical trials in the Sierra Leone context is unique in terms of applying known technologies to the problems of clearly identifying enrolled subjects for correct dose assignment and administration, which could be considered an important breakthrough for the deployment of prime-boost vaccination strategies in similar field conditions.

However, the experts noted that, as the large-scale clinical trials and vaccine launch initially envisioned are now drastically down-sized, EBODAC will not have the opportunity to demonstrate and prove that the platforms work for large-scale implementation. The experts therefore recommended that the project prioritise future activities that will validate the EBODAC system and its components.

EBOVAC1

The experts confirmed that the objectives of the project are still relevant as a possible future outbreak of Ebola virus disease cannot be ignored. Due to the decline in the epidemic, the original plan of testing for efficacy in an outbreak situation had to be revised. The experts validated the new pathway forward that is focusing on an extended collection of immunogenicity and safety data, and applauded what has already been achieved, from regulatory approvals to successful completion of vaccinations of Phase 1 trials in Europe, Kenya, Tanzania, Uganda, and the first stage of a large-scale clinical trial in Kambia District, a remote area of Sierra Leone that was strongly affected by the Ebola outbreak.

In the absence of efficacy data, the experts recognised the evolution of the regulatory framework in moving forward with immunogenicity and safety data and potential bridging to animal data as the most critical factor for the ongoing work.

EBOVAC2

The relevance of the objectives and the importance of the work in EBOVAC2 that is focusing on carrying out Phase 2 clinical trials with the Janssen prime-boost vaccine regimen in both Africa and Europe was emphasised by the experts. In general, the work is proceeding toward the appropriate goals and was considered scientifically credible. The experts noted significant delays that were experienced by the project, due to complexities in relation to regulatory and ethics approvals in various countries linked to a loss of urgency due to the decline in the Ebola outbreak.

EBOMAN

The experts recognised that the scientific and technological achievements of EBOMAN are mainly in terms of preparing a rapid manufacturing response in case of future outbreaks. In this respect, the project has gone beyond the state of the art, i.e. accelerating the development process (from usually 8 years to 2 years). The objectives and milestones have been generally attained except for those related to an increase in manufacturing capacity supporting a large scale phase III efficacy trial with the Janssen prime-boost vaccine. The experts recognised the value of having sufficient manufacturing capacity for a rapid response with different vaccines produced on the same manufacturing platform that could provide supplies quickly for other emergency situations.

EMIF

The project has made good overall progress during the two years following the last review. The technology platform has matured and functionality was extended in response to requirements by the scientific use cases. The consortium appears to be functioning properly with clear evidence of increased collaboration within the project both between the scientific topics as well as with the platform. Numerous scientific publications and presentations contributed to increased public visibility of the EMIF project. As a result, the reviewers concluded that EMIF is making good progress towards establishing an innovative operational framework and infrastructure for data harmonisation and integration in support of biomarker discovery. Nevertheless, in order to have real impact EMIF will have to deliver globally relevant results: this remains a challenge especially in light of competing international initiatives. Thus in its final phase the experts recommended that the project boost its dissemination and sustainability activities to ensure success.

PRECISESADS

The goal of this project is the use of the power of omics and bioinformatics to identify new classifications for diseases known to share common pathophysiological mechanisms such as systemic lupus erythematosus, systemic sclerosis, Sjögren's syndrome, rheumatoid arthritis and others. The mid-term evaluation of the project revealed that the work foreseen was largely being delivered as originally planned. The consortium had already successfully addressed a number of technical laboratory analysis procedures and had achieved a level of clinical and experimental data sharing across multiple sites. It was observed that some new methodologies developed by the consortium, particularly the analysis of multiomic data sets and the standardisation of FACS analysis across multiple sites, represented significant achievements. Moreover, these methodologies will be of relevance to researchers across many disease areas.

ADVANCE

The experts confirmed that the ADVANCE project is making an important contribution to the process of benefit-risk assessment of vaccines in Europe. They congratulated the ADVANCE consortium for the progress made on what is clearly a complex and ambitious project. It was recognised that the partnership of different stakeholders with different objectives was challenging, but the experts were pleased to see that considerable effort was made to achieve engagement of the various stakeholders within ADVANCE and assure good communication between the stakeholders. Methodological work by ADVANCE was much appreciated and will be valuable to the scientific community outside of ADVANCE, including public health stakeholders. A concern was raised around the availability of sufficient data from the various disparate databases to produce valid and reliable results. The experts therefore recommended that the ADVANCE team focus on what can be achieved with the available databases and methods and manage expectations by recognising the limitations.

DRIVE AB

The DRIVE-AB goal of proposing alternative economic strategies and reward models for new antibiotics while simultaneously ensuring appropriate consumption of existing antibiotics was acknowledged as ambitious by the experts. They recognised that the project was playing an important role in stimulating the global discussion in the battle against antibiotic resistance. The experts noted a lack of clarity on what the ultimate tangible results of the project will be, and recommended to the consortium to be more specific on what the DRIVE-AB contribution to the overall international efforts is. The great achievement of DRIVE-AB would be the development of evidence-based policy recommendations briefed with all relevant stakeholder groups and adaptable to various countries and healthcare settings. The planned stakeholder conference in June 2016 was well appreciated by the experts and should help to reach that goal.

PRISM

The PRISM project aims to study the biological correlates of social withdrawal, a common early symptom in schizophrenia and Alzheimer's disease, to identify if underlying, biological causes of this symptom are the same in the two conditions. The hope is that the project's findings will shed new light on the causes of mental illness and their symptoms and facilitate the development of much-needed new treatments, better targeting specific patient groups and possibly going beyond the old disease classifications. The reviewers were requested to examine the first critical milestone of the project, namely the synopsis document for their clinical deep phenotyping study that provides the basis for a full clinical protocol that will be executed in work package 4 of the project. The reviewers were overall satisfied with the proposed approach for the study, but nevertheless proposed some adjustments in the patient population (e.g. inclusion of healthy control participants to add power and enhance understanding of the dimensional neural circuit-behaviour relationships), and in the timing and number of assessments and tests, in order to achieve optimal results within the available time and budget of the clinical study.

SPRINTT

The SPRINTT project aims to improve frailty care and prevention in Europe. At the core of SPRINTT project is a large clinical trial to assess treatment options designed to prevent the frail from becoming disabled and losing their mobility. Ultimately the project will demonstrate how health research and healthcare systems can be adapted to the needs of older people with long-term health problems and provide pharma and SMEs with sound methodologies for developing innovative treatments for frailty and sarcopenia.

The interim review highlighted that several important advances have already occurred. The randomised clinical trial has been set up and recruitment is ongoing. Dissemination to identified target groups has been deployed according to plan and has been successful. The reviewers appreciated that the project team already works closely with medicines regulators to ensure its findings can be rapidly implemented in clinical practice and applied to improve the development of innovative drugs for frailty.

Nonetheless the panel has made some important recommendations mainly related to close follow up and strategies for boosting recruitment of the clinical trial in order to achieve the recruitment targets.

1.4.3 Project reporting

All projects submit a periodic report for the previous year summarising their progress and costs incurred. At the end of the project, a final report is submitted. These reports are analysed in detail by the scientific officer and finance officer responsible for the project, and form the basis for the IMI Programme Office's ex-ante controls.

The table below shows the project reports due in 2016. Most are periodic reports, relating to annual reporting periods (RP). As shown in the final column, some of the reports received in 2016 were final reports.

IMI Calls	1st RP in 2016	2nd RP in 2016	3rd RP in 2016	4th RP in 2016	5th to 7th RP in 2016	Total reports	Of which final reports
IMI1 - 1	0	0	0	0	7	7	5
IMI1 - 2	0	0	0	0	8	8	5
IMI1 - 3	0	0	0	7	0	7	0
IMI1 - 4	0	0	2	5	0	7	0
IMI1 - 5	0	0	1	0	0	1	0
IMI1 - 6	0	0	2	0	0	2	0
IMI1 - 7	0	1	1	0	0	2	0
IMI1 - 8	0	4	0	0	0	4	0
IMI1 - 9	1	3	0	0	0	4	0
IMI1 - 10	1	0	0	0	0	1	0
IMI1 - 11	7	0	0	0	0	7	0
IMI2 - 1	1	0	0	0	0	1	0
IMI2 - 2	7	0	0	0	0	7	0
IMI2 - 3	0	0	0	0	0	0	0
IMI2 - 4	0	0	0	0	0	0	0
IMI2 - 5	0	0	0	0	0	0	0
Total	**17**	**8**	**6**	**12**	**15**	**58**	**10**

1.4.4 Progress against key performance indicators (KPIs) and statistics

The 2016 annual objectives and KPIs, presented in annexes 6, 7 and 8, are linked to the main policy objectives of IMI as set out in its founding legislation[6]. They focus on performance in the following key strategic areas of IMI'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;
(3) performance;
(4) the impact of the IMI programme on the regulatory framework as well as EU competitiveness;
(5) the level of collaboration and SME participation so far;
(6) the level of involvement of patients groups;
(7) the extent of awareness of IMI;
(8) the overall efficiency, budget execution and the level of awareness of the IMI Programme Office.

For the purpose of monitoring IMI's contribution to achieving the H2020 objectives, the Programme Office also collects data to report 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, II, and III of the Council Decision 2013/743/EU establishing Horizon 2020 - the Framework Programme for Research and Innovation.

The Programme Office will continue to measure and track, with the assistance of external consultants and service providers, all aspects of IMI's performance, outputs and impact using different methods for reporting results and outcomes including qualitative assessments, periodic scoreboards, and other metrics. These will continue to reflect the longer term outputs and impacts of both the IMI1 and IMI2 programmes for the ultimate benefit of patients, as well as European competitiveness, economic growth, and the advancement of science and innovation.

Meanwhile, with the goal of enhancing IMI's performance and accountability measures, in 2016 IMI embarked on the development of a logic model and revised its performance measurement framework to ensure the programme's progress against its objectives. Furthermore, the IMI logic model is intended to map IMI's contribution to the intended outputs and outcomes as articulated in the Horizon 2020 intervention logic. The goal here is to ensure that IMI's KPIs are fully aligned with its own objectives and those of the wider Horizon 2020 programme. The KPIs effectively provide a roadmap that shows how IMI's activities will eventually lead to the outcomes and long-term impacts that IMI hopes will result from its work.

[6] See section 2.2 for details.

1.5 Dissemination and information about project results

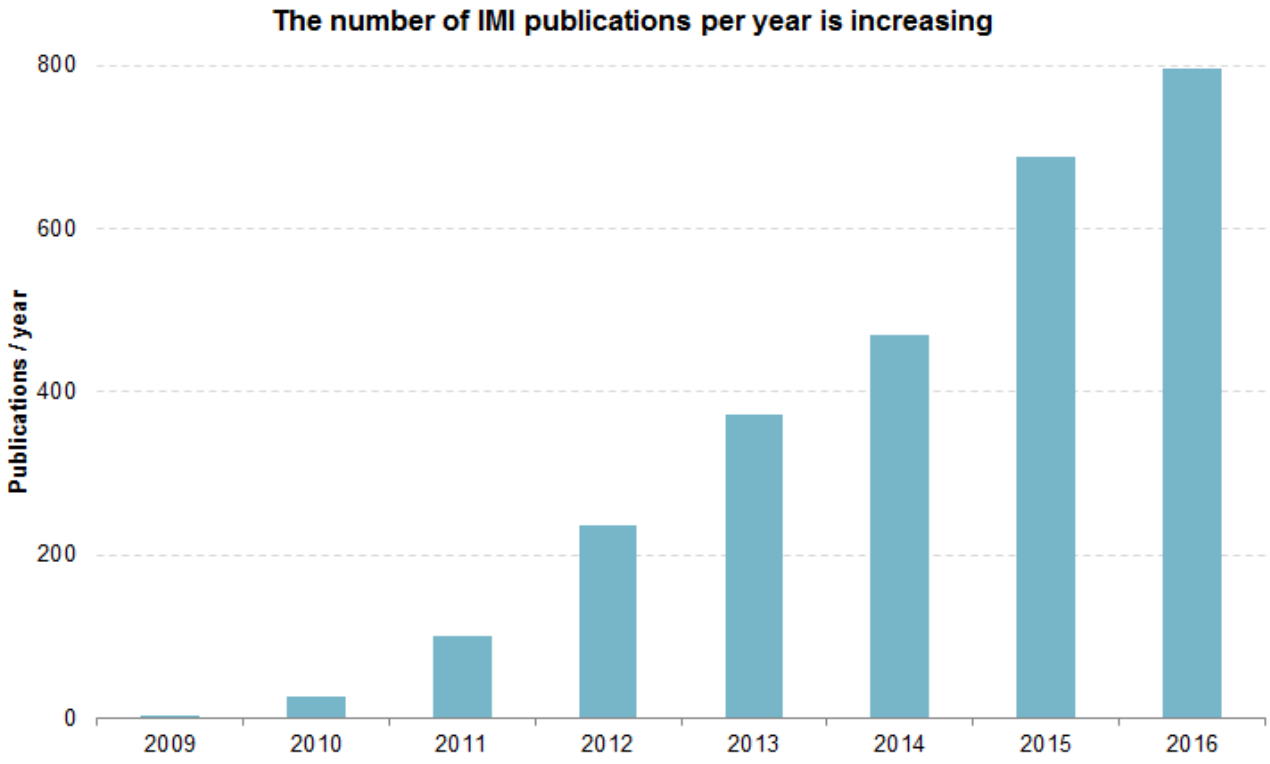
IMI projects are delivering diverse tools, resources and methodologies that are helping to change and improve the way new medicines are discovered and developed. This section describes how these resources, and information on them, are disseminated by both the project partners and IMI. Scientific publications are the key communication and dissemination channel for scientific results. IMI has been analysing the scientific publications emerging from IMI projects for a number of years now.

Many projects are also using discoveries and developments from IMI projects to create new commercial opportunities, for example, through spin-offs and patents.

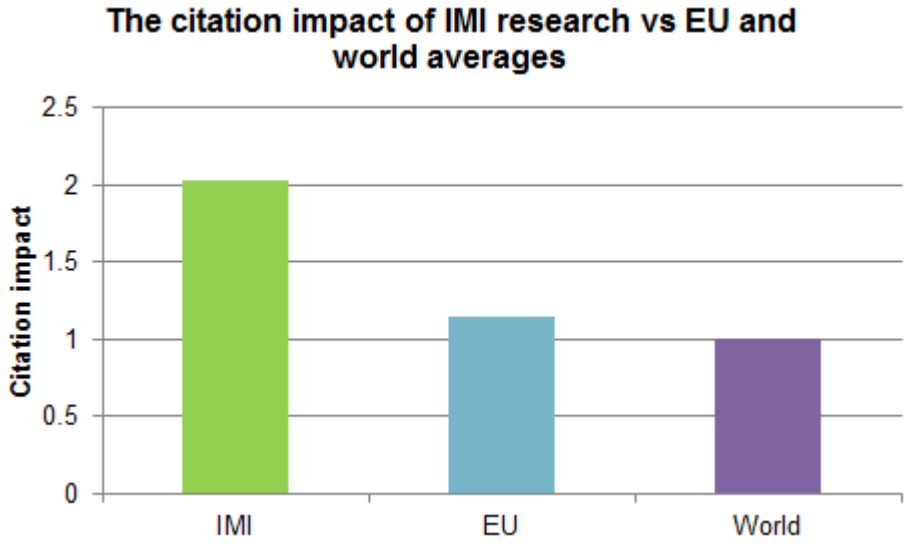
IMI consistently reminds its projects of the importance of dissemination, and in 2016 issued a practical guide on this.

Publications from IMI projects

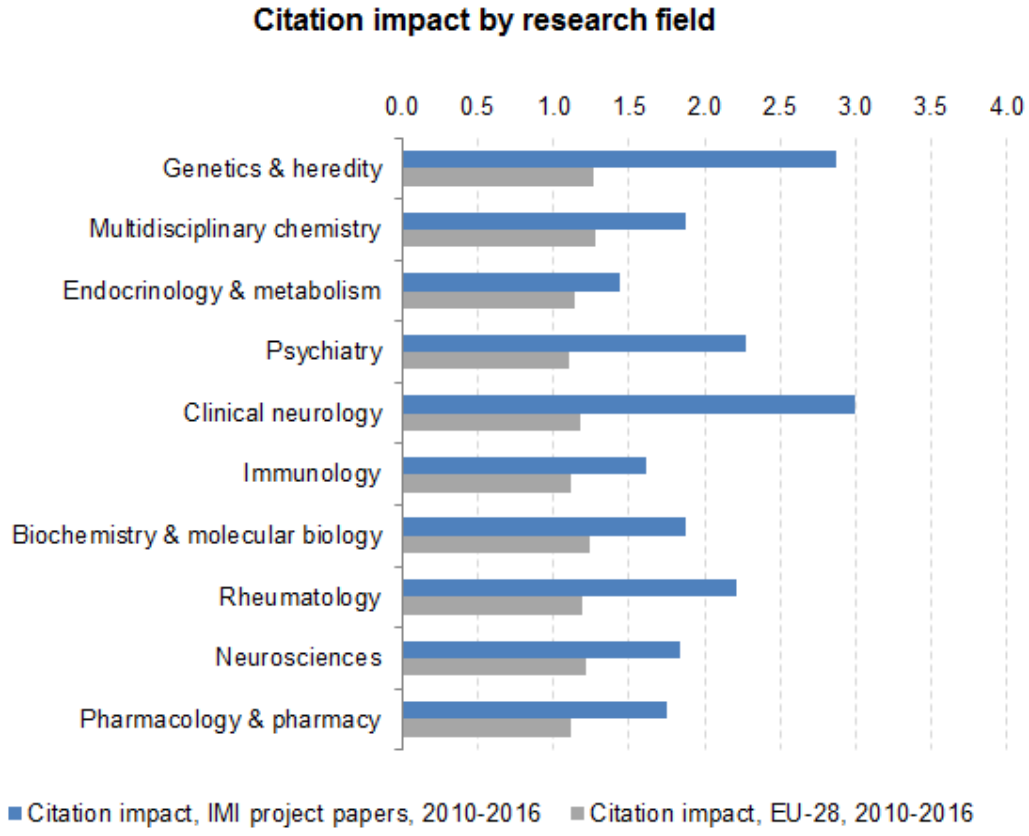
IMI has been monitoring and analysing the papers coming out of its projects since 2012. The analyses, carried out by Clarivate Analytics (formerly Thomson Reuters), have consistently demonstrated both the sheer volume and high quality of research taking place in IMI projects. As the graph below shows, the number of publications is increasing year-on –year. In 2016 alone, IMI projects produced 796 publications, bringing the total number of publications produced by IMI projects to 2 690. With the number of IMI projects on the rise, this trend is set to continue for the coming years.



The field-normalised citation impact for all IMI papers is 2.03 (compared to 1.14 for the EU and the baseline of 1 for the world). This is similar to the result in previous years and shows that IMI is maintaining a high standard even as its output increases.



As the graph below shows, IMI research is published in a range of fields within the biomedical sector. In all fields, IMI research has a higher citation impact than the EU average. This is most notable the case in the fields of genetics and heredity, and clinical neurology, where the IMI citation impact is almost 3.



Other key facts and figures revealed by the latest analysis include the following.

- 26.1% of papers from IMI projects are 'highly cited', meaning they are in the top 10 % of papers by journal category and year of publication.
- IMI projects have published in a total of 796 journals, and the average journal impact factor for IMI research is 5.968.

- Journals with a particularly high impact factor that have published IMI research include: Lancet Neurology, Science Translational Medicine, Nature (and other Nature journals e.g. Nature Genetics, Nature Medicine, and Nature Neuroscience), Science, and the Journal of the American Medical Association (JAMA).
- The collaborative nature of IMI is reflected in the authorship of the papers, with over half of papers (58.4%) recording authors from more than one country.

Project snapshot

Going by the number of papers produced, the most prolific projects are unsurprisingly the older ones. The table below shows the top 10 projects, ranked by number of papers produced. As the figures show, most have citation impacts above 2 and a high percentage of highly-cited papers.

Project	No. papers	Field normalised citation impact	No. highly-cited papers	% highly-cited papers
BTCURE	457	2.03	128	28.0%
EU-AIMS	196	2.47	67	34.2%
NEWMEDS	156	2.24	46	29.5%
EUROPAIN	147	2.16	42	28.6%
IMIDIA	113	1.68	26	23.0%
EMIF	109	3.04	35	32.1%
PROTECT	90	1.26	13	14.4%
SUMMIT	81	1.68	16	19.8%
CHEM21	75	2.32	17	22.7%
eTOX	71	1.81	19	26.8%

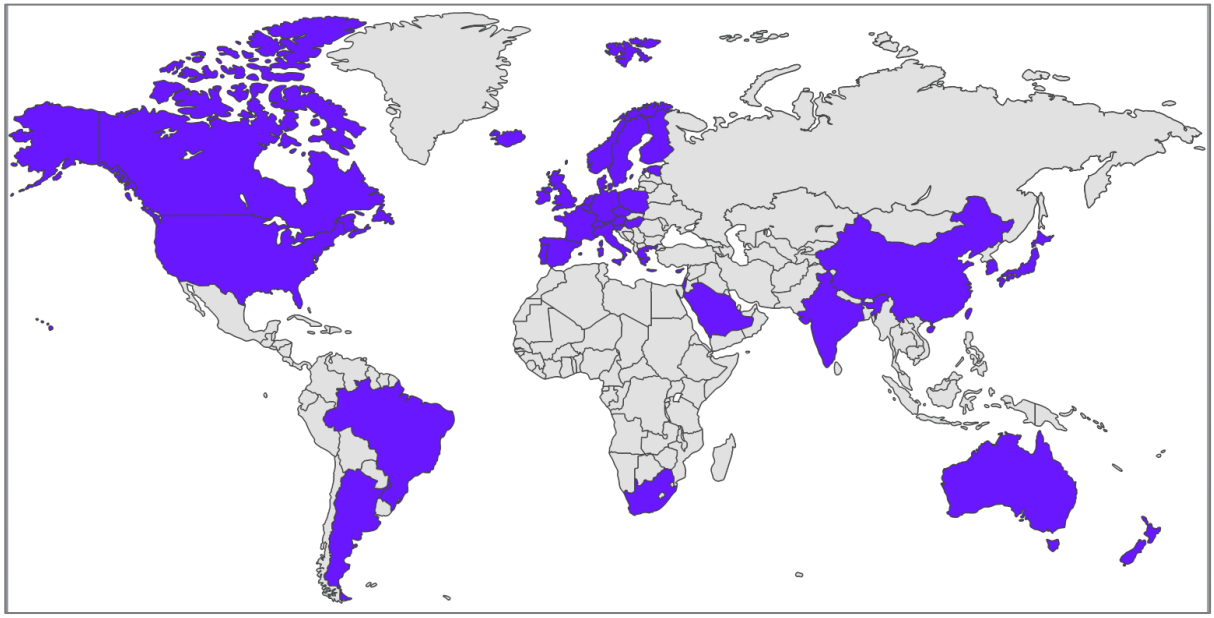
Other projects with fewer publications but impressive citation impacts (i.e. above 2.5) or a percentage of highly-cited papers (i.e. above 30%) are:

Project	No. papers	Field normalised citation impact	No. highly-cited papers	% highly-cited papers
U-BIOPRED	45	2.31	15	33.3%
OncoTrack	43	2.92	18	41.9%
CANCER-ID	34	4.41	14	41.2%
COMPACT	33	3.02	11	33.3%
K4DD	24	2.23	9	37.5%
PROactive	22	2.19	8	36.4%
DIRECT	21	2.64	6	28.6%
DRIVE-AB	9	2.78	3	33.3%
ZAPI	8	4.98	2	25.0%
APPROACH	4	5.48	2	50.0%
SafeSciMET	3	1.53	1	33.3%
ADVANCE	2	3.44	2	100.0%
EUPATI	2	1.42	1	50.0%
VSV-EBOVAC	2	2.10	1	50.0%

WEB-RADR	2	3.06	1	50.0%
EU2P	1	4.17	1	100.0%

Meanwhile, the 2016 report includes the first publications from IMI2 projects, namely three projects from the Ebola+ programme (EbolaMoDRAD, EBOVAC1, and VSV-EBOVAC), as well as ADAPT-SMART, INNODIA, RADAR-CNS and RHAPSODY.

The analysis also reveals the global reach of IMI's research activities. In total, 81 countries have at least one paper funded by IMI. The map below highlights countries with at least 10 papers funded by IMI.



IMI project impacts: spin-offs and commercial exploitation

In early IMI Calls, sustainability and commercial exploitation plans were not specifically part of the project objectives. However, as projects are nearing completion, they are bringing forward sustainability plans and investigating how best to exploit the results generated. Several have identified innovative business solutions for keeping the added value of the project sustainable after the IMI-funded project duration. In addition, the results of several projects have resulted in spin-off activities as well as commercialisation. IMI project highlights in these areas from 2016 are summarised below.

Spin-offs

Companies, foundations and non-profits generated by IMI projects

- **DDMoRe** has established the DDMoRe Foundation that aims to deliver infrastructure to contribute to the quality, efficiency and cost effectiveness for model-informed drug discovery & development (MID3) and therapeutic use. Servier is their first paying member.
- The archiving of **OncoTrack** data after completion of the project will be supported by funds from the government of Luxembourg, creating an ELIXIR hub at the University of Luxembourg.
- **OncoTrack** has founded a new not-for-profit organisation Dahlem Institute for Genome Research and Medical Systems Biology (DCGMS) gGmbH is a not-for-profit, pioneering systems biology research group focused on the analysis, characterisation and modelling of diseases.
- As a result of public screening programme of the **European Lead Factory**, a spin-out company was created, (ScandiCure) whose aim is to further develop molecules discovered via the ELF screen into a

first-in-class anti-diabetic drug. The company has already secured an investment from GU Ventures AB, an investment company and an incubator owned by the Swedish state.

- **EUPATI** has established national platforms in several countries across Europe including Austria, France, Germany, Ireland, Italy, Luxembourg, Malta, Poland, Spain, Switzerland and the UK, and more recently in Denmark, Slovakia and Serbia.
- Resulting from the **StemBANCC** project, Newcastle University has established a company called Newcells Biotech that provides services and products based on iPSC technology for drug discovery and toxicity testing activities of academic and industrial customers.

Follow up projects, grants, or new collaborations

- The **GetReal** consortium has secured €1 million over two years from EFPIA companies to support sustainability activities.
- Researchers from **RAPP-ID** were awarded follow on grants: the ROUTINE project (FP7), on the development of urinary tract infections diagnostics, and ND4ID (H2020) a Marie Curie Initial Training Network grant to develop a unique education programme focused on technological aspects of diagnostics development.
- **K4DD** partners were granted a Partnership for Advanced Computing (PRACE) grant for computational time, enabling faster and more elaborate analysis of the K4DD results.
- **PROactive** signed a Memorandum of Understanding (MoU) among the project partners who wish to continue the collaboration beyond the project lifetime.
- The **ULTRA-DD** consortium has attracted additional funding (€1.5 million for the next two years) via collaborations with disease foundations, including Myeloma UK and The Brain Tumour Charity, to sponsor postdoctoral researchers whose scientific outputs will contribute directly to the ULTRA-DD project.

Commercialisation and exploitation

- New tools have been developed with support from **EU-AIMS** partners:
  (1) new hardware tools for animal behaviour research: PhenoTyper® instrumented cage systems, with add-on sensors and stimulus devices;
  (2) new software tools for animal behaviour research: The Observer® XT, EthoVision® XT, UltraVox™ XT. New and improved versions of these products have been launched on the market and sold to pharmaceutical companies, universities and research institutes around the world.

1.6 Operational budget execution

About IMI's operational budget

IMI's operational budget ('Title 3') reflects expenses linked to the implementation of the IMI research agenda[7]. Here it should be noted that since 2014, IMI has managed two programmes in parallel:

- IMI1 (under the Seventh Framework Programme, FP7)
  FP7 was the EU's research and innovation funding programme for 2007-2013. Through FP7, the EU contributes EUR 966 million to the IMI1 research programme.
- IMI2 (under Horizon 2020, H2020)
  H2020 is the EU's research and innovation funding programme for 2014-2020. The EU has committed to contribute EUR 1.638 billion from H2020 to the IMI2 programme.

IMI's operational budget in 2016

The operational budget approved for 2016 was EUR 297.5 million in commitment appropriations (CA) and EUR 252.4 million in payment appropriations (PA).

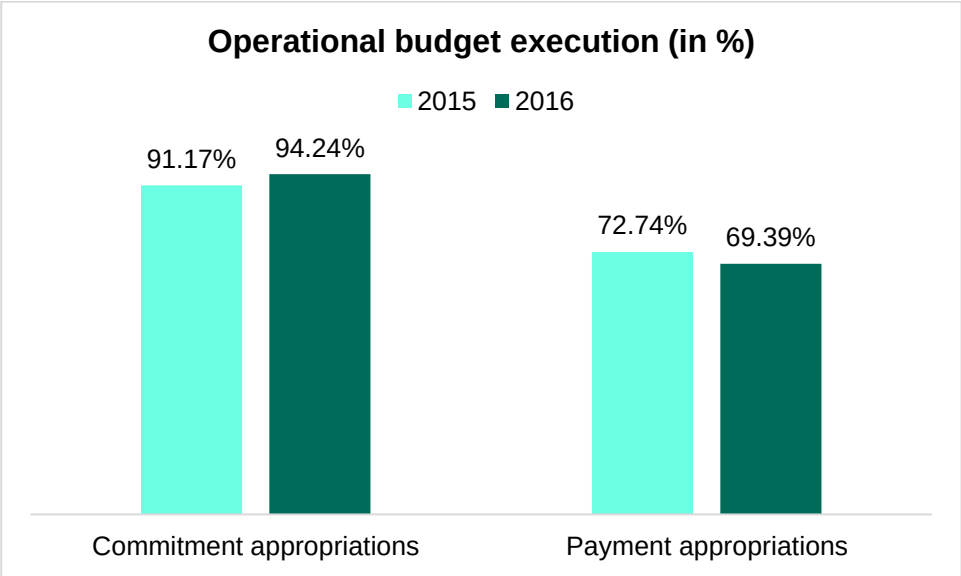
Budget execution of the commitment appropriations reached 94.24 % of the total budget, with payment appropriation execution reaching 69.39 %.

The commitment appropriations linked to the research agenda were consumed by Grant Agreements for projects under IMI2 – Call 3, 5 and 6 and by launching IMI2 – Calls 9 and 10. The launch of IMI2 – Call 11 (Horizon 2020) was postponed to 2017.

The payment appropriations were consumed by intermediate payments for projects from IMI1 – Calls 1–11 and IMI2 – Call 2, as well as pre-financing for projects of IMI2 – Call 3, 5 and 6.

The budgeted payment appropriations were not fully used in 2016 due to significant underspending in the Ebola+ programme, and delays in concluding Grant Agreements for projects under IMI2 - Calls 7 and 8.

Further details about operational financial transactions can be found under section 2.3.



[7] IMI's wider legal and financial framework, and the budget relating to Titles 1 and 2 (which cover IMI's administrative costs), are described in more detail in sections 2.2 and 2.3.

The tables below indicate the operational budget execution (Title 3) per programme.

	Execution of commitment appropriations in EUR							
	Budget			Additional appropriations (carry over + assigned revenue)		Total		
	Voted budget	Execution	%	Appropriations	Execution	Appropriations	Execution	%
IMI1	-	-	-	*85 530*	-	*85 530*	-	-
IMI2	*214 386 590*	*214 348 320*	*99.98*	*83 071 970*	*66 046 050*	*297 458 560*	*280 394 380*	*94.26*
Total	214 386 590	214 348 320	99.98	83 157 500	66 046 050	297 544 090	280 394 380	94.24

	Execution of commitment payments in EUR							
	Budget			Additional appropriations (carry over + assigned revenue)		Total		
	Voted budget [8]	Execution	%	Appropriations	Execution	Appropriations	Execution	%
IMI1	*130 448 760*	*109 792 160*	*84.16*	*85 530*	*54 520*	*130 534 290*	*109 846 680*	*84.15*
IMI2	*69 419 830*	*63 236 040*	*91.09*	*52 510 970*	*2 100 000*	*121 930 800*	*65 336 040*	*53.58*
Total	**199 868 600**	**173 028 210**	**86.57**	**52 596 500**	**2 154 520**	**252 465 100**	**175 182 730**	**69.39**

The commitments carried forward from 2015 to 2016 include the amounts committed at the launch of Calls and the amounts committed based on grant agreements concluded.

The commitments related to Calls launched are consumed by the commitments based on the grant agreements concluded. The commitments related to Calls 7 and 8 were de-committed at the end of 2016 and, based on the N+ 3 rule as set out in the IMI2 Financial Rules, the unused appropriations will be carried over to the 2017 budget.

The table below shows the summary of commitments outstanding for operational expenditure per programme at the end of 2016.

Commitments carried forward from previous year 2015	**Commitment appropriations in EUR**				
	Carry forward	**Commitments made during 2016**	**De-commitments**	**Payments**	**Commitments outstanding at end 2016**
IMI1	*427 949 660*	-	-	*109 846 680*	*318 102 970*
IMI2	*305 757 020*	*280 394 380*	*- 116 802 180*	*65 336 040*	*404 013 170*
Total	**733 706 670**	**280 394 380**	**- 116 802 180**	**175 182 730**	***722 116 150***

[8] Of the total in this column, (EUR 199 868 600): EUR 197 000 000 is from the EU; EUR 2 668 600 is from the Bill and Melinda Gates Foundation as a contribution towards operational expenditure; and EUR 200 000 is a contribution from BMS.

EU funds committed under IMI1 and IMI2

The table below outlines the breakdown per Call of EU committed funds for IMI1 (FP7) as of 31 December 2016.

IMI1 Call	EUR committed
Call 1	116 082 000
Call 2	85 765 000
Call 3	112 839 000
Call 4	97 943 000
Call 5	79 999 000
Call 6	125 417 000
Call 7	12 999 000
Call 8	98 732 000
Call 9	56 440 000
Call 10	6 100 000
Call 11	173 410 000
Total	**965 731 000**

The table below outlines the breakdown per Call of EU committed funds for IMI2 (H2020) as of 31 December 2016. For IMI2 Calls 1 to 6, these figures reflect the commitments as set out in the Grant Agreements. For Calls 7 to 10, the figures represent the commitments as set out in the Call texts.

IMI2 Call	EUR committed
Call 1	17 630 000
Call 2	114 090 000
Call 3	56 060 000
Call 4	1 130 000
Call 5	47 477 000
Call 6	46 696 000
Call 7	46 802 000
Call 8	70 000 000
Call 9	58 328 000
Call 10	173 890 000
Total	**632 103 000**

1.7 In-kind contribution

IMI is a public-private partnership between the EU (represented by the European Commission) and the pharmaceutical sector (represented by EFPIA). Some IMI2 projects also include Associated Partners[9]. In IMI projects, academic institutions, SMEs, and non-profit organisations receive EU funds to support their activities[10].

Large EFPIA companies and Associated Partners do not receive any EU funding from IMI, but contribute to the projects in-kind. These in-kind contributions are costs incurred by EFPIA companies and Associated Partners in the implementation of IMI projects and include the costs of researchers, research equipment and materials.

The EFPIA in-kind contribution[11] can be broken down into the following cost categories:

- **Personnel**: staff employed by EFPIA companies directly working on IMI projects.
- **Other direct costs**: consumables, equipment depreciation, samples, compounds.
- **Subcontracting**: clinical trials, subcontracting to clinical research organisations, subcontracting to data management companies, lab services, communication, project management support, etc.
- **Financial contribution (FC)**: A transfer of funds from an EFPIA company to an academic institution within the same project/consortium. This financial contribution is used by the academics to hire researchers during the lifetime of the IMI project or to buy consumables or equipment.

EFPIA companies are contractually obliged to report to IMI all costs that they claim were incurred in IMI projects. IMI controls the eligibility and regularity of the contributions and carefully monitors the development of the total in-kind contribution to both programmes (IMI1 and IMI2).

For each programme, Council regulations clearly define the matching requirement:

- IMI1: EC funding up to EUR 966 million, to match the equivalent in-kind contributions from EFPIA.
- IMI2: EC funding up to EUR 1.425 billion, to match the equivalent in-kind contributions from EFPIA companies.
  An additional EUR 213 million in EC funding may be provided to match additional contributions from other Members, Associated Partners, or from their constituent entities or their affiliated entities.

IMI1 programme

EFPIA's commitment to the IMI1 programme totalled EUR 953.1 million as of 31 December 2016, down by EUR 43.2 million compared to 2015. This decrease is due to the decision by the COMBACTE-NET project to terminate work on a compound due to scientific (safety or efficacy) reasons.

The IMI1 commitment remains unchanged at EUR 965.7 Million. However commitments for an amount of EUR 20 million were 'frozen' in the COMBACTE-NET project, reducing the IMI1 matching funding to EUR 945.7 million.

As of 31 December 2016, EFPIA companies had reported EUR 487.7 million in-kind contributions, of which EUR 385 million had been formally validated (checked by IMI staff and/or audited by external auditors – see section below on Control). The difference between reported and accepted in-kind contribution illustrated in the table below is due to ongoing review by IMI; missing, incomplete or non-compliant certification of the reported in-kind; and time needed to review and validate the reports.

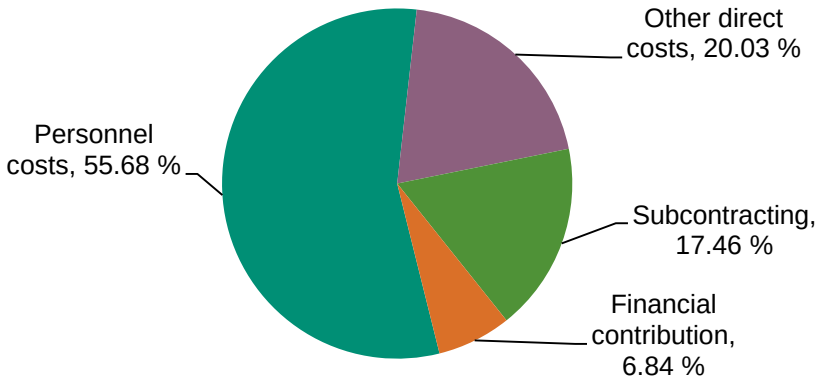
[9] IMI's legal and financial framework is described in more detail in section 2.2.

[10] The management of these funds is described in more detail in section 1.7 and section 4.

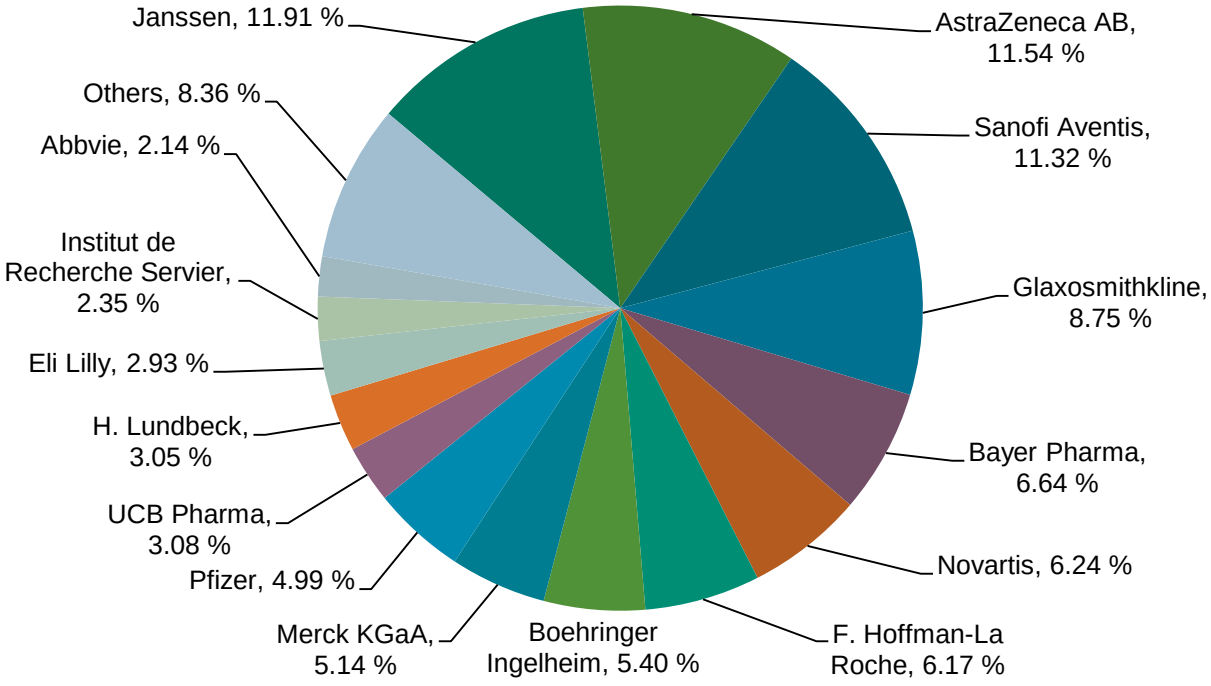
[1111] Details of what can be considered as in-kind contribution are set out in the IMI1 and IMI2 regulations and, for IMI1, in the Financial Guidelines.

The breakdown of the reported EFPIA in-kind contribution to IMI1 projects, by cost category and by company, is shown in the graphs below.

IMI1 in-kind contribution by category



IMI1 in-kind contribution by company



Companies listed under 'Other' are: Abbott, AiCuris Anti-infective Cures GmbH, Almirall, Amgen, Astellas Pharma Europe, Basilea, Biogen Idec, Bristol Myers Squibb, Chiesi Farmaceutici, Eisai, Farmaindustria, Grünenthal, INFARMA, Ipsen, Laboratorios del Dr Esteve, Menarini, Merck Sharp & Dohme, Novo Nordisk, Orion Corporation, Sanofi-Aventis Groupe, Sigma-Tau, Takeda, VFA, Vifor

The table below provides a breakdown by Call of both EU and EFPIA contributions (cost claims only) for the whole IMI1 programme[12].

IMI1		EU (EUR million)			EFPIA in-kind (EUR million)		
Call	Projects	Committed	Accepted	%	Committed	Validated	%
1 - 2008	15	116.1	108.2	93.2%	149.9	117.2	78.2%
2 - 2009	8	85.8	63.1	73.5%	74.3	48.2	64.9%
3 - 2010	7	112.8	70.4	62.4%	73.7	34.8	47.2%
4 - 2011	7	97.9	56.1	57.3%	109.7	58.1	53.0%
5 - 2012	1	80	42.8	53.5%	91.3	81.1	88.8%
6 - 2012	2	125.4	23.5	18.7%	98.2	13.7	14.0%
7 - 2012	2	13	6.2	47.7%	11.9	5.3	44.5%
8 - 2012	4	98.7	21.7	22.0%	49.6	13.1	26.4%
9 - 2013	4	56.4	7.9	14.0%	88.6	5.2	5.9%
10 - 2013	1	6.1	0.6	9.8%	6.1	0	0.0%
11 - 2013	8	173.4	10.7	6.2%	199.7	8.5	4.3%
Total	**59**	**965.7**	**411.2**	**42.6%**	**953.1**	**385.2**	**40.4%**

Of EUR 953.1 million committed by EFPIA, EUR 213 million (or 22 %) comes from outside the EU and FP7-associated countries[13].

IMI2 programme

As of 31 December 2016, 25 IMI2 projects had been launched with EUR 275.8 million in EC funding, and commitments of EUR 249.1 million from EFPIA, and EUR 14.4 million from Associated Partners. The following table provides an overview of EU, EFPIA and Associated Partner contributions to IMI2 projects.

IMI2		EU (EUR million)		EFPIA in-kind (EUR million)		Associated Partners (EUR million)	
Call	Projects	Committed	Paid	Committed	Validated	Committed	Validated
1	1	17.6		12.7		5.6	
2	8	114.0	12.9	100.7	47.2		
3	5	49.0		43.9		7.0	
4	1	1.1		2.0			
5	6	47.5		44.3		1.8	
6	4	46.4		45.3			
Total	**25**	**275.8**	**12.9**	**249.1**	**47.2**	**14.4**	

Of the EUR 263.5 million committed by EFPIA and the Associated Partners as of 31 December 2016, EUR 83.7 million comes from outside the EU and H2020 associated countries[14]. A significant part (21%) of

[12] In this table, the 'accepted' column on the EU side refers to costs reported by beneficiaries and accepted as eligible by IMI.

[13] Under the IMI1 programme, in-kind contributions from outside the EU/FP7 associated countries are subject to IMI Governing Board approval on a case-by-case basis.

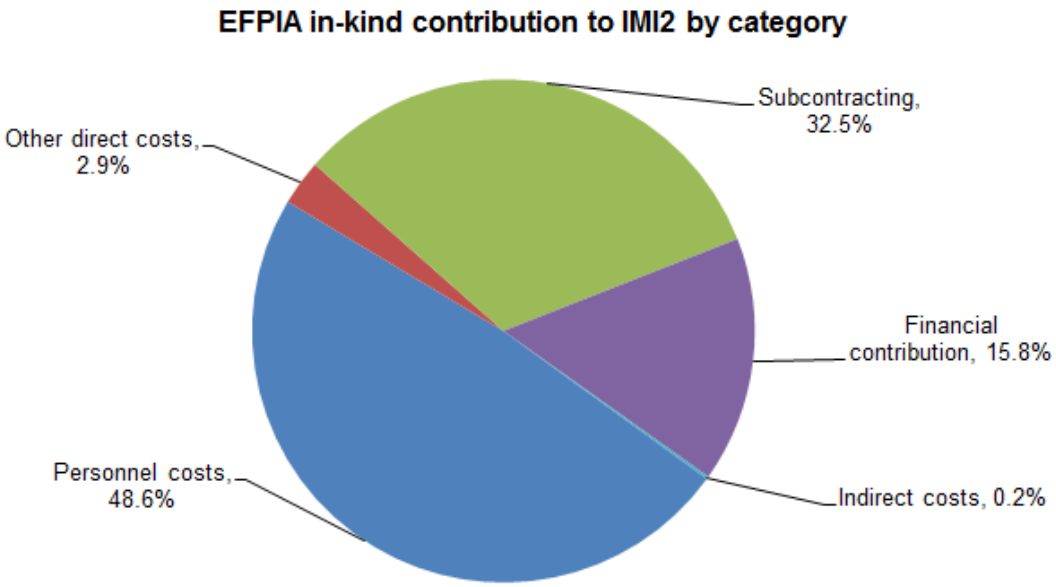
this non EU/H2020 associated countries contribution comes from Switzerland; it is expected that this percentage will decrease once Switzerland becomes a H2020 Associated country on 1 January 2017.

Under the IMI2 programme, beneficiaries of EU funding and EFPIA companies and Associated Partners do not report at the same time. While beneficiaries report according to project deadlines, EFPIA companies and Associated Partners report once a year on 31 January for the previous year. As of 31 January 2016, EFPIA companies had reported EUR 83.5 million and Associated Partners had reported EUR 0.3 million in in-kind contributions.

The table below shows the breakdown of in-kind contributions to IMI2 so far by year and by status.

IMI2 in-kind contribution (all figures in EUR million)	EFPIA companies	Associated Partners	Total
Reported in 2015, certified and validated by IMI	47.2	0.0	47.2
Reported in 2015, not yet certified (estimates)	2.1	0.0	2.1
Reported in 2016, not yet certified (estimates)	34.2	0.3	34.5
Total	83.5	0.3	83.8

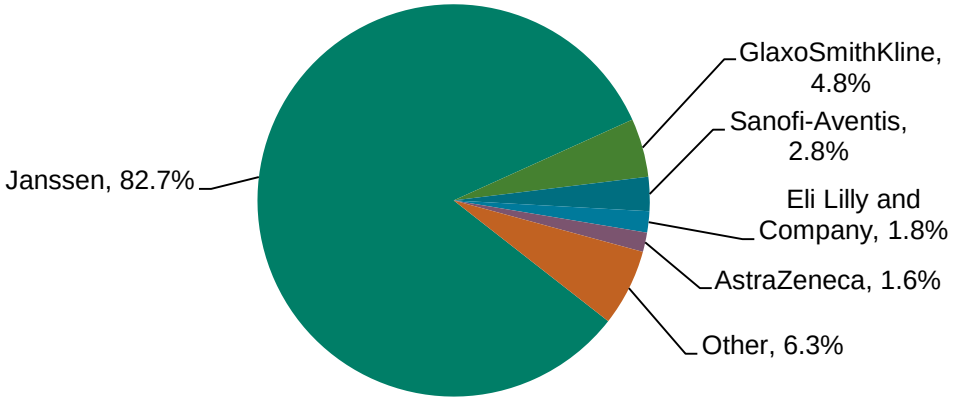
The breakdown of the reported EFPIA in-kind contribution to IMI2 projects, by cost category and by company, is shown in the graphs below. The high percentage of subcontracting costs in IMI2 projects (32.5%) compared to IMI1 projects (17.4%) is due to the particularities of the Ebola projects, where significant tasks were subcontracted.



As the company breakdown shows, 82.7 % of the total reported IMI2 in-kind contribution (or EUR 69.2 million) is provided by one single EFPIA company, Janssen. The remaining 17.3% comes from 29 different organisations.

[14]As set out in Article 4 of the IMI2 regulation: 'In-kind contributions consisting of costs incurred in third countries other than countries associated to Horizon 2020 shall be justified and relevant to the objectives set out in Article 2 of this Regulation, and shall not exceed 30 % of the eligible costs at the level of the IMI2 programme, incurred by the Members other than the Union and by the Associated Partners'.

IMI2 in-kind contribution by organisation



Organisations included under 'Other' are: AbbVie, Actelion Pharmaceuticals, Amgen, Bayer Pharma, Biogen Idec Limited, Boehringer Ingelheim, Bristol-Myers Squibb Company, EFPIA, F. Hoffmann-La Roche, GE Healthcare, Grünenthal, H. Lundbeck, Institute de Recherche Servier, Intervet International, IPSEN Innovation, JDRF International, Merck, MSD IT Global Innovation Center, Novartis Pharma, Novo Nordisk, Pfizer Limited, Piramal Imaging, Takeda Development Centre Europe Ltd., The Leona M. and Harry B. Helmsley Charitable Trust, UCB Biopharma.

Controls of in-kind contributions under IMI1 (FP7)

Ex-ante controls of the in-kind contribution

EFPIA contributions to IMI projects are reviewed from before the start of the project, when proposals for new projects are evaluated by independent experts. During evaluation, experts assess whether the proposed in-kind EFPIA contribution is in line with the work to be carried out in the project.

Once the project is underway, EFPIA companies' in-kind contributions are reported by participating companies for each project as an integral part of the annual project report. All in-kind contributions declared must be accompanied by audit certificates, during or at the end of the project. Furthermore, the IMI Programme Office audits companies providing in-kind contributions. Before validating each annual report and the related contributions, IMI carries out a series of checks to verify the eligibility of in-kind contributions, i.e. that they are in line with the Grant Agreement requirements and the project's description of work.

The IMI Governing Board receives regular updates from the IMI Programme Office on the level of in-kind contributions to projects. The in-kind contributions are also reported in a transparent manner in the annual accounts and the Annual Activity Reports of IMI, both of which are published online. Before their formal approval, the draft annual accounts of IMI are carefully scrutinised by the European Commission. The approval of the annual accounts, including the in-kind contributions, is part of the decision-making process in which the European Commission has a controlling vote at the level of the IMI Governing Board.

The European Court of Auditors audits IMI's accounts. In doing so, the Court has full access to all the documentation linked to the reporting of the in-kind contributions and the validation and auditing of such reports.

Ex-post controls of the in-kind contribution

In addition to the ex-post audits covering IMI funding to beneficiaries, the IMI Programme Office also continually conducts ex-post reviews and financial audits on the declared in-kind contributions by EFPIA companies participating in IMI projects. These companies do not receive any IMI funding but contribute their own resources in-kind to the projects in which they participate.

The purpose of these audits, using a risk-based approach as per IMI's audit strategy, is to independently verify that the in-kind contributions accepted by IMI JU have been effectively committed to the projects.

Each control exercise consisted of two key elements: an ex-post review, followed by a financial audit.

Ex-post review: This is a review of the in-kind methodology used by the EFPIA company to declare in-kind contributions for all the IMI JU projects in which it participates, applying agreed-upon procedures to confirm the factual basis of the responses and descriptions provided in the submitted certificate on in-kind contribution methodology. On this basis, the auditors are able to conclude whether:

- the approach and basis of the actual calculations were as originally described in the accepted methodology;
- whether any mathematical errors or other inconsistencies were noted in the actual calculations made relating to the direct personnel full time equivalent (FTE) daily cost rate;
- the in-kind methodology was consistently applied by the EFPIA company across all research and business activities and in accordance with its usual accounting and management principles and practices;
- the basis of the methodology and calculation was consistent with Article II.13.4 of the Grant Agreement and excludes ineligible costs.

Financial audit: This is a financial audit of a sample of in-kind contributions declared in the financial statements submitted by EFPIA companies to IMI in order to assess and present an opinion on whether these meet the conditions of the Grant Agreement.

Controls carried out by IMI on EFPIA companies' contributions are subject to scrutiny by IMI's internal and external auditors, namely the European Commission's Internal Audit Service (IAS) and the European Court of Auditors (ECA).

Audit coverage of the in-kind contribution

To date IMI, has completed ex-post audits of 13 EFPIA companies, covering a total of EUR 344.3 million of accepted contributions to IMI1 projects or 89 % of all EFPIA contributions. A further three companies' audits are ongoing and due to be finalised in the first and second quarters of 2017. Together the 16 companies' contributions to IMI projects total EUR 365.8 million or 95 % of total contributions.

An overview of the audit coverage of the in-kind contribution (IKC) provided by the EFPIA companies is detailed below:

Company	IKC accepted as of 31/12/2016 (EUR million)
Total finalised audits	344.3
Total ongoing audits	21.4
Total all EFPIA companies audited or under audit	365.8
Total all EFPIA companies	385.4
Audit coverage	**95 %**

The audits finalised to date have identified adjustments, either positive ones thus increasing the contribution or negative ones decreasing it, for a total value of EUR 3 621 519 corresponding to 1.05 % of the total audited amounts.

Accepted IKC (EUR)	Audited IKC (EUR)	Coverage	Negative adjustments (EUR)	Positive adjustments (EUR)	Total absolute adjustments (EUR)	% of absolute adjustments
385 357 733	344 348 701	89.36%	-1 760 634	1 860 885	3 621 519	1.05 %

Controls of in-kind contributions under IMI2 (Horizon 2020)

The framework for the selection and evaluation of proposals in IMI2 (H2020) is the same as described above for IMI1 (FP7). The main change from FP7 is in the reporting of in-kind contributions during project implementation. Under FP7, in-kind contributions are declared on a per-project basis, together with the annual report of each project. By contrast, in IMI2, each EFPIA company and Associated Partner is required to report its in-kind contributions once a year for the totality of all costs generated contributing to IMI2 projects (and so by extension to IMI's operational budget).

All reported costs must be accompanied each year by a certificate from an independent external auditor, confirming that the costs are in line with the requirements of the IMI2 Regulation. The certification must be based on standard terms of reference provided by IMI2. IMI analyses the audit reports and adjusts the amounts where necessary. In-kind contributions are only validated for inclusion in IMI's accounts after these checks and adjustments[15]. IMI may carry out an additional audit itself, before the validation of the in-kind contribution. This is done on a risk basis only, should the audit certificate provided with the cost declaration leave uncertainties as to the valuation of the contribution.

[15] When in-kind contributions are validated by the IMI Executive Director, they are, in accordance with EU Accounting Rule 1, recognised as contributions from Members under the net assets heading of the balance sheet.

2 Support to operations

2.1 Communication and events

In 2016, IMI's communication activities focused on achieving the overarching goal of the IMI Communication Strategy, namely to increase the level awareness of IMI amongst all targeted groups. This goal has been broken down into the following communication objectives:

1. promote IMI and raise awareness levels and perception of IMI among all target groups;
2. attract the best researchers from relevant target groups to apply for funding under IMI 2 Calls for proposals
3. increase the engagement of patients in IMI's activities;
4. increase the engagement of SMEs in IMI's activities;
5. gain support for IMI among key groups of policymakers and opinion leaders.

Although IMI's communication activities are led by the IMI communication team, IMI's successes in this area in 2016 were considerably boosted by the contribution of other IMI staff, the European Commission and EFPIA, as well as the SRG, the Scientific Committee, and the projects.

IMI outreach activities - events

Event	Date & location	Outcome
How IMI is accelerating access to affordable innovative medicines? This lunch debate in the European Parliament featured a presentation of the first results of study on the socio-economic impacts of IMI's projects, followed by a discussion.	24 February Brussels, Belgium	60 people, including Members of the European Parliament (MEPs), opinion leaders, patients, and scientists took part in a lively discussion on how a PPP like IMI offers value for money for European citizens.
BIO 2016 IMI's involvement in BIO was as follows: Educational session on Alzheimer's clinical trials (organised by IMI, featuring IMI's EPAD project) Sponsored workshop on novel anti-infectives (co-organised by IMI, IMI's ENABLE project and CO-ADD, the Community For Open Antimicrobial Drug Discovery) IMI speaker slot in educational session on antibiotic research and development IMI presence at European Commission stand at the BIO exhibition	6-9 June San Francisco, US	The sessions organised by IMI attracted large audiences (over 150 for the session on Alzheimer's disease and 200 for the workshop on anti-infectives) and positive feedback. IMI was also active on Twitter during the event (and an IMI tweet was featured on the BIO homepage for much of the event). IMI's presence at the exhibition also helped to raise IMI's profile at BIO.
Workshop for National Contact Points (NCPs) Held just before the Stakeholder Forum, this event was held to strengthen the links between IMI and this important group of multipliers	28 September Brussels, Belgium	The event was well attended and allowed both IMI and the NCPs to learn from each other and decide on how best to work together in the future.

Event	Date & location	Outcome
IMI Stakeholder Forum 2016 Day 1 of the event focused on IMI2 – Call 10, and on IMI's rules and procedures. Day 2 was dedicated to four parallel consultative workshops designed to gather stakeholders' input on IMI's plans in four key areas: biopreparedness, advanced therapies, digital health, and oncology.	28-29 September Brussels, Belgium	375 people attended the event in person and a further 97 followed it online. The output of the workshops will allow IMI to plan its future activities. The presentations and videos of the event were published on the event web page.
IMI at the European Week of Regions and Cities The joint undertakings, including IMI, featured at the 2016 edition of the European Week of Regions and Cities with a session entitled 'Enhance Regional Innovation and Growth: possibilities for integrated funding through regional cooperation with Joint Undertakings (JUs)'.	11 October Brussels, Belgium	The event explored how synergies between different funding mechanisms such as the European Structural and Investment Funds (ESIF) and the Horizon 2020 programme can help to boost innovation and growth in the regions.
IMI at the European Parliament ITRE Committee IMI Executive Director Pierre Meulien gave a presentation on IMI's work and achievements to the European Parliament's Committee on Industry, Research and Energy (ITRE).	12 October Brussels, Belgium	The meeting was an important opportunity for IMI to present its achievements and added value, and for MEPs to ask questions and give feedback.
Alzheimer's disease: advancing research through collaboration This roundtable held in the European Parliament brought together representatives of IMI Alzheimer's disease projects plus representatives of other major initiatives in the field to discuss the value of EU/IMI collaborative research in tackling the health challenge of Alzheimer's disease.	8 November Brussels, Belgium	The event successfully showcased both IMI's and Horizon 2020's successful track record in building powerful research networks and leveraging investments.

In addition to the events listed above, IMI staff members and multipliers spoke at a large number of events both in Europe and elsewhere. IMI was also involved in a number of events in the European Parliament (in addition to the two events organised directly by IMI, listed in the table above).

- 14 July: IMI Executive Director Pierre Meulien gave a presentation on IMI at a workshop on 'EU options for improving access to medicines' organised by the European Parliament's Committee for Environment, Public Health and Food Safety (ENVI).
- 20 October: IMI helped its eTRIKS project organise a workshop at the European Parliament designed to gather stakeholder input on the value of medical research data re-use.

IMI also organised the following consultative workshops (in addition to those held during the Stakeholder Forum) to gather input from core stakeholders on future plans and activities in key thematic areas:

Date and location	Subject
22 January Stockholm, Sweden	EU-US collaboration on clinical trials related to antimicrobial resistance workshop (with participation of EC, JPI AMR and NIH) See section 1.2.4 for more information
5 April Brussels, Belgium	Paediatric clinical trials

28 April Brussels, Belgium	IMI's patient engagement strategy See section 1.4.2 for more information
7-8 December Lyon, France	Driving infectious diseases diagnostics toward the sustainable development and use of antibiotics workshop (consultation among the major EU diagnostics companies, organised by BioMerieux in collaboration with IMI)
15 December Brussels, Belgium	Safe use of medicines during pregnancy/lactation

Promoting IMI Calls for proposals

IMI started 2016 by continuing the promotion of IMI2 – Calls 7 and 8, which were launched at the end of 2015. IMI subsequently launched its 9th and 10th Calls under IMI2 during 2016. Calls were promoted via the following channels:

- IMI website
- H2020 Participant Portal
- Press
- IMI Newsletter
- Social media (Twitter, LinkedIn)
- Brochures and flyers
- Events organised by others (e.g. SRG members)
- Direct e-mails to stakeholder organisations (e.g. academic societies, patient groups) and relevant individuals
- IMI events
- Presentations by IMI staff at external events

The first day of IMI's Stakeholder Forum was also dedicated to IMI Calls, IMI's rules and procedures, and tips for applicants.

For each Call launched, IMI also organised webinars on all Call topics as well as IMI's rules and procedures. The webinars represent an important opportunity for potential applicants to learn more about the topics, ask questions, and network with fellow participants. The webinars are also recorded and published on the IMI website and YouTube channel, further maximising their reach. The table below shows the number of registrations for the Call-related webinars in 2016.

Call	Dates	Registrations
IMI2 – Calls 7 & 8	11-29 January	645
IMI2 – Call 9	11-29 April	546
IMI2 – Call 10	7-20 December	821*

* Note that the figure for IMI2 – Call 10 webinar registrations does not include registrations for two webinars held in January 2017.

Promoting IMI projects and their successes

The Communications team promotes IMI projects and their successes through a variety of channels:

- IMI newsletter
- IMI website
- Social media (Twitter, LinkedIn)
- IMI press releases
- Other organisations' press materials (e.g. European Commission)
- Press and scientific articles by the IMI office
- Examples given to journalists writing about IMI
- IMI events

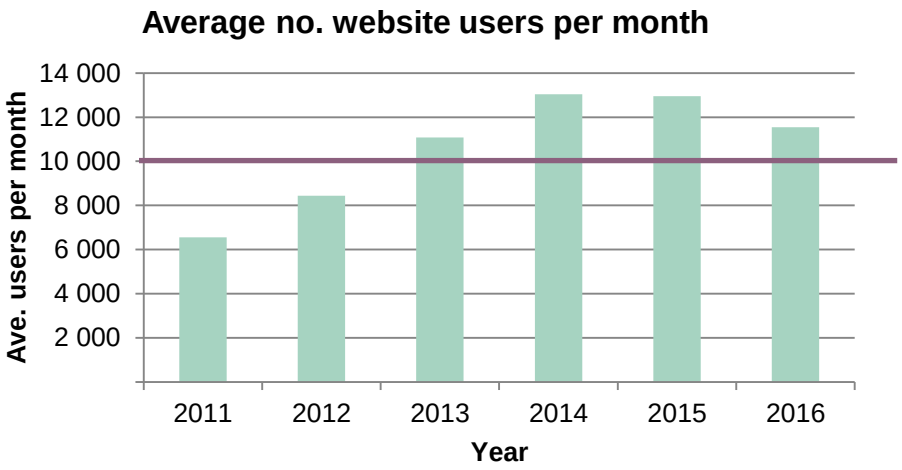
- Presentations by IMI staff and ambassadors at external events

IMI website

In 2016, the most significant additions to the IMI website were as follows:

- launch of the ideas submission portal, which allows external organisations to submit ideas for IMI projects;
- creation of project pages for new projects;
- updates of factsheets of projects that had finished to reflect their results and impacts (see the dissemination and results section for more information);
- promotion of the IMI consultation on Advanced Therapies and the public consultation on IMI.

The average number of visitors ('users') to the website per month in 2016 was 11 546.

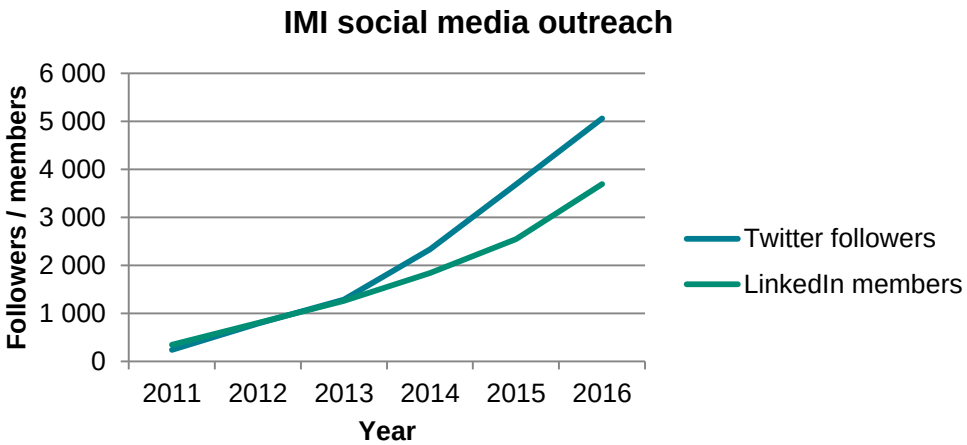


Note: the purple bar represents IMI's KPI for average website visits per month

As the graph shows, IMI has achieved its goal of attracting an average of 10 000 unique visitors (users) per month every year since 2013. Although the number of visitors is lower in 2016 than in 2014, this can be explained by the fact that IMI only launched two Calls for proposals in 2016 (compared to four in each of the two previous years).

IMI social media

IMI's social media reach continues to expand. By the end of 2016, @IMI_JU had 5 058 followers on Twitter, up from 3 684 the year before. IMI tweets on a range of subjects, including new Calls for proposals, project successes, IMI events (including live tweets on the day) and more. The LinkedIn group also continued to grow, and had 3 692 members at the end of 2016.



IMI Newsletter

IMI sent out 11 newsletters during 2016, as well as a 'newsflash' focusing on the Stakeholder Forum. There are currently around 6 500 newsletter subscribers.

Publications

Publications produced by IMI in 2016 include:

- A brochure entitled 'The Innovative Medicines Initiative and patients - a partnership', published in April 2016
- A factsheet on IMI's dementia project portfolio, published in June 2016
- An update of the factsheet on IMI's antimicrobial resistance programme, published in May 2016
- A new leaflet presenting IMI, which includes quotes from key stakeholders including Commissioner Carlos Moedas, published in July 2016
- A supplement for Parliament Magazine on the contribution of public-private partnerships to economic growth in Europe's regions, created jointly by all joint undertakings and published in October 2016 during the European Week of Regions and Cities
- Contributed to a study by Deloitte entitled 'How do EU agencies and other bodies contribute to the Europe 2020 Strategy and to the Juncker Commission Agenda?', published in December 2016

IMI also sent out flyers to advertise new Calls for proposals.

In addition, IMI Executive Director Pierre Meulien featured in two videos relating to events: one on the 5e Rencontres du G5 santé and one on the 6th Pharmaceutical Science World Congress (PSWC).

Media relations

In 2016, IMI issued the following press releases and statements:

- 21.12.2016 - Autism, diabetes, cancer & pain in new IMI Call for proposals
- 13.12.2016 - Have your say – contribute to the consultation on IMI
- 27.08.2016 - Increased momentum in antimicrobial resistance research (letter co-authored by European Commission, EFPIA, European Investment Bank and IMI, published in The Lancet)
- 18.07.2016 - IMI research remains top-notch, while output grows rapidly
- 04.07.2016 - IMI statement on the outcome of the referendum of the United Kingdom's membership of the European Union
- 18.05.2016 - Major new report reveals socio-economic impact of Innovative Medicines Initiative projects
- 28.04.2016 - IMI statement on the European Parliament vote on IMI's budget implementation and accounts for 2014
- 27.04.2016 - IMI launches €60 million Call for proposals on major challenges in drug development

In addition, IMI published the following interviews:

- 15.11.2016 - PROactive draws to a close, delivers on its promises – an interview with project coordinators
- 11.10.2016 - 'It's been a great first year' - an interview with Pierre Meulien
- 11.08.2016 - 'Without IMI this would have never happened' – an interview with U-BIOPRED's Peter Sterk

In terms of media coverage, IMI was mentioned in over 800 articles in the EU press in 2016. IMI's headline / opening presence was 11% and the tonality was 93% neutral and 7% positive. Subjects that attracted particular interest include Brexit, IMI's Calls for proposals, and the launch of new projects. A selection of some of the most significant articles is listed below; a fuller list can be found in the Annexes.

- Nature (UK), 9 November 2016
  How to defeat dementia
- Science| Business (EU), 2 November 2016
  In the lab: a big data project is trying to improve outcomes for patients
- Euronews - Business Planet (EU), 28 October 2016
  The vital role of SMEs in medical research

- Drug Discovery World (UK), 25 October 2016
  Reconfiguring drug discovery through innovative partnerships
- Financial Times (UK), 14 September 2016
  Europeans are among those most sceptical of vaccine safety
- Scrip (UK), 24 August 2016
  View From The Top of IMI: Heading Up Life Sciences' Biggest Public-Private Partnership
- Nature (UK), 13 July 2016
  Neuropathy: A name for their pain
- The Lancet (UK), 30 May 2016
  Better together for better dementia research and care
- Financial Times (UK), 20 May 2016
  EU exit would lessen the influence of UK scientists
- Financial Times (UK), 19 May 2016
  Big pharma hits back at tax to tackle superbugs
- Science Business (EU), 19 May 2016
  Innovative Medicines Initiative says its early goals being met
- Novi List (Croatia), 19 May 2016
  Nova mobilna aplikacija HALMED-a: Prijave nuspojava lijeka odsad i putem smartphonea (HALMED's new mobile app: from now on it will be possible to report side effects via smartphone)
- Nature (UK), 11 May 2016
  Competition: Unlikely partnerships
- Corriere Della Sera (Italy), 29 April 2016
  Uno smartphone anti-depressione (An anti-depression smartphone)
- Financial Times (UK), 25 April 2016
  Experimental Ebola vaccines need testing
- Science (US), 12 April 2016
  European mental health project targets biological roots of social withdrawal
- Manufacturing Chemist (UK), 11 April 2016
  IMI project recommends caution when assessing medicine impact studies from different databases
- Il Sole 24 Ore (Italy), 15 March 2016
  Big data per la salute. L'Europa cerca la cura più efficace (Big data for health. Europe seeks the most effective cure)
- Nature Biotechnology (UK), 10 March 2016
  Community crystal gazing
- The Malta Independent (Malta), 14 February 2016
  Explaining the enigma in medicines research & development
- La Libre (Belgium), 3 February 2016
  Un projet européen pour mieux comprendre le diabète de type 1 (A European project to better understand type 1 diabetes)

IMI was also cited in political and policy documents, most notably:

Council conclusions on AMR: In their June Council conclusions on antimicrobial resistance, EU health ministers underlined 'that in order to stimulate the development of new antimicrobials, alternative therapies and (rapid) diagnostics, EU and global coordination and cooperation on research programmes and incentives are needed and recognises the work done by the Innovative Medicines Initiative (IMI) project DRIVE-AB (Driving reinvestment in research and development and responsible antibiotic use), the proposals of the Antimicrobial Resistance Review team and the Joint Programming Initiative on Antimicrobial Resistance among others'.

UK Labour Party questions on Brexit: In October, the UK Labour Party published a list of 170 questions on Brexit. No. 141 mentions IMI: 'Will the government seek to negotiate continued access for UK research institutions to the Innovative Medicines Initiative and other EU-funded research and collaboration programmes, both to safeguard the funding streams they provide and to continue bringing together institutions from different EU countries together to pool their expertise and research?'

2.2 Legal and financial framework

Legal framework

IMI2 JU is a PPP between the EU (represented by the EC) and the European pharmaceutical industry (represented by EFPIA).

IMI2 JU was established, within the meaning of Article 187 of the Treaty on the Functioning of the European Union, by Council Regulation (EU) 557/2014 of 06/05/2014[16] for the implementation of the Joint Technology Initiative on Innovative Medicines.

PPPs are an instrument foreseen by H2020, established by Regulation (EU) No 1291/2013 of the European Parliament and of the Council[17] to achieve a greater impact with respect to research and innovation by combining EU public funds and private sector funds in key areas where research and innovation can contribute to the Union's wider competitiveness goals, leverage private investment and help tackle societal challenges.

IMI2 JU is established for a period until 31 December 2024. However, in order to take into account the duration of Horizon 2020, Calls for proposals by IMI2 JU shall be launched at the latest by 31 December 2020. In duly justified cases, Calls for proposals may be launched until 31 December 2021.

IMI2 JU replaced and succeeded the IMI JU, established by Regulation (EC) No 73/2008. However, according to Article 19.2 of Regulation 557/2014, actions initiated under Regulation (EC) No 73/2008 and financial obligations related to those actions shall continue to be governed by that Regulation until their completion.

Regulation (EU) No 1290/2013[18] shall apply to the actions funded by IMI2 JU. In accordance with that Regulation, IMI2 JU shall be considered as a funding body and shall provide financial support to indirect actions as set out in Article 1 of the Statutes.

Financial framework

IMI2 JU has a budget of EUR 3.3 billion for the period 2014-2024[19]. Of this:

- up to EUR 1.425 billion comes from Horizon 2020 to match at least EUR 1.425 billion from EFPIA companies;
- up to EUR 213 million comes from Horizon 2020 to match additional contributions from other Members and Associated Partners,

EFPIA companies and Associated Partners do not receive any EU funding[20], but contribute to the projects 'in kind', for example by donating their researchers' time or providing access to research facilities or resources.

In accordance with Article 209[21] of Regulation (EU, Euratom) No 966/2012[22] on the financial rules applicable to the general budget of the Union and Commission Delegated Regulation (EU) No 110/2014[23], IMI2 JU has adopted specific financial rules.

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[16] OJUE 07/06/2014 L 169/54.

[17] Regulation (EU) No 1291/2013 of the European Parliament and of the Council of 11 December 2013 establishing Horizon 2020 — the Framework Programme for Research and Innovation (2014-2020) and repealing Decision No 1982/2006/EC (OJ L 347, 20.12.2013, p. 104).

[18] Regulation (EU) No 1290/2013 of the European Parliament and of the Council of 11 December 2013 laying down the rules for participation and dissemination in 'Horizon 2020 — the Framework Programme for Research and Innovation (2014-2020)' and repealing Regulation (EC) No 1906/2006 (OJ L 347, 20.12.2013, p. 81).

[19] During its first phase (2008-2013 established by Regulation 73/2008), IMI JU had a budget of EUR 2 billion, half of which came from the EU's Seventh Framework Programme for research (FP7), and half of which came from in kind contributions by EFPIA companies.

[20] For precise reference to IMI2 JU rules on eligibility of funding, please refer to Article 1 of Commission Delegated Regulation (EU) No 622/2014 of 14 February 2014.

[21] By way of derogation from Article 60.7 and Article 209 of Regulation (EU, Euratom) No 966/2012, the discharge for the implementation of the budget of the IMI2 Joint Undertaking shall be given by the European Parliament, upon recommendation of the Council in accordance with the procedure provided for in the financial rules of the IMI2 Joint Undertaking.

2.3 Budgetary and financial management

2.3.1. 2016 budget approved

The total IMI budget for 2016 was EUR 307 052 760 in commitment appropriations (CA) and EUR 263 423 489 in payment appropriations (PA). The budget execution of the commitment appropriations reached a level of 94.08 %, and payment appropriations reached a level of 69.60 %.

The IMI budget is divided into three Titles.

- Title 1 covers staff expenditure such as salaries, training, costs associated with recruitment procedures, and staff well-being.
- Title 2 covers the costs associated with functioning of IMI JU such as renting of premises, IT needs, expenses related to external communication, expert fees and costs of ex-post audits.

Titles 1 and 2 together form the administrative expenditure.

- Title 3 covers IMI's operational activities.

The 2016 budget was approved by the Governing Board on 13 January 2016. The first budget amendment was approved by the Governing Board 27 April 2016 in order to include the carry over amounts from previous year. A second budget amendment, approved by the Governing Board on 5 December 2016, included financial contributions from Associated Partners and other members. The Staff Establishment Plan 2016 was also amended and was approved by the Governing Board on 10 November 2016.

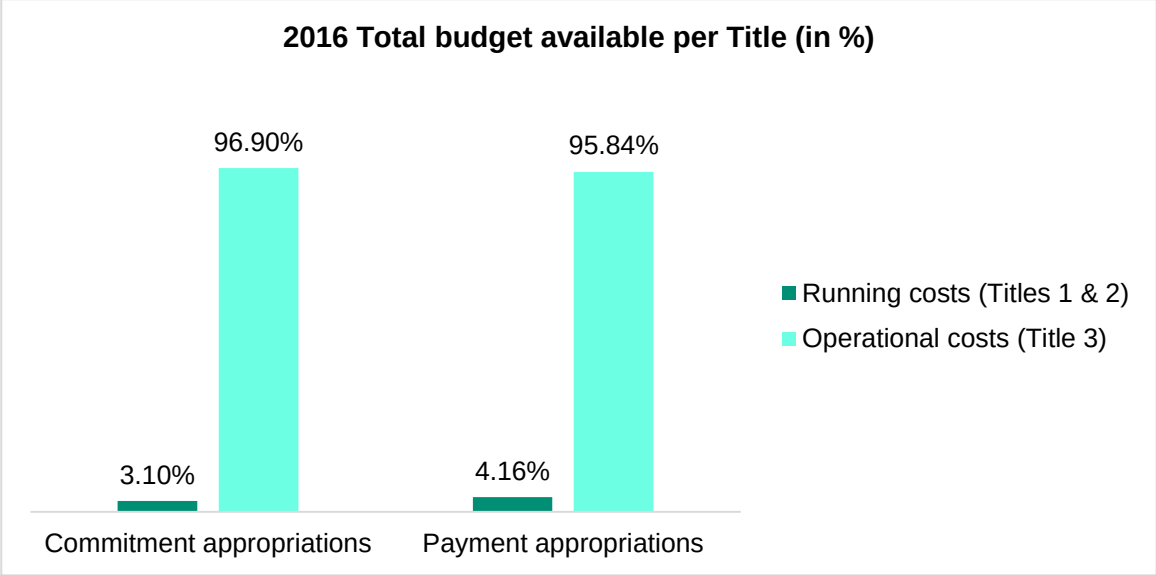
[22] Regulation (EU, Euratom) No 966/2012 of the European Parliament and of the Council of 25 October 2012 on the financial rules applicable to the general budget of the Union and repealing Council Regulation (EC, Euratom) No 1605/2002 (OJ L 298, 26.10.2012, p. 1).

[23] Commission Delegated Regulation (EU) No 110/2014 of 30 September 2013 on the model financial regulation for public-private partnership bodies referred to in Article 209 of Regulation (EU, Euratom) No 966/2012 of the European Parliament and of the Council (OJ L 38, 7.2.2014, p. 2).

Budget 2016 in EUR

Budget 2016 in EUR										
	Voted budget		Carry over Amending budget no 1		Amending budget no 2		Assigned revenue		Final budget	
	CA	PA	CA	PA	CA	PA	CA	PA	CA	PA
Revenue										
EC contribution	207 927 000	201 740 000	80 972 000	51 861 000					288 898 000	253 601 000
EFPIA contribution	4 740 000	4 740 000							4 740 000	4 740 000
Assoc. Partners					7 000 000	2 669 000			7 000 000	2 669 000
Other members					4 200 000	200 000			4 200 000	200 000
Total revenue	**212 667 000**	**206 480 000**	**80 972 000**	**51 861 000**	**11 200 000**	**2 869 000**			**304 838 000**	**261 209 000**
Expenditure										
Title 1	5 353 000	5 353 000		220 000					5 353 000	5 573 000
Title 2	4 127 000	4 127 000		1 229 000			29 000	29 000	4 156 000	5 385 000
Title 3	295 359 000	199 869 000		50 411 000			2 186 000	2 186 000	297 544 000	252 465 000
Total expenditure	**304 839 000**	**209 349 000**		**51 861 000**			**2 214 000**	**2 214 000**	**307 053 000**	**263 423 000**

The assigned revenue shows the amounts recovered during the year from suppliers. The graph below shows the total 2016 budget available per Title in %.



2.3.2. Budget transfers

One budget transfer from Title 1 to Title 2 was made during 2016; this was below the 10% threshold. Budget transfers between chapters were authorised in 2016 which led to the following changes:

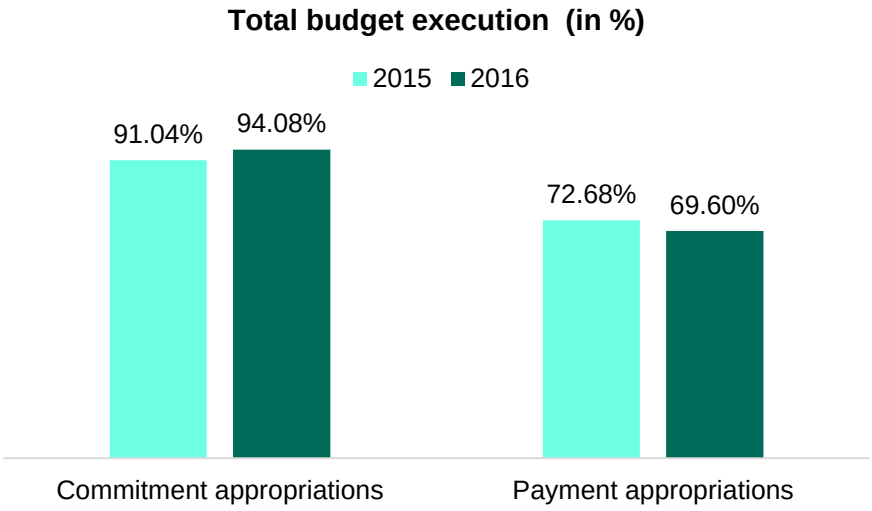
Chapter		Budget voted EUR	Budget transfer EUR	Budget after transfers EUR
11	Staff in active employment	4 893 000	- 104 000	4 789 000
13	Missions	190 000	- 90 000	100 000
14	Socio-medical structure	230 000	176 000	406 000
20	Investments in immovable property rental of buildings	660 000	21 000	681 000
21	Information Technology purchases	560 000	154 000	714 000
22	Movable property	153 000	- 143 000	10 000
23	Current administrative expenditure	123 000	10 000	133 000
24	Postage and telecommunications	68 000	- 24 000	44 000
25	Expenditure on formal meetings	158 000	- 48 000	110 000
26	Expenditure in connection with operational activities	300 000	48 000	348 000
27	External communication information and publicity	625 000	- 25 000	600 000
28	Studies	780 000	- 1 000	779 000
29	Expert contracts and meetings	700 000	26 000	726 000

2.3.3. 2016 budget execution

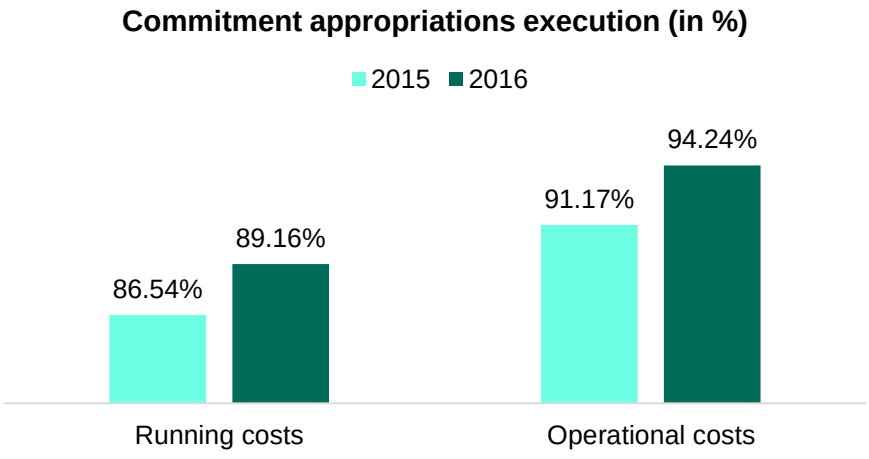
The table below shows the execution of the 2016 budget per Title.

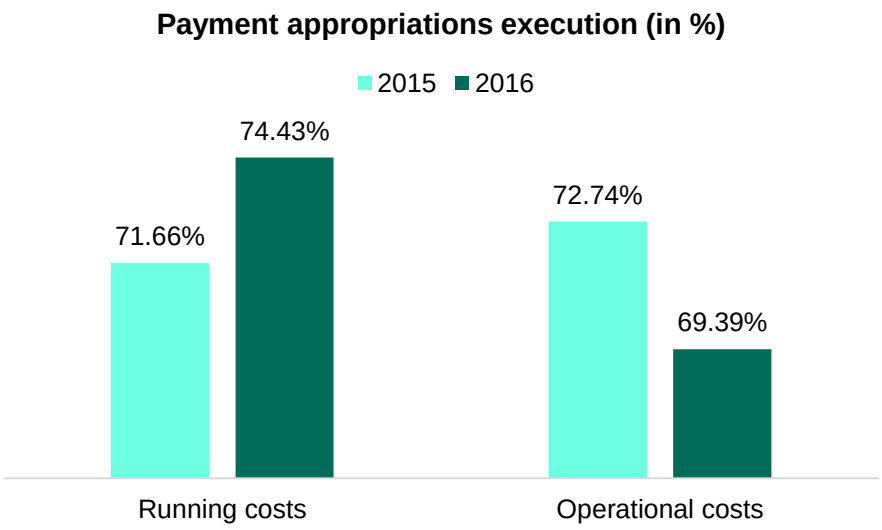
Title	2016 final budget execution per title in EUR					
	Commitment appropriations	Execution	%	Payment appropriations	Execution	%
Title 1	5 334 540	4 707 100	88.24	5 554 850	4 648 750	83.69
Title 2	4 174 140	3 771 010	90.34	5 403 540	3 507 070	64.90
Subtotal administrative costs	*9 508 670*	*8 478 100*	*89.16*	*10 958 390*	*8 155 810*	*74.43*
Title 3	297 544 090	280 394 380	94.24	252 465 100	175 182 730	69.39
Total (Title1, 2 and 3)	**307 052 760**	**288 872 480**	**94.08**	**263 423 490**	**183 338 540**	**69.60**

The graph below shows the 2016 total budget execution compared with 2015.



The graphs below show the 2016 budget execution for operational activities (project-related) and for administrative costs (staff and infrastructure) compared with 2015.





The performance objectives of the annual budget execution as established in the Annual Work Plan 2016 were: ≥95% for commitment appropriations for administrative costs and operational costs, and ≥95% for payment appropriations of operational costs.

The total budget execution of the commitment appropriations reached a level of 94.08 %, and of the payment appropriations a level of 69.60 %. As regards operational expenditure, details are set out in section 1.7.

Regarding the administrative costs, despite some recruitments carried in 2016, the number of staff employed at the end of 2016 was lower than the maximum authorised, resulting in lower execution than planned.

IMI continued to execute its budget applying principles of sound financial management, resulting in savings in the organisation of events, communication and administrative expenditure.

It is important to note that the EC part of unused appropriations for administrative costs will be made available for operational activities in the 2017 budget – see section 2.3.5 for details.

The table below shows the summary of commitments outstanding at the end of 2016.

	EUR
Commitments carried over from previous year	735 156 390
De-commitments	- 117 157 480
Payments made during 2016 related to commitments carried forward	- 158 822 020
Commitments made during 2016	288 872 480
Payments made during 2016 related to commitments made during 2016	- 24 516 520
Total commitments outstanding at the end of 2016	**723 532 860**

2.3.4. Cash contributions

The table below outlines the breakdown of the cash contributions received in 2016 up to 31 December.

	EC contribution EUR	EFPIA contribution EUR	Associated Partners & other members EUR
FP7 (IMI1)			
Administrative up to 31/12/2015	27 211 950[24]	15 839 470	
Administrative 2016	3 540 000	2 108 610	
Operational up to 31/12/2015	570 671 000		
Operational 2016	126 143 190		
H2020 (IMI2)			
Administrative up to 31/12/2015	1 180 300	1 180 300	
Administrative 2016	1 200 000	1 200 000	
Operational up to 31/12/2015	62 000 000	-	
Operational 2016	70 856 810	-	2 868 600
Total up to 31/12/2015	661 063 260	17 019 770	-
2016	201 740 000	3 308 610	2 868 600
Total up to 31/12/2016	**862 803 260**	**20 328 390**	**2 868 600**

The administrative costs are covered through financial contributions divided equally (50%-50%) between the EC and EFPIA. If part of the EC contribution is not used, it may be made available for Research Activities.

The total amount of the unused administrative costs of EC contribution during 2009-2015 has been transferred to operational costs for a total amount of EUR 11 372 477. This results in an EC contribution to administrative costs of EUR 15 839 474.

The amount of EUR 188 531 of EFPIA cash contributions was booked in 2016 although it relates to 2015 (balance of 2015); it is included in 2016 cashed contribution.

The amount of EUR 954 772 of EFPIA balance cash contributions related to 2016 (recovery order issued in 2017) is not included in 2016 cashed contribution.

[24] This amount includes EUR 992 966 of EC subsidy for running costs before IMI autonomy.

2.3.5. Overview of the carry over appropriations to 2017

The N+3 rule for the PPP bodies states that the unused appropriations may be entered in the estimate of revenue and expenditure of up to the following three financial years. IMI will re-enter into the 2017 budget the unused commitment and payment appropriations from 2016.

Administrative expenditure:

- Payment appropriations of EUR 1 416 709, corresponding to the amount of commitments carried forward from the 2016 to the 2017 budget.

Operational expenditure:

- Unused commitment and payment appropriations to be carried over to 2017 budget of EUR 134 478 277* corresponding to commitment appropriations, and EUR 77 282 291* corresponding to payment appropriations.

	Commitment appropriations (EUR)	Payment appropriations (EUR)
Unused appropriations (operational and administrative)	*134 467 000	*78 699 000

*estimated; subject to Governing Board approval

2.4 Procurement and contracts

The large majority of IMI's procurements in 2016 were carried out under existing multi-annual framework contracts (FWCs). In terms of volume, the FWCs used most were on the provision of IT services and audit services; these were concluded jointly with other JUs to avoid duplication and minimise administrative effort.

Additionally, in February 2016 IMI signed, also on behalf of five other JUs, a multiannual JU FWC for the provision of interim staff services. This new FWC replaces the JUs' previous FWC which expired in Q4/2015.

Where possible, IMI also made use of the European Commission's framework contracts that it is party to. During 2016, the most significant of these in usage volume terms were in IT development, software licenses, and travelling services. IMI also used an EC FWC to sign a specific contract for the creation of a new IMI website, and used DG Budget's FWC to sign a specific contract for the verification of IMI's annual accounts.

Apart from the contracts mentioned above, a significant number of specific contracts were concluded for the rental of meeting premises for organising project evaluations under a framework contract IMI tendered on its own in 2012.

The table below shows tender procedures in 2016 outside existing FWCs with a value exceeding EUR 15 000.

Reference and subject	Procedure	Contractor	Amount	Signature date
Purchase of access to scientific publications	Low value	EBSCO	19 920.16	08/01/2016
Purchase of access to POLITICO Pro Health Care	Low value	POLITICO Pro	16 689.00	09/09/2016
FWC for Printing services	Negotiated procedure (<134.000 EUR) – Service contract	-	-	Closed without contract award

2.5 IT and logistics

The objective of IMI's ICT team is to deliver value to the organisation 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 to make all IMI processes simpler and more efficient.

The IT team's activities in 2016 were filled with the project management of the transition of IMI2 calls and projects to the Horizon 2020 IT tools; enhancements of in-house developed applications for core and administrative processes; IT infrastructure and helpdesk support; and ICT procurement aspects.

2.5.1 Transition to H2020 IT tools

The project progressed significantly; thanks to close collaboration with the various EC IT teams supporting the H2020 applications, IMI succeeded in launching IMI2 - Call 10 in SEP in December 2016. The use of SyGMA application is planned to take place in Q1 2017 with the grant agreement preparation of Call 9.

Use of the H2020 IT applications is expected to deliver a number of benefits, including the streamlining of processes related to grant applications, experts and grant management; improved end user experience through the participant portal; replacement of paper signatures with electronic signatures in expert contracts, grant agreements, accession forms, amendments, financial statements and technical reports; and the transfer of data for statistical purposes directly to CORDA.

Furthermore, in 2016 significant progress was made with the enhancement of IMI's reporting application, QlikView, in order to provide it with data after the full migration to H2020 IT tools. Part of this project is the transfer to QlikView of the SOFIA ILG Overview, which is used by the EFPIA managers and provides a complete view about the IMI projects that their companies are participating in. The first version of an 'EFPIA Manager' dashboard was implemented in QlikView at the end of 2016. In addition, integration with CORDA is expected to take place in 2017.

2.5.2 Enhancements of in-house applications

The team handled several new enhancement and service requests regarding the further development and maintenance of applications developed in-house that support core and administrative processes. In particular, 91 change and service requests were delivered related to SOFIA (Submission of Information Application), which will continue to be used for the management of IMI1 projects, and 39 related to DORA (Document Repository Application), ISA (Information System for Absences), eMA (electronic Missions Application), and the web collaborative platforms for Strategic Governance Groups (SGGs) and States Representatives Group (SRG). The following list presents the most important developments:

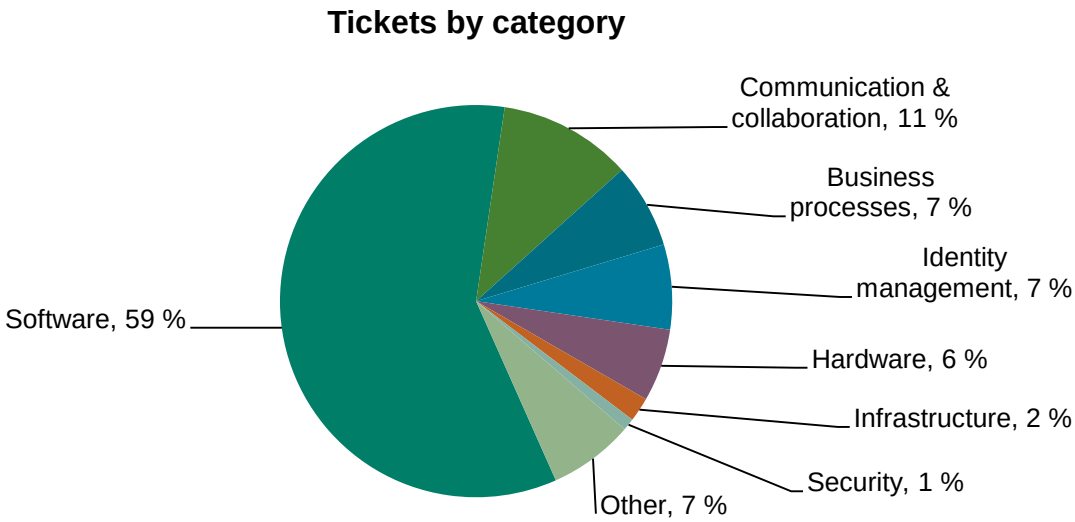
- SOFIA: implementation of IMI2 beneficiaries' periodic reporting; implementation of EFPIA reporting for IMI2 projects; adjustments to form C; XML export of IMI2 data for integration with CORDA; improvements to ex-post audit process.
- ISA: new version of application for time and absence management implementing common requirements of the HR teams of all Joint Undertakings.
- eMA: various improvements of the application for mission management.
- Migration of the back-end server to a newer version due to product end-of-life.

Furthermore, the gathering and analysis of the requirements for the new IMI's website took place. These are going to be used for the implementation of a new website, which is going to take place in 2017.

2.5.3 IT Infrastructure and helpdesk support

In 2016, a total of 1 410 requests for support were sent to the IMI IT Helpdesk (helpdesk@imi.europa.eu), which had been set up in 2015 as a single point of contact and incident management system.

The following figure depicts the various categories related to the tickets generated.



Moreover, the IT team cooperated closely with the IT staff of the other JUs located in the same building, in order to safeguard together the uninterrupted operation of the common ICT infrastructure. The following were achieved in 2016:

- Transfer of the TESTA network infrastructure to the new provider under the corresponding EC framework contract.
- Implementation of a backup-as-a-service (BaaS) solution, i.e. online backup system, in order to improve the backup strategy of the JUs and the recovery point objective serving the requirements of the business continuity planning
- Definition of the strategy and architecture related to common IT infrastructure to be implemented in 2017 due to end of life of currently used hardware. An Infrastructure as a Service (IaaS) approach was selected, which is going to be implemented in 2017.
- Alignment of office automation software licenses that JUs had initially purchased with the current situation based on headcounts and repartition keys.

Last but not least, IMI utilises an online infrastructure in order to host its business operations information systems, and the collaboration, communication and administration information systems mentioned above. A cyber-capability assessment exercise of this infrastructure started in December 2016 and will be completed by end of January 2017.

2.6 Human resources

Staff and recruitment

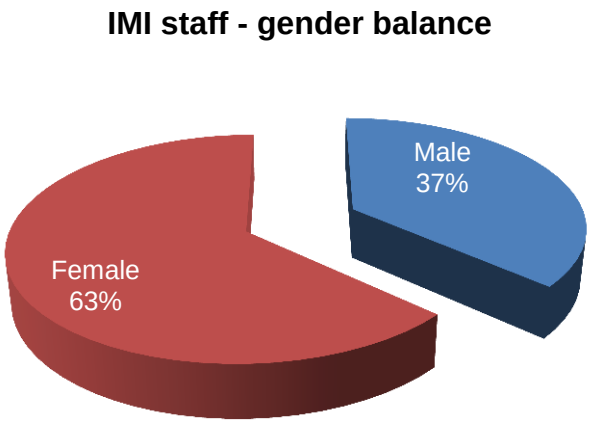
The initial staff establishment plan for 2016 had 47 positions. To take account of the overall increase in IMI's workload, the IMI Governing Board approved in November 2016 a new staff establishment plan with 52 positions. On 31 December 2016, 41 positions were occupied.

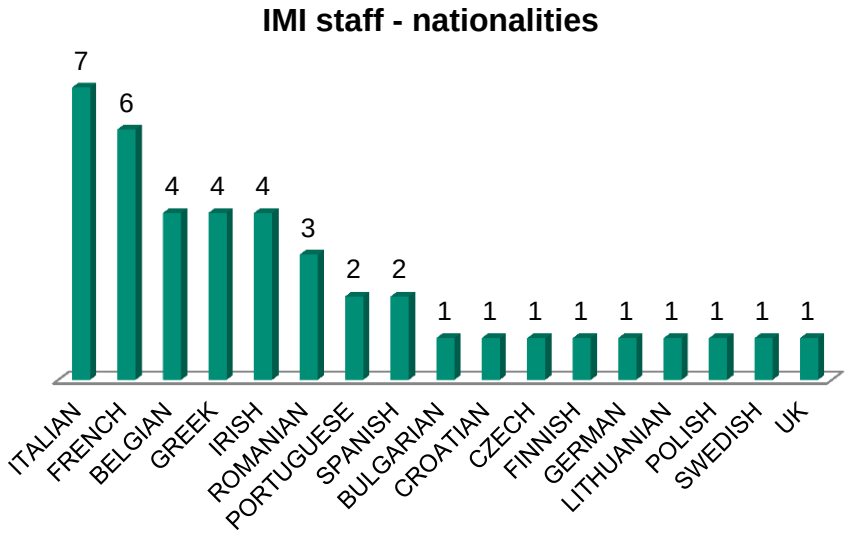
A total of 12 vacant positions were filled in 2016 as follows:

- Head of Scientific Operations on 1 January 2016;
- Head of Communication and Institutional Relations on 1 March 2016.
- The science team was reinforced with the recruitment of a senior scientific project manager, a scientific programme officer, and three scientific project officers.
- the communication team was reinforced with the recruitment of a writer/editor
- The support and project management support team was reinforced with an ex-post audit assistant and three administrative assistants.

In addition, 5 new staff members were appointed at the end of 2016 and will take up duties in q1 2017: one scientific project officer and four financial assistants (assigned to the operational finance team).

The two graphs below show the gender and geographical balance within IMI on 31/12/2016:





Learning and professional development

Organisational efficiency is dependent upon learning and professional training in order to keep staff members up-to-date. The main areas covered were:

- Operational and legal context: H2020 new environment, financial regulations. In the context of the ongoing transition of IMI2 JU operations to the European Commission H2020 IT tools, specific attention was given to training of staff on the Horizon 2020 IT tools (SEP, SyGMA, Compass);
- IT skills (Word, Excel, MS Project or ABAC and any IT tool developed by IMI);
- New staff members also benefit from induction training as well as training on ethics and integrity.

The European Commission's 'EU Learn' system was implemented in 2016. It replaces Syslog and is expected to facilitate IMI staff in the selection of their training needs, on both hard and soft skills.

Staff regulations and implementing rules

IMI, in cooperation with other EU agencies and JUs, is working on a second set of rules to be adopted in line with the new Staff Regulations and the EC's DG HR (Directorate-General for Human Resources and Security) guidelines.

2.7 Data protection

In 2016, IMI pursued the implementation of data protection principles within its activities involving the processing of personal data.

Regular communication with IMI staff, with the network and the JUs' data protection officers, and with the European Data Protection Supervisor (EDPS) services, enabled the continuing implementation of data protection principles. In particular, there were regular internal consultations with the data protection officer (DPO) in the areas of science, human resources, communication and IT.

Prior checking activities: In 2016, IMI continued to follow up the notifications to the EDPS and issues related to existing processing operations. There is no specificity on the IMI processing of personal data to report. Recommendations from the EDPS as an outcome of IMI notifications are being implemented.

Notifications to the DPO: Notifications from the staff to the DPO cover IMI activities including communication with IMI bodies, the organisation of meetings, remuneration schemes, audits, grants and procurement schemes, business trips, conflicts of interest & confidentiality, HR matters, and invitations of experts.

Consultations: There were no formal consultations of the EDPS in 2016 to report. The DPO continued to collaborate on the work developed by the projects through consultation and advice.

Inspections: There were no site visits by the EDPS in 2016.

Complaints: There were no complaints to the EDPS in relation to IMI's processing of personal data to report in 2016.

Network activities: The DPO network meetings are an important forum to exchange best practices between DPOs and get guidance and information about EDPS activities. Developments related to the implementation of the new data protection Regulation were addressed during the two meetings held in 2016. The DPO also participated in meetings hosted by the DG RTD common support service to discuss updates on the privacy statements on experts and grants, in view of publication / update on the European Commission participants' portal.

Training / communication activities: In 2016, the DPO provided systematic data protection training for newcomers. Information on developments in data protection activities was provided to the IMI Programme Office staff.

Thematic guidelines

EDPS Guidelines	Status of notification to EDPS	Comments
Tasks, duties and powers of the DPO	closed	
Recruitment	closed	
Health data at work	Waiting EDPS closure	
Staff evaluation	Waiting EDPS closure	
Leave & Flexitime	Waiting EDPS closure	
Conflict of interest	Pending	Adoption by HR of specific guidelines
Anti-harassment procedures	Pending	Procedures being developed in IMI
Administrative inquiries and disciplinary proceedings	Pending	Procedures being developed in IMI

EDPS Guidelines	Status of notification to EDPS	Comments
Whistleblowing procedure	preparatory work	Procedures being developed in IMI
Electronic communications	preparatory work	Common approach to be discussed / agreed with other JUs
Mobile devices	preparatory work	Common approach to be discussed / agreed with other JUs
Mobile applications	preparatory work	Common approach to be discussed / agreed with other JUs
Web services	preparatory work	Common approach to be discussed / agreed with other JUs
Security measures for data processing	preparatory work	Common approach to be discussed / agreed with other JUs
Video surveillance	not applicable	IMI is not the controller of the data

3 Governance

3.1 Governing Board

The Governing Board is the main decision-making body of the IMI2 JU. It carries the overall responsibility for the operations and oversees the implementation of its activities. It therefore guarantees the fulfilment of the objectives set by the organisation.

In 2016 the Governing Board held six meetings. The main decisions taken by the Governing Board in 2016 can be found on IMI website for the 1st semester 2016 and the 2nd semester 2016.

The role of Chair of the Governing Board in 2016 was assumed as follows:

Dates	Chair & Deputy Chair
1 January – 30 April	Chair: Rudolf Strohmeier (EC) | Deputy Director-General responsible for Research Programmes within the Directorate-General for Research and Innovation Deputy Chair: Marc de Garidel (EFPIA) | Chairman of Ipsen Group, member of the EFPIA Board and Vice-President of EFPIA
1 May – 6 July	Chair: Robert-Jan Smits (EC) | Acting Deputy Director-General for Research Programmes within the Directorate-General for Research and Innovation Deputy Chair: Marc de Garidel (EFPIA)
7 July – 2 October	Chair: Marc de Garidel (EFPIA) Deputy Chair: Robert-Jan Smits (EC)
2 October – 31 December	Chair: Marc de Garidel (EFPIA) Deputy Chair: Ruxandra Draghia-Akli (EC) | Deputy Director-General responsible for Research Programmes within the Directorate-General for Research and Innovation

More information on the composition of the Governing Board and on its representatives can be found on the IMI website as well as in the factsheet at the beginning of this document.

3.2 Executive Director

Pierre Meulien was Executive Director of IMI throughout 2016.

3.3 States Representatives Group

The IMI2 JU States Representatives Group (SRG) is composed of one official delegate of each Member State and of each country associated to the EU's research programmes. It provides opinions to the Governing Board, especially on the IMI2 programme orientation, progress and achievements.

Information on the membership can be found at on the SRG page of the IMI website; in 2016, IMI started to publish the CVs of SRG members to the website.

The position of Chair is held by Marta Gómez Quintanilla (Spain) and the position of Vice-Chair by Gunnar Sandberg (Sweden).

In 2016, the SRG met in March, May and September. At the meetings, detailed updates on IMI2 JU activities with a specific focus on involvement of SMEs were provided. During 2016, the SRG was consulted on the Call topics and documents and on the Annual Work Plan.

3.4 Scientific Committee

The Scientific Committee provides strategic science-based recommendations to IMI and advises on the continued relevance of the Strategic Research Agenda and the scientific priorities, which are the basis for the Call topics. The Committee is appointed upon suggestions made by the States Representatives Group. There were three Scientific Committee meetings in 2016.

In 2016, seven new Scientific Committee members were appointed to replace members whose mandates were due to end during the year. As of the end of the year, the full list of members was as follows:

- Isabelle Bekeredjian-Ding, Head of Division Microbiology, Paul-Ehrlich-Institut, Langen, Germany
- Andreas Bernkop-Schnurch, Head of the Institute of Pharmacy University of Innsbruck and CSO, ThioMatrix Forschungs & Beratungs GmbH, Innsbruck, Austria
- Maria Blasco, Director, Spanish National Cancer Research Centre (CNIO) and head of Telomeres and Telomerase Group, Madrid, Spain
- Dolores Cahill, Professor of Translational Science, School of Medicine, University College Dublin (UCD) and Principal Investigator, UCD Conway Institute of Biomolecular and Biomedical Research, Dublin, Ireland; Co-founder PROTAGEN AG, Dortmund, Germany
- Anna Chioti, Head of the Department of Public Health, Luxembourg Institute of Health, Luxembourg
- Maria Beatriz Da Silva Lima, Professor of Pharmacology and Pharmacotoxicology, Lisbon University, Lisbon, Portugal
- Hans-Georg Eichler (ad hoc member), Senior Medical Officer, European Medicines Agency, London, United Kingdom
- Markus Perola, Research Professor in the Institute for Health and Welfare, University of Helsinki, Finland
- Torsten Schwede, Professor for Bioinformatics, Biozentrum, University of Basel, Switzerland
- Tanel Tenson, Professor of molecular biology at Institute of Technology, University of Tartu, Estonia
- Annamaria Vezzani, Head of Experimental Neurology Laboratory, Department of Neuroscience, Mario Negri Institute for Pharmacological Research, Milano, Italy

The members have expertise in a range of medical fields, including bioinformatics, cancer, microbiology, molecular biology, neurology, pharmacology, proteomics and public health. The bios of all members are published on the Scientific Committee page of the IMI website. A new chair and vice-chair will be elected in early 2017.

3.5 Stakeholder Forum

There were over 500 registrations for IMI's Stakeholder Forum 2016, which was held in Brussels, Belgium on 28-29 September. It featured a presentation of IMI's more rules and procedures as well as four parallel workshops on biopreparedness, advanced therapies, digital health, and oncology.

More information on the event can be found in the Communication and Events section (2.1).

3.6 Strategic Governing Groups (SGGs)

IMI2 Strategic Governing Groups (SGGs) are advisory groups to the Governing Board. These are 7 thematic platforms addressing defined areas under the umbrella of the IMI2 Strategic Research Agenda.

The SGGs are made up of representatives of companies active or interested in the area covered by the scope of the SGG as well as representatives from the European Commission, the IMI Programme Office and the IMI Scientific Committee. The SGGs were created in 2014 on the basis of Article 7.3.p of the legislation establishing the IMI2 JU programme.

The work of the SGGs is focused on facilitating an efficient translation of the IMI2 JU Strategic Research Agenda and developing a coordinated strategy for selected diseases which will lead into annual strategic priorities. They also provide recommendations for high quality and concrete call topics, taking into account proposals from industry, Associated Partners and third parties.

In 2016 the GB adopted a new SGG charter that clearly defines the tasks, composition, operations, requirements for confidentiality and reporting to GB of an SGG. The GB also approved the foundation of an SGG in the area of oncology. Several cross-SGG meetings were held during the year to facilitate cross-SGG coordination.

In 2016 the seven established SGGs were focused on the following areas:

- Neurodegeneration
- Immunology
- Data and knowledge management
- Infections control
- Diabetes / metabolic disorders
- Translational safety
- Oncology

SGG Neurodegeneration

The SGG Neurodegeneration met three times in plenary session during the year. An IMI scientific officer participated in all meetings. The SGG Neurodegeneration provided input to the IMI Governing Board regarding the scientific priorities for 2017, and developed one topic that was launched in the IMI2 – Call 9. A focus group focussed on Neurodegeneration and Pain was created. The group developed three topics that were launched in the IMI2 – Call10.

SGG Immunology

The SGG Immunology held 4 meetings in 2016, two of which were face-to-face. In addition to discussion on priorities for the area and the development of topic ideas, one topic was launched as part of Call 9 they proposed the topic. Several sub group meetings were held to support the development of topics to be included future calls.

SGG Data and knowledge management

In 2016, the SGG Data and Knowledge Management met twice. Discussions on several new topics and prioritisations took place, resulting in the BD4BO Prostate Cancer topic in IMI2 Call 10 and input to the scientific priorities for 2017. Speakers were invited from other funding agencies and initiatives to discuss challenges regarding the sustainability of databases resulting from IMI projects. The SGG also actively engaged with several new EFPIA partners in research.

SGG Infection Control

The SGG Infection Control held two face-to-face meetings and two teleconferences during 2016. An IMI scientific officer participated in all meetings. At the meetings, the existing IMI project portfolio in the field of infectious diseases and ideas for potential IMI call topics submitted by third parties or from SGG members were discussed. One topic, Joint influenza vaccine effectiveness studies, was launched in IMI2 Call 9. The SGG Infection Control also provided input into the scientific priorities for 2017.

SGG Diabetes and Metabolic Disorders

The Diabetes and Metabolic Disorders met four times in plenary session during the year. An IMI scientific officer participated in 3 of those meetings. The SGG provided input to the IMI Governing Board regarding the scientific priorities for 2017, and developed two topics that were launched in the IMI2 – Call 9 and IMI2 – Call 10.

SGG Translational Safety

The SGG Translational safety met three times in 2016. The IMI office and the EC were represented at these meetings. Discussions focused on the development of new topics, one of which was launched under Call 9. Input to the IMI Governing Board regarding the scientific priorities for 2017 was also provided. In addition, to the development of topic ideas and scientific priorities discussions were also held on bringing non-EFPIA partners into the SGG and how they could contribute to IMI going forward.

SGG Oncology

The SGG Oncology met three times in 2016. Discussions focused on the SGG scientific strategy to prioritise and implement new topics to be launched in future IMI calls. The newly-formed SGG brainstormed on objectives and deliverables for project to support the agreed strategy.

3.7 Associated Partners

Under the IMI2 programme, any legal entity (except for EFPIA companies) can become an IMI Associated Partner. Like EFPIA partners in IMI projects, Associated Partners do not receive any funding from IMI, but contribute to the projects, mainly through in-kind contributions (such as their experts' time, access to resources / equipment). In addition, on an IMI programme level, contributions Associated Partners put into a project are matched by an EU contribution, making this a good way of leveraging precious resources. As contributors to the project, Associated Partners are involved in the definition of the project, and can participate as observers in IMI Governing Board meetings during discussions relating to the projects they are involved in.

As of the end of 2016, the following organisations had become IMI Associated Partners:

- Autism Speaks
- Bill and Melinda Gates Foundation
- JDRF
- Leona M. and Harry B. Helmsley Charitable Trust
- Simons Foundation Autism Research Initiative (SFARI)
- T1D Exchange

4 Internal Control Framework

4.1 Financial procedures

In accordance with the EU financial regulation, IMI has adopted specific financial rules and a Manual of Procedures for Financial Operations which describes the financial processes and procedures of the Programme Office and provides guidance to staff. These documents also highlight in detail the responsibilities of financial actors and internal controls as well as specific methods to safeguard IMI's assets; check the accuracy and reliability of recorded accounting data; and promote efficiency in financial operations.

Specific standard operating procedures (SOPs) with written instructions (e.g. 'Assessment and approval of periodic and final reports', 'Preparation, submission and approval of CFS', etc.) are also adopted to assist operations and assure compliance.

Finally, IMI applies the principles and rules of the H2020 framework research programme as set out in the Regulation (EU) No 1291/2013.

4.2 Ex ante controls on operational expenditure

The IMI internal control framework is embedded across the organisational structure and relies on a combination of ex-ante and ex-post controls, as summarised in the table below.

Ex-ante controls aim to prevent errors and avoid the need for ex-post[25] corrective actions. Ex-ante verifications cover both the financial and operational aspects of each transaction handled by IMI. According to the IMI Financial Rules, ex-ante controls are executed at the primary control level and are also performed for every commitment and payment. These controls consist of desk reviews and on-the-spot controls and aim to assess compliance with legality, regularity and sound financial management (economy, efficiency, and effectiveness).

	Ex-ante controls	Ex-post controls
When	Before the transaction is authorised.	After execution of the authorised transaction.
Frequency	Mandatory for all transactions.	Made on a sample basis.
Methodology	At least a desk review of documents (e.g. proposal received, reports, etc.) and available results of controls already carried out relating to the operational and financial aspects of the operation.	On-the-spot checks at the beneficiary's premises.
Impact	Errors detected should be rectified before the transaction is approved.	Errors detected are corrected. Where the error caused an ineligible expenditure, a recovery order is issued or an offset is made with future payments
Level of assurance	Primary means of ensuring sound financial management and legality and regularity of transactions, but less evidence as usually based on desk review.	Secondary means of ensuring sound financial management and legality and regularity of transactions, but more robust as normally carried out on-the-spot

[25] Ex post controls are described in Section 4.3 below.

IMI's annual budget is implemented through operational expenditure (i.e. related to the management of the research programme – Title 3 of the budget) and administrative expenditure[26] (i.e. staff and other expenses which support day-to-day activities – Titles I and II of the budget).

Operational expenditure relates to payments made to beneficiaries of IMI funding. In this context, it should be noted that IMI is currently managing actions funded and regulated under two different framework programmes, with different obligations and *modus operandi*:

- IMI1 programme: Actions initiated under Regulation (EC) No 73/2008 - which implements the FP7 for research and innovation - and financial obligations related to those actions are governed by the above Regulation until their completion. In particular, 'actions arising from calls for proposals provided for in annual implementation plans adopted under Regulation (EC) No 73/2008 shall be regarded as actions initiated under that Regulation'[27].
- IMI2 programme: Actions funded by the IMI2 Joint Undertaking shall be subject to Regulation (EU) No 1290/2013[28] laying down the rules for participation and dissemination in Horizon 2020. In accordance with that Regulation, the IMI2 Joint Undertaking shall be considered as a funding body and shall provide financial support to indirect actions[29].

The two tables below compare the balance between the two running programmes (IMI1/FP7 and IMI2/H2020) in terms of operational expenditure for the year 2016.

Operational expenditure in 2016 (EUR)					
	Project portfolio		**Pre-financing payments 2016**	**Interim / final payments (against cost statements) 2016**	**Total paid in 2016**
IMI1 (FP7)	Running at 31/12/2016	38	0	109 847 000	109 847 000
	Concluded at 31/12/2016[30]	21			
IMI2 (H2020)		25	52 339 000	12 997 000	65 336 000
Total		**84**	**52 339 000**	**122 844 000**	**175 183 000**

Comparative table of operational expenditure 2010 - 2016 (EUR millions)								
	2010	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**Total**
IMI1 (FP7)	35.242	68.979	103.809	121.468	120.051	88.562	109.847	**647.958**
IMI2 (H2020)	/	/	/	/	/	45.953	65.336	**111.289**
Total	35.242	68.979	103.809	121.468	120.051	134.515	175.183	**759.247**

[26] More details on the structure and implementation of the administrative budget can be found in Section 2.3.1 above. From the control point of view, all transactions related to administrative expenditure are subject to an ex ante control in accordance with the principles of four eyes and segregations of duties and are subject to the procedures and controls described in the Manual of Procedures.

[27] Council Regulation 557/2014, Article 19.2.

[28] Regulation (EU) No 1290/2013 of the European Parliament and of the Council of 11 December 2013 laying down the rules for participation and dissemination in 'Horizon 2020 — the Framework Programme for Research and Innovation (2014-2020)'.

[29] Council Regulation 557/2014, Article 17.

[30] In the final phase of presentation of the final report.

A detailed description of the functioning of ex-ante controls performed during the grant agreement implementation phase is given in the following section. However, ex-ante controls are also embedded in all programme management activities.

Call management and Selection and evaluation phase (SEP): Here the goal is to make sure that the best proposals are selected; that they match the conditions set out in the Call for proposals; and that the beneficiaries are capable of completing the projects successfully and on time. To this end, the following checks are performed.

- Eligibility checks, to make sure that the proposals are submitted according to the rules and that they are in compliance with the eligibility criteria defined in the work programme.
- Evaluation of the proposals by external experts. Controls ensure the quality of the experts selected to evaluate the proposals. The JU also makes sure that the experts do not have any conflict of interest in evaluating proposals.

Grant award preparation phase (GAP): Here, the financial officer checks the budget and administrative data submitted and validates each participant, and reviews the full proposal. The financial officer then sends to the coordinator his/her comments, together with a request for any documents needed for the financial viability check (if applicable). The result of the check performed is documented in the grant preparation report. The pre-financing payment is made to the beneficiary as soon as the grant agreement has been signed.

As of IMI2 - Call 10, launched in December 2016, both processes are carried out by the IMI Programme Office through the common H2020 IT tool for submission and evaluation of proposals (SEP)[31].

Control indicators at this stage are as follows:

Indicator	Results 2016	Target 2016
% of coverage of annual call topics identified in AWP 2016	93% (14 out of 15)	100% (15)
Number of redress procedures on the result of the evaluation and selection procedure	None	None
Total average time to Grant (TTG)[32]	232 days	243 days

4.2.1 Ex-ante controls of the grant agreement implementation phase

The control of costs claimed by beneficiaries is triggered when IMI receives the periodic or final report. The checks focus on the deliverables, the technical report summarising the work done, and the costs reported (Form C) by beneficiaries as well as by (EFPIA) companies (the so-called in kind contribution) and Associated Partners.

The ex-ante controls procedure is performed in accordance with the workflow, checklists and templates defined in a standard operating procedure (SOP) on the assessment and approval of periodic and final reports of IMI projects[33]. According to this procedure, controls are carried out before authorising any payment and aim to verify that:

[31] Actions started before the implementation of the H2020 IT tool were, so far, managed through the internal IMI IT system and will progressively migrate to the H2020 IT system in the course of 2017.

[32] According to the H2020 Vademecum on Grant preparation, the time-to-grant (TTG) is the period between the Call deadline and grant signature. That period cannot exceed a maximum of 8 months (equivalent to 243 days). Further detailed information on grant preparation, in particular on time-to-inform (TTI) applicants and on time-to-prepare and sign (TTS) grants (which has to remain within the period of 8 months) is provided in Annex 6.

[33] Last version: IMI2/INT/2016-00952 of 31/03/2016

- the project is progressing as planned, as demonstrated through the project deliverables and other reports submitted (external reviewers can be involved in this assessment to ensure that project implementation is on track and that the project objectives continue to be achieved);
- resources are being used according to the indicative plan in the DoW (e.g. FTEs associated to each of the work packages, subcontracts, 'other direct costs', etc.); costs are plausible and are assessed against the initial description of work and the scientific progress made;
- costs reported are eligible according to the rules (i.e. Grant Agreement).

The assessment of the scientific officer (SO) and financial officer (FO) is facilitated by an assessment template that also allows them to identify high risk profile beneficiaries and to assess[34] other inherent risks.

On that basis, they can adapt their controls to verify if the use of resources reported by beneficiaries (for personnel, consumables, equipment, subcontracting, etc.) is clearly scientifically justified in relation with each specific task, deliverable and milestone.

Depending on the type and rating (high, medium or low) of the risk identified, the SO and FO can therefore take the most appropriate measures[35].

Once the report is accepted by the SO ('certified correct' visa), the accepted costs are reimbursed to beneficiaries (interim payment) following a standard financial circuit outlined in the financial rules and in the IMI Manual of Procedures for financial operations.

As the ex-ante control is based on a desk review of the self-declarations of beneficiaries and on the results of controls of the operation as known at the moment the payment is authorised, IMI can only have the reasonable assurance that the costs claimed are accurate and in compliance with the applicable legal and contractual provisions. Additional level of assurance on costs paid can only be achieved through ex-post audits carried out at the beneficiaries' premises, after the costs have been incurred and declared (below Section 4.3).

Furthermore, during the implementation of projects, IMI monitors the progress of their work plan not only through the systematic review of the periodic (annual) technical reports but also through interim reviews of each project. The review is performed by independent observers and their recommendations are closely followed up by the project managers.

All the interim reviews accomplished in 2016 made positive conclusions on the progress made and the early achievements of IMI1 - Calls 4, 7, 8, 9 and IMI2 - Calls 2 and 3 projects, as well as on the additional measures that could be taken to ensure successful completion of the projects by the end of the respective funding periods[36].

a) Volume of operational transactions

The number of operational transactions performed in 2016 gives an overview of the increasing levels of work carried out by the IMI Programme Office. Each transaction results from the control workflow described above. The IMI verification process is complex due to the nature of the projects implemented, amounts at stake and the number of participants per project (average 26).

Another element to take into consideration while assessing control workload is the percentage of final payments (8) handled during the year. Final payments of balance due conclude the project life cycle and therefore need a more in depth and extensive analysis and assurance elements in comparison to interim payments.

[34] Main criteria applied are: materiality, complexity and capacity to manage.

[35] Based on a risk control matrix which covers the majority of operational cases.

[36] For more information, see section 1.5.2.

The table below provides details of the number of pre-financing, interim and final transactions made by IMI or compensated against previous pre-financing payments[37] from 2012 to 2016.

	2012	2013	2014	2015	2016
Pre-financing payments	12	14	18	16	**16**
Interim and final payments[38]	26	33	32	30	**59**
Total	38	47	50	46	**75**

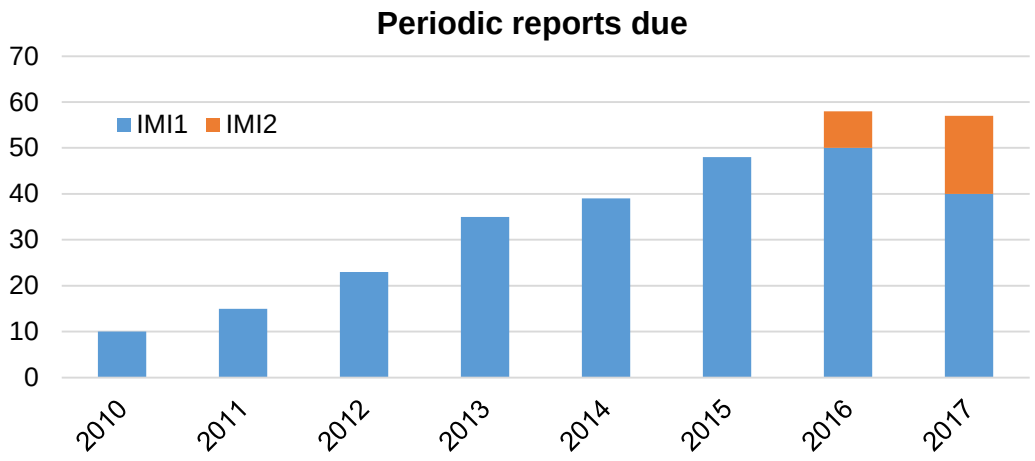
The analysis shows that the volume of transactions executed in 2016 is significantly (by 63%) higher than in 2015[39]. The considerable increase in the number of transactions was managed with the same number of staff available in the IMI Programme Office, resulting in a major increase in workload. This increasing trend in terms of workload will continue in the coming years.

The table and graph below demonstrate the current pipeline on the reporting due by ongoing projects. The number of payments does not correspond to reports received in year N. New projects are gradually added to the pipeline as Calls will continue to be launched up till 2020 and project implementation runs respectively till 2024.

Cumulative planning of periodic reports presented and due in 2016

Project periodic reports (RP) due in 2016						Of which
1st RP in 2016	2nd RP in 2016	3rd RP in 2016	4th RP in 2016	5th / 7th RP in 2016	Total reports	Final report due 2016
17	**8**	**6**	**12**	**15**	**58**	**10**

Graph showing periodic reports due from 2010 to 2017



[37] This implies that, in some cases, payments for the interim periods are fully or partially compensated ("clearing"). In 2016, the total amount of the costs cleared against pre-financing was EUR 18.348 million.

[38] Including 5 transactions concluded with full compensation against previous pre-financing payments.

[39] In this table, the transactions concluded with full compensation against previous pre-financing payments were not considered to assure consistence with the figures of previous years when there were no cases of full compensations.

b) Value of operational transactions

The total value of the operational transactions made in 2016, as well as the value of costs reported and accepted by IMI, is presented in the two tables below.

The 75 financial transactions managed amount to EUR 195.530 million, of which EUR 175.183 million represents the 70 effective payments to project beneficiaries.

Overview of operational transaction made in 2016

		No of Transactions		Value of Payments (EUR)	Value of Transactions (EUR)
IMI1 (FP7)	Pre-financing payments		**0**	0	0
	Interim payments	**39**			
	Final payments	**8**	**52**	109 847 000	128 194 000
	Clearing	**5**			
IMI2 (H2020)	Pre-financing payments		**16**	52 339 000	52 339 000
	Interim payments		**7**	12 997 000	12 997 000
TOTAL			**75**	175 183 000	195 530 000
		Budget execution %		**69.38%**	

Although the effort made during the year in terms of volume of transactions (see above) was 1/3 higher than in previous years, the corresponding budget execution rate remained at 69.38%. That was mainly due to three connected and objective factors.

- The number and intensity of Calls launched under IMI2 (10 Calls between 2014 and 2016) had an impact on the timeline of the Grant award phase, delaying the signature and payment of some pre-financing planned in the previous financial year. This issue has been now addressed by IMI services, but the effect of corrective measures will be visible only in future work plans and reports.
- The accumulated backlog of periodic and final reports received since 2015; this backlog will be however addressed with the increase of staff resources starting in Q1 2017.
- The unexpected decrease in cost claims of certain projects (mainly in IMI2 - Call 2) that reported less than foreseen in their work plans.

Interim and final costs reported and accepted in 2016 (EUR)

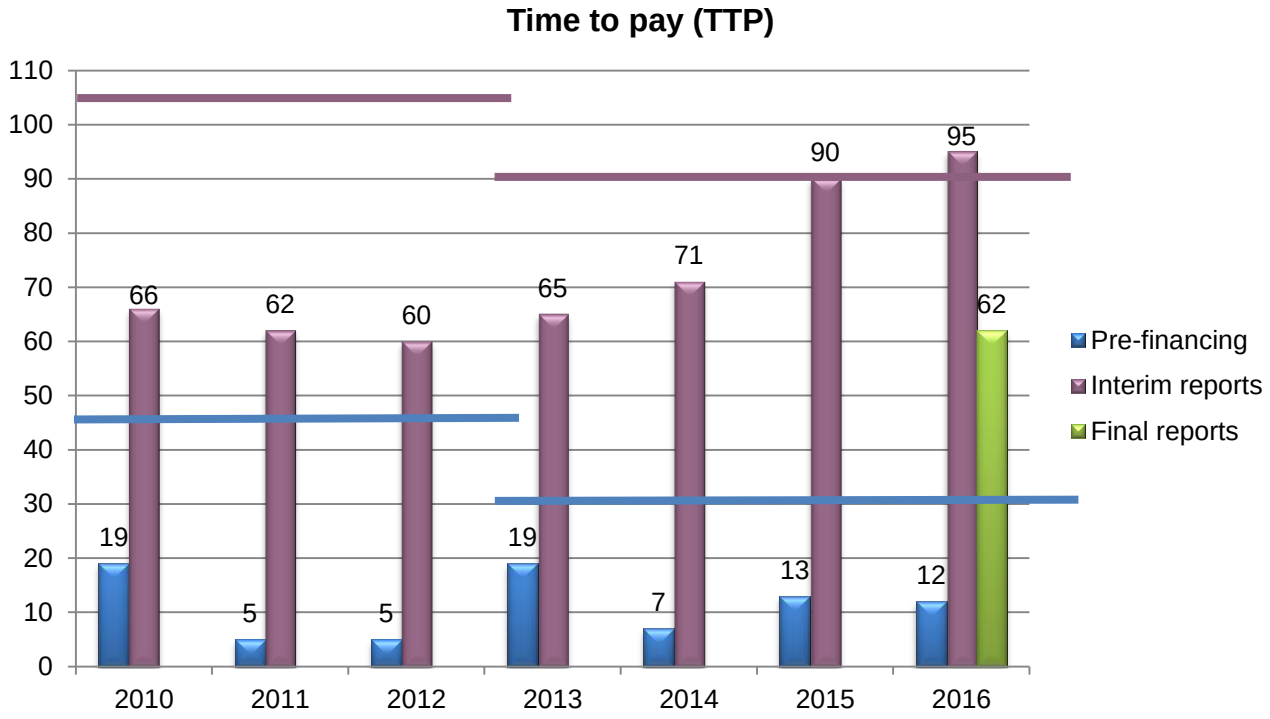
	2016
Total of reported costs	200 522 390
Of which covered by CFS	117 251 598
Accepted costs	198 985 169
Of which covered by CFS	116 688 760
Rejection	1 537 220
Rejection (in %)	**0.77%**

c) Time to Pay (TTP)

In 2016, on average it took 12 days to process pre-financing payments of the new projects implemented. That shows an efficient approach of the Programme Office to speed up the financing of beneficiaries and the implementation of grant agreements signed.

As for interim and final payments of cost claimed by beneficiaries, in 2016 the average time to pay (TTP) was 95 days, which is slightly above the time limit. The reasons for this partially match with those cited above to explain the budget implementation rate. They were mainly due to the combination of an increasing number of periodic and final reports submitted since 2015, and limited manpower available in 2016 within the financial team. This gap was finally bridged in the last quarter of the year when the Governing Board approved a new organisational structure presented by the Executive Director and authorised the recruitment of new financial officials who are expected to take join IMI in Q1/2017.

IMI management made a thorough review and follow up of the payments strategy in order to achieve the payment execution target and related 'time to pay'. However, despite those measures and the mitigating actions implemented, it was not possible to prevent the delay and late interests were paid to six beneficiaries.



Note:

- The purple lines ▬ represent the target for making interim and final payments.
  From 2010 to 2012, the target was 105 days. From 2013 onwards, the target was 90 days.
- The blue lines ▬ represent the target for making pre-financing payments.
  From 2010 to 2012, the target was 45 days. From 2013 onwards, the target was 30 days.

4.2.2 Control efficiency and cost-effectiveness

a) Cost-effectiveness of ex-ante controls

In terms of resource allocation, 11.5 FTEs (scientific and financial officers including the Heads of both sectors) are involved in the ex-ante control of the project implementation phase and payment cycle.

As described below, the number of FTEs involved in ex-ante controls represents 42.5% of the FTEs allocated to the operational programme management and around 1/6 of the total staff.

FTEs allocated to ex-ante controls as at 31/12/2016

Sector	Staff in the sector	FTE allocated to ex-ante control
Science	9	4
Operational Finance	4	4
Support activities (legal, AST, IT, internal control and audit)	11	3,5
Total	**24**	**11.5**

Average number of projects managed by staff member as at 31/12/2016

Operational sector	Staff in the sector	Average no. projects managed by staff member
Science	9	9.3
Operational finance	4	21

While IMI administrative costs represent 4.2 % of the total IMI budget, the costs for ex-ante controls can be estimated in standard costs at EUR 1.495 million/year (of which EUR 1.445 million is for FTEs' standard salaries[40], and EUR 50 000 on average for costs of externalised reviews and audits).

The cost for ex-ante controls would then represent around 0.85 % of the IMI operational budget.

Compared to the IMI project portfolio, the cost of the ex-ante control corresponds to EUR 16 797/year per project.

IMI2 JU budget 2016 (Payments in EUR)		% in total budget	Total costs of ex-ante control	Cost of ex-ante control as % of annual budget
Administrative budget	8 155 810	4.45 %	1 495 000	18.33 %
Operational budget	175 182 730	95.55 %		0.85 %
Total	**183 338 540**	**100 %**	**/**	**0.81 %**

[40] For this calculation we have used the methodology set out by DG BUDG in the Circular Note RUF/2015/34 of 09.12.15 where "average costs" include the so-called "habillage" Real estate expenses, furniture, IT, etc.).

b) Cost-effectiveness of controls of the programme management cycle

A complete assessment of the cost-effectiveness of IMI's control efficiency implies a consideration of all costs related to control of the programme life cycle, from submission, evaluation and selection to ex-post audit.

Sector	Estimated FTE allocated to ex-ante control	FTEs costs	Other costs related to controls	Total
		(Costs are indicated in EUR)		
Call management, Selection and evaluation phase	1.5	201 000	16 000*	
Grant award	1	134 000	/	
Grant management	11.5	1 445 000	40 000*	
Ex-post control	2	204 000	386 000	
Total	**15.5**	**1 984 000**	**442 000**	**2 426 000**
Cost-effectiveness ratio	**Cost of controls / Administrative costs budget**			**22.14%**
	Cost of controls / Total operational budget			**0.96%**
	Cost of controls / Operational payments 2016			**1.38%**

* Estimates

The assessment of these controls can be an important indicator of the sound financial management of the budget implemented. More baseline data, collected for a sufficient period of time, will be available by using consistently the methodology described above.

4.3 Ex-post control of operational expenditure and error rates identified

Ex-post controls are the final stage of IMI's control strategy in the project lifecycle. This stage includes the ex-post audits as well as the recovery/correction of any unduly paid amounts. Ex-post audits are carried out on the cost claims accepted and paid following the ex-ante controls described above.

Since the legal bases and the budgetary frameworks are different, IMI reports separately on the IMI1 programme under FP7 and the IMI2 programme under Horizon 2020. Separate chapters below address the ex-post controls under IMI (FP7) and IMI2 (H2020).

Ex-post control of operational expenditure under IMI1 (FP7)

Ex-post controls: audit and corrective actions

Ex-post audits have three main objectives:

(1) to assess the legality and regularity of expenditure on a multi-annual basis;
(2) to provide an indication of the effectiveness of the ex-ante controls;
(3) to provide the basis for corrective and recovery mechanisms.

IMI mainly uses two types of audits in order to arrive at a substantial representative coverage across beneficiaries as well as to identify and correct irregularities by providing coverage of certain participants' risk profiles.

- **Representative audits**, which contribute to an error rate representative of the whole population. This kind of audit is conducted by IMI on the basis of representative samples in accordance with the sampling methodology identified in the ex-post audit strategy. Each sample includes a combination of the largest cost claims by beneficiaries and randomly selected entities.
- **Corrective audits**, which aim to identify and correct irregularities and allow the coverage of certain risk profiles through **risk-based audits**. There may be populations which are not sufficiently covered by representative audits and which might present specific risks. This kind of audit provides IMI with enough flexibility, ensuring that specific populations are properly covered.

The main legality and regularity indicators for payments made to beneficiaries, as defined in the ex-post audit strategy, are the **representative** and **residual error rates** detected through financial ex-post audits.

- The ***representative error rate*** **(RepER)** is the detected error rate resulting from the representative audits. It provides a reasonable estimate of the level of error in the population relating to the accepted IMI contributions on completion of the audits, but does not take into account the corrections and follow-up undertaken by IMI. The formula for the calculation of the representative error rate, under the IMI ex-post audit strategy approved by the Governing Board, is shown in Annex 10 – Materiality Criteria.
- The ***residual error rate*** (**ResER**) is the level of error remaining in the population after deducting corrections and recoveries made by IMI JU. This includes the extension of audit results to non-audited financial statements of the audited beneficiaries to correct systematic errors. The formula for the calculation of the representative error rate under the IMI ex-post audit strategy approved by the Governing Board is shown below in Annex 10 – Materiality Criteria.

Given the multi-annual nature of both the IMI programme and its individual research projects, the **residual error rate** calculated on the duration of the programme provides the most meaningful indication of the financial impact of errors. It takes into account the corrections made by IMI and the fact that IMI extrapolates the systematic findings of the audits, significantly increasing the cleaning effect of audits. Moreover, as the programme advances, beneficiaries learn from their errors. Furthermore, drawing from the lessons learned from the audit findings, IMI also works continuously to better inform beneficiaries of any pitfalls to help them report their costs correctly.

Resources

Since the lean structure of IMI does not allow for the setting up of an internal team of auditors for these purposes, ex-post audits are outsourced to external audit firms. Nevertheless, the IMI Programme Office remains responsible for the management of ex-post audits, namely:

- the selection of audits;
- coordination with the EC;
- the preparation of the audit input files;
- contract management and the monitoring of the external audit firms' progress and deliverables (regular follow up of the audit status, interaction with audit firms on technical questions, and quality checks of audit reports);
- the analysis of errors detected and the implementation of audit results.

Indicators for the cost of control are provided in chapter 4.2.2.

Indicators of coverage: Number of audits and audit coverage (cumulative)

For the calculation of the audit coverage of the total costs claimed, the cumulative audited value of finalised ex-post audit assignments is compared to the total cumulative validated costs claims as of the cut-off date of 22 June 2016, corresponding to the last audit sample from which finalised audits were included in the current AAR.

	Total population[2]	Audited	Audit coverage
Beneficiaries	608	187	30.8 %
Projects	59	42	71.2 %
Costs accepted by IMI up to 22 June 2016 (EUR, cumulative)	297 818 980	67 771 342	22.8 %

The following table gives an overview of the status of individual audit assignments as of the cut-off date of 31 December 2016:

Sample	Audits finalised[1][2	Of which		Of which finalised in 2016	Audits ongoing	Total	Of which	
		Representative	Risk-based				Representative	Risk-based
2011	58	56	2	0	0	58	56	2
2012	35	34	1	1	0	35	34	1
2013	37	35	2	12	0	37	35	2
2014	24	24	0	7	1	25	24	1
2015	22	19	3	14	4	26	22	4
2016	11	10	1	9	5	16	15	1
Total	**187**	**178**	**9**	**43**	**10**	**197**	**186**	**11**

[2] Beneficiaries in IMI1 projects (FP7)

[1] An audit is considered finalised when the audit adjustment and the related 'error rate' is final. This comprises either audits with 'final audit reports' accepted by IMI or if not received or accepted, with a 'pre-final audit report' (after contradictory procedure with the beneficiary) approved by the JU and therefore with a definitive audit adjustment and error rate.

In the first half of 2016, IMI launched 15 representative audits based on the validated costs claims as of 30 April 2016. One further risk-based audit was launched. A second sample of 15 audits was drawn at the end of 2016 based on cost claims paid before 15 November 2016. These will be launched in early 2017.

Representative and residual error rates as of 31 December 2016

At this point, the **cumulative representative error rate** (RepER) resulting from 178 representative audits finalised is 2.12 % in terms of IMI contribution. The **cumulative Residual Error Rate** (ResER: error remaining in the population after corrections and recoveries) is 1.67 % in terms of IMI contribution. The residual error rate is thus below the 2 % materiality threshold established in Annex 10 of this report.

Implementation of audit results

Following the finalisation of each audit by an external audit firm, IMI launches the necessary corrective actions to recover or offset against subsequent claims of the same beneficiaries any amounts that have been found to be unduly paid.

The table below summarises the status of implementation of audit results on a cumulative basis as of the cut-off reporting date of 31 December 2016.

Number of cases of unduly paid amounts identified in audits	Number of cases implemented	Percentage of cases implemented	Amount implemented (EUR)
133	122	92%	1 188 222

Implementation of extrapolation

IMI extrapolates the systematic findings of the audits to all other cost claims by the same beneficiary. The unduly paid amounts thus identified are recovered or offset against subsequent cost claims of the beneficiary.

The status of the implementation of extrapolation of audit findings is shown in the table below.

Implementation of extrapolation of systematic findings	Beneficiaries
Audits finalised	187
Pre-information letters / letters of conclusion sent	178
Of which affected by systematic errors[41]	44
Extrapolation feedback received from beneficiary	34
Of which implemented[42]	33

[41] This does not include positive systematic errors and systematic errors below materiality threshold.

[42] Systematic errors are considered implemented when the complementary letter confirming the submitted adjustments is received from the external audit firm that performed the desk review.

Ex-post control of operational expenditure under IMI2 (H2020)

Ex-post control framework under IMI2

As regards the IMI2 programme, IMI's ex-post controls of grants are aligned with the harmonised strategy adopted for the entire H2020 Programme[43]. The Common Support Centre of the European Commission, more specifically its Common Audit Service (CAS), carries out the H2020 audits in accordance with the strategy for all entities implementing the H2020 programme, including IMI2 JU.

Under the coordination of CAS, IMI has throughout 2016 cooperated with the other stakeholders of the H2020 research family to contribute to the update of the H2020 Common Audit Strategy and to the definition of its implementing rules (Audit Approach for Bankruptcy Cases; Materiality Threshold for Extrapolations; Indicative Audit Programme instructions on the audit findings; Sampling methodology; Working Arrangements for H2020 Processes; Coordination of Horizon 2020 audits). IMI works in close cooperation with CAS to develop and implement its annual audit plans.

Ex-post controls in 2016

The first cost claims for the IMI2 programme went through ex-ante checks and were paid out in the third and fourth quarters of 2016. In order to acquire an element of assurance for the IMI2 programme early on, IMI agreed with CAS to launch four audits in 2016. With a view to covering, cost efficiently, a maximum amount at risk, the largest cost claims from a population of four projects were selected for audit

The total IMI contribution audited is EUR 2 976 456. This represents 23% of the total of EUR 12 997 000 of costs accepted as of 31 December 2016. One audit was finalised by the reporting deadline for the current report; no errors were detected. All four audits will be considered in the error rate calculation for 2017 when the population and the sample become more representative to meaningfully draw error rates.

[43] Horizon 2020 Ex-post Audit Strategy (2016 – 2025).

4.3 Audit of the European Court of Auditors (including IMI external auditors)

On 14 November 2016 the European Court of Auditors (ECA) published its report on IMI2 JU's annual accounts for the financial year 2015. In the report, the ECA issued an unqualified 'clean opinion' on the reliability of the accounts as well as on the legality and regularity of all transactions underlying the annual accounts.

Without calling into question its clean opinion as outlined above, the ECA also provided some general comments on the following:

- *Presentations of the accounts* – the auditors highlight a need for Commission guidelines on budgetary reporting.
- *Implementation of the 2015 budget* – the auditors note some delays in negotiations which impacted individual commitments and payments of pre-financing, and affected budget execution results (91% for commitment appropriations and 73% for payment appropriations as reported in AAR 2015).
- *Key controls and supervisory systems* – acknowledges that IMI2 JU has set up ex-ante control procedures and performs ex-post audits which are key tools for assessing the legality and regularity of the underlying transactions including in-kind contributions. Internal procedures are in place to provide reasonable assurance on the prevention and detection of fraud and irregularities.
- *Commission's Internal Audit Service* – the auditors note IMI2 JU actions to implement previous audit recommendations.

IMI strongly supported the Court's recommendation on horizontal guidelines for the budget reporting. In view of the Court's remarks, in December 2016 the Commission prepared and issued a set of guidelines for the content of the annual accounts and for the content of the report on budgetary and financial management. IMI will follow those guidelines for the 2016 accounts and report.

IMI addressed all previous audit recommendations as further specified in Part 4.4.

In accordance with the revised IMI2 Financial Rules, IMI's 2016 annual accounts are audited by the external audit company (Ernst&Young), who are contracted under EC DG Budget framework contract for a period of two financial years. The preparatory work started in November 2016. The Court of Auditors will draw its audit opinion on the accounts on the basis of the work of independent external auditors and report upon it in October 2017.

4.4 Internal audit

The Internal Audit Service (IAS) of the European Commission performs the internal audit function for IMI as specified in the Financial Rules.

The IAS issued the final audit report on ‘Controls over in-kind contributions in IMI2 JU’ on 21 January 2016.

The audit assessed whether management control procedures on in-kind contributions were adequately designed, compliant with the regulatory framework, and effectively and efficiently implemented under the IMI1 programme.

The auditors recognise IMI's efforts in simplifying the administrative burden for participants (both beneficiaries and EFPIA companies) and the efficiency of IMI staff in dealing with ex-ante checks of in kind contributions (IKC), at both financial and scientific levels. IAS confirmed that the arithmetic and reconciliation controls performed re accurate and performed well. The monitoring controls on the evolution of IKC at programme level, and its reporting to the Governing Board, were considered adequate and well documented.

The audit concluded that the set-up of the controls complies with the broad lines of IMI's founding regulation, but identified some weakness and issued four recommendations for improvements, three of which were classified as ‘very important’ and one as ‘important’.

The IAS recommended that IMI:

- provide clear and comprehensive instructions on the certification methodology to be applied by the external auditors and strengthen the review and approval process of the certificates;
- develop a strategy, procedures and guidance for the control of in-kind contributions;
- increase the value of operational and financial ex-ante and ex-post controls;
- perform checks on the quality of accounting data.

IMI prepared an action plan approved by the IAS on 26 February 2016. All four recommendations were implemented within the agreed deadlines in the course of 2016, thus mitigating the residual risk towards reasonable assurance.

In the course of 2016, the IAS carried out a preliminary survey and fieldwork at the IMI premises for the audit on ‘H2020 Grant Process in IMI2 JU’. The audit aimed to assess the design and implementation of the management and control systems set up by IMI to support the grant process, in terms of adequacy, efficiency and effectiveness. The final report is due in 2017.

Follow-up of previous internal audit recommendations

There are no outstanding recommendations from previous audits.

The implemented audit recommendations stem from the audits on ‘Grant management ex-ante controls’ and ‘Controls over in-kind contributions in IMI2 JU’. The implementation is confirmed by the IAS in the issue-tracking system.

In summary, six recommendations were implemented. This helped to improve IMI’s internal control system and mitigated residual risks to the Authorising Officer’s reasonable assurance.

4.5 Risk management

Background and methodology

Risk management is intended by IMI to be a proactive process of identifying and assessing any event that could pose a threat to the achievement of its objectives, and determining how the corresponding risks should be managed.

The JU implements a robust Enterprise Risk Management (ERM) process based on an annual Risk Assessment Exercise (RAE)[44] which consists of all the actions connected to setting up objectives, identifying risks, and the measurement, review, handling, reporting, follow-up, monitoring and reaction to risks.

In 2016 as in previous years, the annual risk assessment was an important step in the definition of the annual objectives and priorities for IMI. The exercise provided a comprehensive analysis of the weaknesses and threats that could undermine IMI's performance and capacity to deliver. In accordance with the methodology adopted, during the assessment risks are broken down to manageable levels in order to involve as much as possible staff at all levels. Risks are then reassessed at corporate level in order to facilitate the elaboration of tailored mitigating actions. The result is twofold.

- At operational level, each sector (e.g. science operations, communication, HR, finance, IT, etc.) produces and manages an **Operating Risk Register (ORR)** that identifies and ranks the risks they might have to face when implementing the annual work plan. The ORR includes a risk mitigation plan which details for each risk the assigned responsibility and recommended actions to reduce either the probability of a risk materialising into a problem, or the severity of the exposure if the risk does occur.
- At corporate level, the JU management makes a strategic, cross-sectional assessment of the JU's objectives and of the risks reported in each ORR. Cross-cutting and policy risks scored above a critical threshold are considered strategic as representing a threat at corporate level. These risks and the related mitigation plan are included in the **Strategic Risk Register (SRR)**, which is directly monitored at senior level.

Periodic monitoring and updates are planned during the year in order to keep the risk management dynamic and able to respond to internal/external influences or evolving priorities (as was the case, for example, for Brexit; its potential impact was promptly communicated to project participants and is monitored by IMI). In this respect, the risk register is supposed to capture risk information from the 'bottom up' within each service area where actions and risks are assessed and controlled. Risks are escalated when new circumstances prevent objectives from being achieved.

Key results

An overall assessment of the 2016 exercise shows that some risks tend to persist within the JU. This is because they are correlated with the specific objectives of IMI as a public-private partnership. Some strategic risks in particular are typically associated with the IMI mission and have therefore to be accepted as such and addressed in a way that allows the JU to reduce or partially transfer their impact where needed. This is the case, for example, for the risk of unbalance between the in-kind contribution from industrial members and the financial contribution of the EU at the end of the programme, or the risk of insufficient leverage of private contributions.

With the aim of preventing adverse impacts on IMI's planned activities, the strategic and operational risk factors identified in the assessment exercise and the associated control measures were monitored throughout the year to allow a deeper analysis and understanding.

The result of these monitoring and management activities is reported below together with the action taken. Certain risks have been merged or reformulated according to the changing environment (e.g. alignment of operating procedures with H2020 and implementation of common IT tools SEP, SYGMA and COMPASS).

[44] The annual risk assessment is performed in accordance with the methodology defined in the Guideline for risk management approved by the Executive Director.

Risk factors	Mitigation measures implemented
Potential unbalance at the end of the IMI Programme between the in-kind contribution from industry and the financial contribution of the EU.	The risk is mitigated through: ▪ continuous monitoring of in-kind contributions (committed and reported) at project level through the annual periodic reports and interim reviews, which are periodically reported to the Governing Board; ▪ at the request of the Governing Board, EFPIA has developed a contingency plan addressing potential imbalance at the end of the IMI1 Programme, including operational and financial actions.
IMI's operational and financial planning process may be delayed, influencing negatively the achievement of the JU's activities and objectives (e.g. topic definition, Call launch, budget implementation, etc.).	The operational planning of the JU may be impacted by external factors that are outside the control of the JU (such as Brexit). However, this risk is controlled through: ▪ extensive consultations with and between the JU's Members; ▪ the role of the SGGs in the Call topic definition process was enhanced (new charter) so that they have become interactive thematic platforms addressing defined areas within the IMI2 SRA; ▪ periodic revision and simplification of the planning and budgeting process.
Various external and internal factors may jeopardise the grant life cycle (from submission to project management) affecting the participation of key stakeholders (e.g. SMEs), the efficient use of resources, or the sustainability and dissemination of scientific results and IMI's expected socio-economic impact.	IMI addresses this risk at various levels: ▪ facilitating the participation of the largest possible number of stakeholders through communication activities (info days, webinars, etc.) and providing assistance during the preparation of full proposals; ▪ monitoring activities during project implementation to prevent and resolve possible deviation or disputes; ▪ promoting the participation of SMEs through dedicated support measures.
The rapidly increasing portfolio of projects and reporting activities may generate a backlog and operational delays, affecting the effectiveness and efficiency of the entire project management process.	▪ Regular monitoring and reporting of the pipeline in cost claims management and prioritisation of tasks to meet TTP target. Enhanced management supervision. ▪ Planning adequate staff resources and back-up. This measure was fully implemented in Q4 2016 and new staff members will take up duties in Q1 2017. ▪ Implementation of the H2020 IT tools in operational activities as from IMI2 - Call 10. Data on previous Calls will be progressively moved to the system over Q1-Q2 2017.
The reorganisation of the Programme Office to meet the evolving objectives of its stakeholders may be delayed in the decision-making process and encounter difficulties in the implementation phase.	▪ Set up of a new Management Team to meet and anticipate operational and strategic needs. ▪ An internal reorganisation, including an updated Establishment Plan was presented by the Executive Director and will be progressively implemented. ▪ A review of job descriptions to align staff tasks with needs and improve their skills was performed in parallel with the reorganisation.
Negative external perception of IMI added value and criticism.	▪ Communication strategy continuously implemented. ▪ Information and public comments on IMI activities monitored closely and reported systematically to management and Governing Board. ▪ Communication services proactive in correcting misconceptions, promoting success stories and ensuring that decision makers, stakeholders and European citizen have an accurate view of how IMI works.

4.6 Fraud prevention and detection

IMI has an Anti-Fraud Strategy aligned with the Common Anti-Fraud Strategy of the Directorate-General for Research & Innovation (DG RTD)[45].

This strategy is implemented at JU level in close coordination with DG RTD and other research agencies through a multiannual action plan.

IMI has adopted a proactive approach to managing the risk of fraud, which is assessed through the annual risk assessment exercise of JU activities and is also embedded in the ex-ante control of periodic and final project reports as described above in the section on operational expenditure.

Regular information on fraud-related risks is communicated to all staff concerned who are encouraged to attend tailored training on fraud prevention and detection in the research area.

IMI has appointed an anti-fraud and OLAF[46] correspondent to support internal activities and to coordinate relations with European Commission, other agencies and OLAF.

In 2016, an instance of suspicion was communicated to OLAF which decided not to open any investigation based on the documentation provided and the result of a financial audit performed by the JU.

[45] This Strategy has been adopted for all the Research family (DG RTD, DIGIT, REA, ERCEA, etc.) by the Executive Committee of the Common Support Centre of DG RTD on 07/02/2015.

[46] Office européen de lutte antifraude (European anti-fraud office).

4.7 Compliance and effectiveness of internal control

IMI implements an internal control framework intended as a process applicable at all levels of management and designed to provide reasonable assurance that operations are effective, efficient and aligned with strategy; financial reporting is reliable, and the JU is in compliance with applicable laws and regulations.

This system is based on 16 Internal Control Standards (ICS) adopted by the Governing Board[47] in line with equivalent standards laid down by the European Commission. Those standards underpin the Internal Control Framework set up by the Executive Director, taking into account the structure and size of IMI, the nature of the tasks entrusted to it and the amounts and financial and operational risks involved.

The Executive Director steers and supervises control and risk management functions assisted by a management team, the Audit Manager and the Internal Control Coordinator. However, all staff members are to implement internal control processes at their respective level of competencies.

Management's key internal control activities performed include:

- overall supervision and monitoring of operations, checks and reporting on the functioning of the internal control systems;
- implementation of the annual Internal Control Action Plan and the self-assessment of the effectiveness of the internal control system;
- risk assessment and management.

This model is embedded across IMI's organisational structure which relies in particular on a combination of ex-ante and ex-post controls, segregation of duties, documented processes and procedures, control of deviations, promotion of ethical behaviour, and sound financial management.

The 2016 annual self-assessment of the effective implementation of the Internal Control Standards was based on the following points.

- Bilateral interviews with the staff concerned, based on a pre-defined questionnaire focusing the 16 ICS. For each standard, a number of questions were asked with the aim of assessing the degree of effective implementation.
- An objective examination of reports and assessment carried out by management and by internal and external auditors. The reports produced in 2016 are:

    - management reports on control results, including the results of internal control monitoring at the JU level;
    - the observations and recommendations reported by the Internal Audit Service (IAS) and by the European Court of Auditors (ECA) as well as a management overview on progress made on the implementation of the corresponding action plans.

In order to assure that all aspects of IMI operations and internal control were covered by the assessment, the 16 standards have been analysed separately and then as a whole. Through this approach, a diagnostic of strengths and weaknesses of the IMI's internal control framework was made. It provides sufficient guarantees as to the completeness and reliability of the information reported on control management of IMI activities.

The overall objective set out in the Annual Work Plan 2016 for internal control was to monitor and improve the robustness of the system to reflect the evolving needs of the JU and to better meet the expectations of its members and stakeholders in terms of efficiency, effectiveness and flexibility. In order to address this objective, the action plan for the implementation of the Internal Control 2016 focused on the prioritisation of some key standards.

[47] GB Decision of 10 July 2014 extending to IMI2 JU the control standards adopted for the IMI1 JU.

ICS 3 and ICS 7 (Staff allocation and organisational structure)

ICS 3 on staff allocation and recruitment and ICS 7 on the effectiveness of the operational structure have been prioritised to monitor the effective implementation of the reorganisation of the Programme Office. Management assessment and monitoring were specifically focused on:

- customisation of procedures to the evolving needs of the JU programming and timely implementation of the staff establishment plan;
- compliance and effectiveness of control processes especially in the field of staff recruitment;
- adoption of appropriate implementing rules adapted to the IMI environment.

ICS 8 (Processes and procedures)

By nature, the effectiveness and efficiency of internal processes and procedures is an ongoing process that requires continuous monitoring and improvement to keep IMI effective, efficient and relevant to the evolving needs of its stakeholders. During the year, the following actions were taken to ensure the effective monitoring, measurement and testing of the established procedures:

- control of overrides and deviations from policies and procedures;
- assessment among the staff of the level of awareness and understanding of updated documented procedures including the risks linked to changes in procedures;
- follow up and monitoring of the operating procedures and guidance adopted to reflect the new environment and requirements of H2020, in particular the implementation of the common IT Tools (SEP, SyGMA and COMPASS) for the management of Calls, evaluation, grant awarding, etc.;
- revision of some specific policies and SOPs to improve the general effectiveness of the office.

ICS 13 (Accounting and financial reporting)

The outsourcing of the accounting function and the recruitment of a new Budget Officer suggested focusing during 2016 on financial management and reporting to ensure the reliability and completeness of the accounting information as well as the production of accounts. For this purpose, the JU management performed regular reviews with periodic meetings at operational level (‘business meetings’) and on-the-spot checks of samples of files in selected processes (particularly in the field of ex-ante operational checks and operational expenditure). Emerging risks were also systematically analysed to mitigate possible negative effects. The self-assessment of the effectiveness of this standard can be considered positive although the validation of the accounting system planned with DG BUDGET was postponed to Q1-Q2 2017 due to the overlapping reporting, audit and evaluation activities affecting the Programme Office in Q4 of 2016.

In conclusion, the results of periodic management supervision, the annual self-assessment of the effectiveness of internal control system, and the overall assessment report of the management, lead to the conclusion that IMI is in compliance with all ICS, the controls in place are working as intended, and the internal control system is providing an effective framework for managing the risks to the achievement of the JU's objectives.

Risks identified through the annual risk assessment exercise (RAE) and that might pose a threat to the achievement of IMI’s mission and objectives were also systematically assessed and managed through appropriate controlling and mitigating actions.

5 Management assurance

5.1 Elements supporting assurance

This section reviews the assessment of the elements reported in Parts 2 (Support to operations) and 4 (Internal control framework) and draws conclusions supporting the declaration of assurance.

Reasonable assurance is a judgement by the Executive Director, the IMI2 JU's Authorising Officer, based on all the information at his disposal.

The management assessment is based on the following sources supporting assurance, specifically:

- governance, risk management process and internal control framework;
- findings and opinions from internal and external audits;
- independent external reviews;

The information reported covers both the operational budgets related to FP7 and H2020 programme, as well as the administrative budget managed by IMI in 2016, and supports the statement of the Declaration of Assurance.

Management assessment provides the results of key indicators related to budget execution, addressing the statement on the 'use of resources for the intended purpose'. It further assesses the 'sound financial management' and the 'legality and regularity of underlying transactions' per process stages and reports on measures implemented to prevent, detect and correct fraud.

As demonstrated throughout the report, the results of performance and control indicators positively support the statement of the declaration of assurance. Although a few indicators, relating to the efficiency component of sound financial management, show slight deviations from targets, these do not impair the declaration of assurance. Fraud prevention and detection mechanisms in place did not reveal anything that would impair the declaration of assurance.

Management has reasonable assurance that overall, adequate controls are in place and work as intended; risks are being mitigated and/or monitored; and improvements and reinforcements are being implemented. The audit results, the internal control self-assessment and the control indicators did not reveal any significant weaknesses and do not fulfil any of the materiality criteria laid down in Annex 10. The overall cumulative residual error rate is below 2 %. The control strategy foresees the implementation of further controls during subsequent years designed to detect and correct these errors.

Taking into account the lessons learned from the indicators of ex-ante and ex-post controls, together with the strengths and weaknesses highlighted in the audits conducted in 2016 and the expected corrective capacity of the controls to be implemented in subsequent years, it is possible to conclude that the internal control system implemented by , IMI provides sufficient assurance to adequately manage the risks relating to the legality and regularity of the underlying transactions, taking into account the multiannual character of the programmes.

5.2 Reservations

There are no reasons for introducing any reservations.

5.3 Overall conclusion

In conclusion, IMI's management has reasonable assurance that, overall, suitable controls are in place and work as intended; risks are being appropriately monitored and mitigated; and necessary improvements and reinforcements are being implemented. The Executive Director, in his capacity as the Authorising Officer, has signed the Declaration of Assurance.

6 Declaration of assurance

I, the undersigned,

Executive Director of the Innovative Medicines Initiative 2 Joint Undertaking

In my capacity as authorising officer

Declare that the information contained in this report gives a true and fair view[48]*.*

State that I have reasonable assurance that the resources assigned to the activities described in this report have been used for their intended purpose and in accordance with the principles of sound financial management, and that the control procedures put in place give the necessary guarantees concerning the legality and regularity of the underlying transactions.

This reasonable assurance is based on my own judgement and on the information at my disposal, such as the results of the self-assessment, ex-post controls, the observations of the Internal Audit Service and the lessons learnt from the reports of the Court of Auditors for years prior to the year of this declaration.

Confirm that I am not aware of anything not reported here which could harm the interests of the Joint Undertaking.

Brussels, 28 February 2017

Pierre Meulien

[48]True and fair in this context means a reliable, complete and correct view on the state of affairs in the Joint Undertaking.

Annexes

Annex 1 – Organisational chart

Annex 2 – Establishment plan

Annex 3 – Project outputs

Annex 4 – Publications from projects

Annex 5 – Patents from projects

Annex 6 – Scoreboard of H2020 common KPIs

Annex 7 – Indicators for monitoring cross-cutting issues

Annex 8 – Scoreboard of KPIs specific to IMI

Annex 9 – Draft/final annual accounts

Annex 10 – Materiality criteria

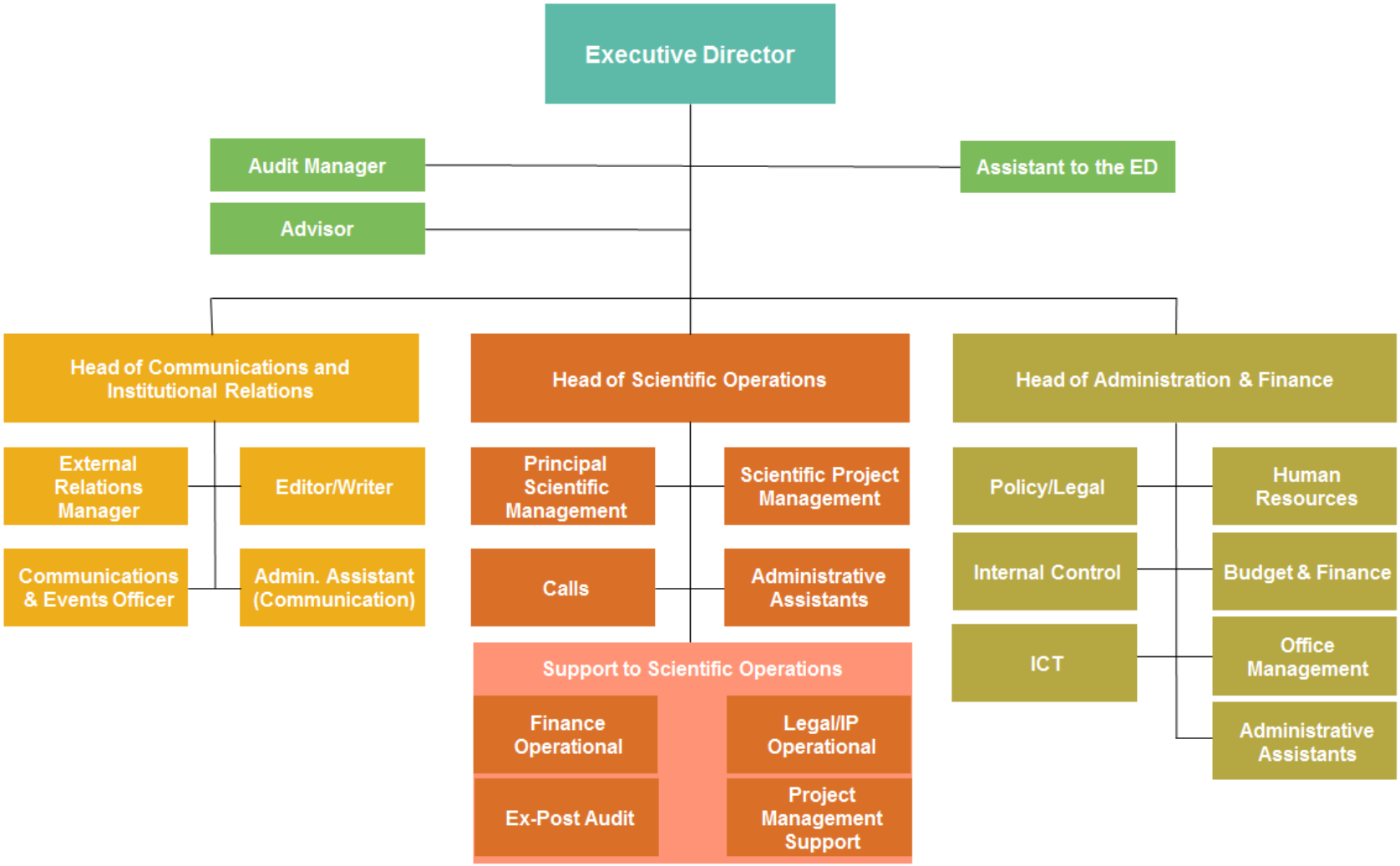
Annex 11 – Media highlights

Annex 12 – List of acronyms

Annex 13 – Table of IMI projects

Annex 14 – Assessment of the consolidated Annual Activity Report by the IMI2 JU Governing Board

Annex 1 – Organisational chart



Annex 2 – Establishment plan

Grade	Year 2015			Year 2016											
	Establishment plan 2015			Evolution in posts						Organisational evolution			Establishment plan 2016		
				Promotion / career advancement			Turnover (departures / arrivals)			New posts (per grade)			Requested budget		
	Perm.	TA	Total	Perm.	TA - LT	TA - ST	Perm.	TA - LT	TA - ST	Perm.	TA - LT	TA - ST	Perm.	TA	Total
AD16															
AD15															
AD14		1	1											1	1
AD13															
AD12		2	2											2	2
AD11		4	4											2	2
AD10															
AD9		3	3											3	3
AD8		7	7											7	7
AD7		5	5											6	6
AD6															
AD5		7	7											11	11
Total AD		29	29											32	32
AST11															
AST10															
AST9															
AST8		1	1											1	1
AST7															
AST6															
AST5															

AST4														
AST3		5	5										4	4
AST2														
AST1													1	1
Total AST		6	6										6	6
SC6														
SC5														
SC4														
SC3														
SC2														
SC1														
Total SC		0	0										0	0
Overall total		35	35										38	38

Notes:

Perm. = permanent staff

TA = temporary agent

LT = long-term contract

ST = short-term contract

Contract agents

Grade	2014	2015	2016
CA FG IV	2	2	2
CA FG III	5	6	11
CA FG II	1	1	1
CA FG I	0	0	0
Total CA	**8**	**9**	**14**

Notes:

CA = contract agent

FG = function group

Annex 3 – Project outputs 2016

The following tables provide a snapshot of the successes generated by IMI1 and IMI2 projects in 2016. Results are classified according to the following categories:

- Identification and validation of new drug targets and novel hit and lead discovery
- Establishment of robust validated models and tools for drug discovery and development
- Development of biomarkers and tools predictive of clinical outcomes (efficacy and safety)
- Clinical trials - improved design and process
- Big data solutions to leverage knowledge / implementation of data standards
- Impact on regulatory framework
- Implementation of project results inside industry
- Education and training for new generation of R&D scientists

Some results stories are told in greater detail as success stories in section 1.2 of this report.

IMI1 projects

Identification and validation of new drug targets and novel hit and lead discovery

Project title	Description of result(s)
AETIONOMY (Alzheimer's disease and Parkinson's disease)	Created a pathway terminology system to retrieve pathway information from literature mining, and used it to mine biomedical papers and patents with focus on Alzheimer's disease (AD). This demonstrated its utility to identify a putative mechanism explaining the mode-of-action of the approved drug Rasagiline, and for fingerprinting patents to support the discovery of pathway knowledge for AD.
AETIONOMY (Alzheimer's disease and Parkinson's disease)	Identified a total of 180 putative disease mechanisms for Alzheimer's and Parkinson's disease. Six of these have been selected for validation in biological samples from the clinical study.
DIRECT (diabetes)	Discovered that human gut microbiome impacts the serum metabolome and associates with insulin resistance. Identified *Prevotella copri* and *Bacteroides vulgatus* as the main species driving the association between biosynthesis of BCAAs and insulin resistance, and demonstrated in mice that *P. copri* can induce insulin resistance, aggravate glucose intolerance and augment circulating levels of BCAAs. These findings suggest that microbial targets may have the potential to diminish insulin resistance and reduce the incidence of common metabolic and cardiovascular disorders.
EMIF-AD (Alzheimer's disease)	MicroRNAs (miRNAs) in cerebrospinal fluid (CSF) have been suggested as Alzheimer's disease (AD)-specific biomarkers. Using large, independent sample cohorts of AD patients, people with mild cognitive impairment and controls from three different centres, several confounding factors were identified which impeded showing differences in miRNA levels between the groups.
EMIF-METABOLIC (metabolic syndromes)	Demonstrated that in obese women, circulating and white adipose tissue (WAT)-secreted CC chemokine ligand 18 (CCL18) correlates with insulin resistance and metabolic risk score. Because CCL18 is macrophage-specific and associates with adipose immune gene expression, it may constitute a marker of WAT inflammation.
EMIF-METABOLIC (metabolic syndromes)	Demonstrated that harmful saturated, ceramide-enriched liver lipidome is a marker of metabolic non-alcoholic fatty liver disease (NAFLD). This suggests that the ceramide pathway is a key mediator of hepatic insulin

Project title	Description of result(s)
	resistance (IR) that in humans characterises increases in liver fat due to IR, and associated increased risk of type 2 diabetes and cardiovascular disease.
ENABLE (antimicrobial resistance)	In 2016, 10 new antibiotic discovery programmes, including 7 from SMEs, were submitted to ENABLE. Of these, 4 were approved for funding, and 4 are currently under evaluation. Nine programs were actively funded at different stages during 2016. A University of Oxford programme discovered through the IMI project ELF was approved for ENABLE's hit-to-lead effort. Since the project started, 27 different antibiotic drug discovery programmes were reviewed by ENABLE's Portfolio Review Committee; 16 were funded, and 11 terminated again.
EU-AIMS (autism spectrum disorders)	Provided important insights into the mechanisms by which neuroligin-4-dependent gamma-aminobutyric acid (GABA)ergic synapses may contribute to autism phenotypes, suggesting new strategies for therapeutic approaches.
EU-AIMS (autism spectrum disorders)	Performed the first translational *in vivo* magnetic resonance spectroscopy (MRS) study in rodent models and adults with Autism Spectrum Disorders (ASD), demonstrating similar abnormalities in the excitation-inhibition (E/I) balance. Human and rodent data together lend further support to the notion that E/I imbalance may be a biological mechanism of ASD and a potential treatment target.
EU-AIMS (autism spectrum disorders)	By applying perfusion-based functional magnetic resonance imaging (fMRI) and quantitative magnetic resonance spectroscopy (MRS), identified in the BTBR mouse model of autism specific circuitry and neurochemical alterations that may underlie the severe stereotypies observed in these animals. Treatment with N-acetylcysteine, i.e. a modulator of cysteine-glutamate antiporter of glial cells, normalised repetitive behaviour and circuit-specific dysfunctions.
ELF (drug discovery)	Ran a screening programme on dengue fever for an SME. There are currently no treatments for dengue fever, which causes flu-like symptoms and can turn into the more serious, potentially fatal 'severe dengue'. In a bid to contribute to the development of treatments for neglected tropical diseases (NTDs), the European Lead Factory is waiving fees for drug discovery programmes on the World Health Organization list of NTDs. The diseases on the list, which includes sleeping sickness, rabies, leprosy, and dengue fever, are found in 149 (mainly tropical and sub-tropical) countries and affect one billion people worldwide.
ELF (drug discovery)	A potential target within Gram-negative bacteria was screened against the ELF library, leading to the identification of hits with very promising activity against the target. These highly potent compounds were then accepted by the ENABLE project, which aims to develop attractive antibacterial candidates for testing in the clinic.
ELF (drug discovery)	An academic researcher who benefited from ELF screening activities by identifying a drug candidate series for type 2 diabetes, went on to create a spin-out company based on these findings. A set of selective and potent small molecules which interfere with this target were identified as part of the screen and a spin-out company, ScandiCure, was created to further develop these molecules into a first-in-class anti-diabetic drug.
K4DD (drug discovery)	Developed and studied a series of molecules to bind the adenosine A2A receptor, a therapeutic target for several diseases including Parkinson's and cancer. This enabled the project to understand the factors which cause some potential drug molecules to disconnect from the receptor, knowledge which can probably be applied to similarmechanisms which exist in a broad range of other receptors similar to A_2A. This will lead to the development of

Project title	Description of result(s)
	safer and more effective drugs to target receptors in general.
ULTRA-DD (drug development)	Discovered a potent inhibitor of a Class I protein arginine methyltransferase fragment - a promising target class in oncology and other disease areas. As a result of a fragment-based screening approach, chemical moieties occupying the substrate arginine-binding site were found to act as efficient fragment inhibitors. Subsequent screening of a 2040 fragment library against PRMT6 (Protein arginine N-methyltransferase 6) produced a 300 nM inhibitor (ligand efficiency of 0.56) that decreased global histone 3 arginine 2 methylation in cells, and can serve as a tool for the development of PRMT chemical probes.
ULTRA-DD (drug development)	Thoroughly validated the protein methyl transferase 5 (PRMT5) as a drug target for new treatments in glioblastoma. In addition, a set of other epigenetic targets have been implicated as suitable intervention points in more pure inflammatory disorders, and validation is ongoing.
ULTRA-DD (drug development)	Jointly with the Structural Genomic Consortium (SGC), launched the chemical probes portal (www.chemicalprobes.org) to make high quality data available to the chemical biology community. Fragment based co-crystal structure data is available from the SGC website.
ULTRA-DD (drug development)	Delivered a three-dimensional view of polycystin-2 (PC2), a protein that causes autosomal dominant polycystic kidney disease (ADPKD) when mutated. This work revealed a novel substructure called the tetragonal opening for polycystins (TOP domain). 27 of the known ADPKD-causing mutations map to this region of the protein. These structural insights will help scientists begin to understand how mutations in PC2 cause disease, and more importantly, generate ideas for how the disease can be treated, thereby enabling development of medicines to help patients with ADPKD.
ULTRA-DD (drug development)	Generated convincing data regarding the role of PRMT5 in glioblastoma, validating its role in disease progression, and thus providing a new target intervention point for the initiation of drug discovery programmes. PRMT5 was recently implicated as a potential target using genetic approaches, and now the case has been significantly strengthened through this study using drug-like chemical probes in patient-derived stem cell assays.
ZAPI (infectious diseases)	Identified key immunogens against new potential zoonotic disease (i.e. Rift Valley fever, Schmallenberg virus and Middle East Respiratory Syndrome). Neutralising antibodies and potential vaccines against these targets will be designed and optimised in later phases of the project.

Establishment of robust, validated tools for preclinical drug development

Project title	Description of result(s)
COMPACT (drug delivery)	Developed a toolbox of reliable and quantitative assays to monitor cytosolic delivery of biopharmaceuticals. The toolbox includes assays on split green fluorescent protein (GFP) or split enzyme complementation as well as assays based on selective cytosolic biotinylation. These assays directly contribute to a better understanding of the intracellular fate of drug delivery systems (DDSs) newly developed by COMPACT, as well as indirectly contribute to the improvement of DDS for future use.
DDMoRe (knowledge management)	105 models available via http://repository.ddmore.eu/models The project also hosts models from the PreDiCT-TB and OrBiTo projects.
EBiSC	Launched the European induced pluripotent stem cell (iPSC) bank

Project title	Description of result(s)
(stem cells)	catalogue, which is a collection of human iPS cells being made available to academic and commercial researchers for use in disease modelling and other forms of preclinical research. Cell lines are available for ordering on a not-for-profit basis. Cell phenotyping data available to biopharma partners, free for service provision.
eTOX (drug safety)	The main project output, the eTOXsys database consists of over 7 000 animal toxicity reports provided by the industry partners and approx. 80 computer models. Both the database and the models are now extremely valuable tools to allow for the prioritisation of toxicology studies on drug candidates.
eTRIKS (knowledge management)	Created the first broadly applicable 'data catalogue' for datasets associated with projects from both IMI1 and IMI2 as well as other published sources. The catalogue provides a searchable metadata repository that encompasses a wealth of cross-project study information, allowing investigators to quickly find and assess datasets pertinent for their research endeavours.
EU-AIMS (autism spectrum disorders)	Reprogrammed and genome edited 8 patient derived induced pluripotent stem cell (iPSC) lines, with 5 more currently being reprogrammed (target: 12 lines). Furthermore, successfully derived morphogenetic, electrophysiological, and pharmacological phenotyped neurons from these cells.
EU-AIMS (autism spectrum disorders)	The SME Noldus Information Technology continued its development of EthoVision XT as a tool for automating behavioural tests with rodent models of ASD, leading to the release of version 11.5.
EU-AIMS (autism spectrum disorders)	Radioligands for oxytocin receptor imaging have been designed, synthesised and evaluated pre-clinically *in vivo* and *in vitro*. These are being used to investigate the brain penetration of oxytocin-like peptides by comparing intranasal and intravenous routes of administration.
ELF (drug discovery)	Compound library expanded further to a total of 460 000 diverse compounds. 79 public target programmes accepted, 50 high throughput screens finished, and 51 hit lists with associated data reports handed over to the target owners. In total, 3 408 qualified hits have been granted to public and private target owners (1 256 and 2 152 respectively).
EUROPAIN (pain)	Demonstrated that sleep deprivation is a valid model for generalised hyperalgesia in rodents and humans with sensory profiles similar to fibromyalgia.
IMIDIA (diabetes)	Generated third generation human beta-cell lines with conditional growth-arrest control.
IMIDIA (diabetes)	Identified culture conditions and *in vivo* factor that control beta cell progenitor differentiation.
IMIDIA (diabetes)	Identified novel human genes differentially expressed in islets from diabetes patients, and their role in human beta cell function.
IMIDIA (diabetes)	Developed new imaging tools for beta cell mass and demonstrated their validity as beta- cell markers *in vitro* and as imaging agents *in vivo* using various animal models and MRI approaches.
K4DD (drug discovery)	The K4DD database now holds almost 1 500 data endpoints. A key K4DD objective is to make the scientific findings publicly available after the end of the project phase.

Project title	Description of result(s)
	In total 26 different assays have been developed for 12 soluble targets, and 34 assays for 10 different GPCRs have been developed.
MARCAR (drug safety)	Used genome-wide profiling of changes to DNA methylation to detect early markers of non-genotoxic carcinogens activity in rodents. These studies contribute to understanding the scale and nature of drug-induced epigenetic changes in an *in vivo* setup relevant for drug safety assessment.
MARCAR (drug safety)	Identification of mRNA signatures which indicate the initiation of cancer. These biomarker candidates improve the understanding of the effects non-genotoxic carcinogens have on the liver and how they may induce cancer.
MARCAR (drug safety)	Established that a mechanism of drug metabolism, previously shown to be important in the rodent liver, is also active in cultured human liver cells. These cells therefore represent a powerful tool to evaluate toxicity of drugs directly in human cells.
MARCAR (drug safety)	Established that superoxide may contribute to the promotion of liver cancer.
MIP-DILI (drug safety)	Developed and extensively characterised an easily scalable 3D primary human hepatocyte (PHH) spheroid system, a versatile and promising *in vitro* system to study liver function, liver diseases, drug targets and long-term drug induced liver injury (DILI)
MIP-DILI (drug safety)	Conducted for the first time a study across multiple industry and academia laboratories of the utility of cell models currently used in safety assessment of drug induced liver injury (DILI). Using a panel of 13 compounds (9 implicated and 4 non-DILI implicated in man) it was showed that none of the cell models could distinguish faithfully between DILI and non-DILI compounds. The study provided clearer insights into the usability of simple cell culture tests for the pharmaceutical industry, by providing robust results validated by two or more independent sites. The public-private approach of the project uniquely enabled this multinational multicentre approach, involving six industry partners and one academic partner.
Open PHACTS (knowledge management)	The Open PHACTS project has published a wide variety of apps to streamline preclinical research. For example, the Open PHACTS Explorer is designed to help answer the critical pharmacological questions of academic and pharmaceutical industry scientists.
OrBiTo (drug delivery)	Completed a landmark study of existing physiologically based pharmacokinetic modelling (PBPK) tools to determine the most appropriate parameters for *in silico* prediction of drug absorption and plasma concentrations as a result of the uptake of a drug. Model-based drug development and regulation in the biopharmaceutics area will help to reduce the need for *in vivo* studies and improve the design of *in vivo* studies that are still needed. The gap analysis was performed jointly by 15 OrBiTo partners and included 43 active pharmaceutical ingredients (APIs) representing over 165 human studies, and over 600 human study arms.
OrBiTo (drug delivery)	Gained novel understanding of human gastro-intestinal physiology and its impact on drug formulation behaviour and drug absorption. The data showed highly variable gastrointestinal parameters even under clinical fasting conditions which must be considered when evaluating clinical studies and developing biorelevant *in vitro* tests. Ultimately, these results will enable the development and assessment of *in vivo* tools for better prediction of *in vivo* drug formulation and dosage behaviour.
PREDECT	Created the first successful xenografts of oestrogen receptor (ER+) breast cancer where the tumour cells are not under selection pressure to change

Project title	Description of result(s)
(cancer)	phenotype. Developed a standardised workflow for tumour tissue slice preparation and culture, using filter support in atmospheric oxygen. This enables the implementation of a robust and routine platform, so that multiple samples from the same tissue of origin or from different pathologies can be compared.
PreDiCT-TB (infectious diseases)	Individual patient level data continues to be received from data custodians with n=15 studies in-house.
StemBANCC (stem cells)	466 participants, including healthy people and people from several clinically-characterised disease cohorts (Alzheimer's, neuropathy, diabetes, Parkinson's, migraine and bipolar, autism, schizophrenia) have been recruited for reprogramming and production of induced pluripotent stem cells (iPSC) in order to produce models of human diseases. Some cells lines have already been fed into the EBiSC project and are part of the EBiSC catalogue.
SUMMIT (diabetes)	Developed and characterised two new diabetic mouse strains with altered insulin metabolism based on altering the expression of the sulfonylurea receptor (SUR) 1 with other metabolic genetic risk factors. The SUR1 model proved useful for studies on epigenetic modifications in the kidney.
SUMMIT (diabetes)	Rodent models of diabetic cardiovascular complications have been pharmacologically validated with standard of care compounds and negotiation for a licensing agreement with a commercial vendor has started to allow the commercialisation of one the models.
TRANSLOCATION (antimicrobial resistance)	Development of assays and tools to understand penetration of antibiotics in bacterial cells is a goal of TRANSLOCATION. Key examples are 1. uptake of fluorescent drugs on a single cell level via a synchrotron light source; 2. mass spec based intracellular bacterial accumulation assays; 3. permeation of charged compounds.

Development of biomarkers and tools predictive of clinical outcomes (efficacy and safety)

Project title	Description of result(s)
ABIRISK (drug safety)	Biopharmaceuticals can trigger an immune reaction in some patients, leading to the production of antibodies (ADAs) that neutralise the drug. ABIRISK identified age and sex as risk factors of anti-IFNbeta and anti-Natalizumab ADA development, something which had never been observed before. Scientists discovered that males and older adults are at a higher risk of developing an immune response when receiving the biopharmaceutical IFNβ. Females and older people are at a higher risk when receiving Natalizumab.
BioVacSafe (vaccines)	Investigated the role of neutrophils and other cell types in a mouse model of infection & immunisation, and showed that IFN-γ from brain leukocytes enhances meningitis by type 4 *Streptococcus pneumoniae* infection.
BioVacSafe (vaccines)	Defined molecular signatures in animal models both in whole blood and in skin that distinguish the safe live viral human vaccine (Varilrix) from upper inflammatory mediators such as Poly I:C and LPS.
BioVacSafe (vaccines)	Among numerous species used in the laboratory setting, only the ferret model is equally well suited for studying the pathogenicity and transmissibility of influenza viruses. The consortium generated real-time polymerase chain reaction (qPCR) reference reagents for the ferret studies, including unique genes that have been published on GenBank.

Project title	Description of result(s)
BTCURE (rheumatoid arthritis)	Uncovered a new mechanism which triggers rheumatoid arthritis, opening the way for the development of more targeted treatments. The researchers discovered that antibodies, which can be detected in the blood of some individuals years before disease onset, contribute to the development of the disease. These antibodies are able to induce joint pain and signs of bone loss before chronic inflammation in the joints occurs.
DDMoRe (knowledge management)	The value of modelling and simulation in reducing the cost of developing new drugs and improving the speed of the process can only be achieved by providing reproducible, qualified models to serve as a strong evidence base for regulatory submission and marketing approval. The DDMoRe framework has been developed to meet this important need for the Model-Informed Drug Discovery and Development (MID3) community.
DIRECT (diabetes)	Developed a remission prediction model for patients undergoing gastric bypass that consists of only 4 pre-operative parameters that provide higher prediction accuracy for remission at 3 months, compared to 9 logistic regression approaches that have previously been published for predicting remission 12 months after surgery.
DIRECT (diabetes)	Developed and partially validated a mass spectrometry-based targeted metabolomics assay for 45 eicosanoids and polyunsaturated fatty acids. It has been scaled up to high throughput format and fully validated according to FDA standards. This assay will allow the absolute quantification of type 2 diabetes relevant inflammatory/anti-inflammatory metabolites of all relevant oxylipin pathways.
DIRECT (diabetes)	Identified potential biomarker candidates based on a GWAS of 695 non-diabetic individuals: 13 loci of potential interest were identified as associated with tolbutamide-stimulated insulin secretion. Moreover, data from a proteomics study investigating 758 antibodies selected by the biomarker task force for DIRECT studies identified 23 antibodies that are significantly associated with measures of insulin secretion and or insulin sensitivity as measured with hyperglycaemic clamps.
EMIF-AD (Alzheimer's disease)	In a cross-sectional multicentre study, showed that cerebrospinal fluid levels of the soluble variant of the triggering receptor expressed on myeloid cells 2 (sTREM2) are a potential biomarker for microglia activity in early-stage Alzheimer's disease (AD) and associate with neuronal injury markers and thus could have value to mark the transition from preclinical AD to dementia.
EMIF-METABOLIC (metabolic syndromes)	Generated, approved and disseminated a standardised protocol to examine the natural history of liver safety biomarkers in industry clinical trial data and the covariates that affect them. This will facilitate the interpretation of liver safety signals in clinical trials, as well increasing the understanding of liver biomarkers as endpoints for non-alcoholic fatty liver disease (NAFLD).
EPAD (Alzheimer's disease)	Developed and presented to regulators (EMA) the EPAD Neuropsychological Examination (ENE) for assessing cognitive performance in people with preclinical and prodromal Alzheimer's disease, which will be a valuable tool for the evaluation of subjects in clinical trials for this challenging population.
EPAD (Alzheimer's disease)	Published a consensus statement on the recommended cognitive outcomes in preclinical Alzheimer's disease for use in both future drug trials and research into the area. To counteract the lack of evidence-based guidelines for measuring cognitive change in a preclinical population where the cognitive decline is 'silent' and occurring years before memory problems arise, the team has identified appropriate cognitive measures for use on preclinical population, based on both cognitive correlates of preclinical brain changes from imaging studies, and cognitive changes observed over time in non-dementia population cohorts developing incident

Project title	Description of result(s)
	dementia.
eTOX (drug safety)	Part of the project achievements in 2016 are the linkage of animal studies to human clinical safety outcomes
EU-AIMS (autism spectrum disorders)	The metabolic glutamate receptor 5 (mGluR5) radioligand FPEB has been validated for human use and will be used for the case control studies in Autism Spectrum Disorder (ASD) and typical subjects in addition to a rare discordant twin population.
EU-AIMS (autism spectrum disorders)	Studied as part of the Eurosibs cohort (www.eurosibs.eu) early sex differences in markers previously shown to relate to emerging autistic symptoms, finding sex-specific relationships with later autistic traits, with prediction to outcome in males but not in females. These data suggest that so-called early autism markers may only act as markers in boys.
EU-AIMS (autism spectrum disorders)	Examined more than 20 infants in one clinical centre for their light reflexes, and showed that infants at risk for autism had hypersensitive pupillary light reflexes. This result, if replicated in the larger Eurosibs cohort, may indicate an early behavioural risk marker for ASD.
EU-AIMS (autism spectrum disorders)	Approximately 600 individuals carrying either a predefined neuropsychiatric copy number variation (CNV), some other large or genic CNV, no CNV, or a point mutation in a gene of interest to autism or related neurodevelopmental disorders, have been recruited for neurocognitive assessment. For 129 individuals, this was followed by structural and functional magnetic resonance imaging (MRI), and a further 72 individuals were also scanned with diffusion tensor imaging (DTI). RNA sequencing is ongoing and approximately 285 individuals have so far been processed.
FLUCOP (vaccines)	In order to achieve the standardisation of assays to assess human influenza vaccines, put in place a toolbox comprising a biobank of clinical serum samples and appropriate protocols. The toolbox is accessible to the project partners.
iABC (antimicrobial resistance)	A collection of 1 018 cystic fibrosis (and bronchiectasis) pathogens, more than half of which have been collected during the project, and susceptibility testing of these micro-organisms against 9 antibiotics has been completed.
MIP-DILI (drug safety)	Demonstrated that the rho-kinase/myosin light chain kinase pathway plays a key role in the impairment of bile canaliculi dynamics induced by cholestatic drugs, paving the way to new predictive biomarkers of drug-induced cholestasis. Intrahepatic cholestasis represents a frequent manifestation of drug-induced liver injury; however, the mechanisms underlying such injuries are poorly understood and predictive biomarkers are not available.
PHARMA-COG (Alzheimer's disease)	Identified a harmonised multimodal biomarker platform for future clinical trials, including cognitive tests, imaging (Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET)), electroencephalography (EEG) and blood biomarkers useful for assessment of both symptomatic and drug-disease-modifying drugs
PHARMA-COG (Alzheimer's disease)	Demonstrated the translational usability of the multimodal battery in animals, healthy volunteers and patients
PreDiCT-TB (infectious diseases)	Fine-tuned a method that offers a much faster way to diagnose tuberculosis (TB) and has the potential to improve both the speed and effectiveness of preclinical and clinical TB trials. The method is based on measuring ribosomal RNA which is part of the structure of the organisms' protein synthesis machinery. The RNA is easy to detect even when there are very few organisms present, and unlike the DNA, it does not survive long after the bug is killed by antibiotics.
PreDiCT-TB (infectious diseases)	Further developed a test which can diagnose TB within 4 hours and therefore may contribute to the speeding up of the evaluation of new drugs. It also has the

Project title	Description of result(s)
	potential to improve clinical management of hard to treat patients by ensuring they receive the most appropriate treatment as early as possible.
QUIC-CONCEPT (cancer)	Elaborated an imaging biomarker (IB) roadmap for cancer studies which includes 14 key recommendations for accelerating the clinical translation of IBs, which highlight the role of parallel (rather than sequential) tracks of technical (assay) validation, biological/clinical validation and assessment of cost-effectiveness; the need for IB standardisation and accreditation systems; the need to continually revisit IB precision; an alternative framework for biological/clinical validation of IBs; and the essential requirements for multicentre studies to qualify IBs for clinical use.
RAPP-ID (infectious diseases)	Completed 2 early-stage prototypes of platforms for point of care testing, as a major step towards the development of diagnostic tests for use in the clinical setting. Influenza breath sampler a rapid (<30 min), highly sensitive, qualitative breath-based test detecting influenza. The platform features a breath sampler, capable of collecting viral particles from exhaled breath into a tube containing a lysing buffer, which improves patient comfort over the use of nasopharyngeal swabs, which is the standard of care. VAP NA-POCT (Ventilator associated pneumonia nucleic acid point of care test) a highly multiplexed molecular platform capable of detecting rapidly (<2 hours) the most important pathogens and resistance markers related to ventilator associated pneumonia (VAAP) from a clinical sample (up to 2 ml endotracheal aspirate of sputum).
SUMMIT (diabetes)	Identified several genetic and epigenetic factors influencing the development of diabetic kidney disease both in type 1 and type 2 diabetes patients.
SUMMIT (diabetes)	Identified a panel of six biomarkers with improved prediction of type 2 diabetic cardiovascular disease (CVD) over and above clinical covariates, to improve prediction and thus facilitate selection of patients for enrolment in clinical trials.
SUMMIT (diabetes)	Evaluated the performance of a large set of serum biomarkers for the prediction of rapid progression of chronic kidney disease (CKD) in patients with type 2 diabetes, and identified several novel associations of biomarkers with CKD progression and the utility of a small panel of biomarkers to improve prediction and thus facilitate selection of patients for enrolment in clinical trials.
SUMMIT & DIRECT (diabetes)	Identified a genetic variant of the glucose transporter gene SLC2A2 that affects how well a type 2 diabetes patient responds to the drug metformin. In addition, showed that the genetic variant had a stronger effect in overweight people. These results indicate the potential of the genetic allele as a biomarker for stratified medicine.
WEB-RADR (pharmacovigilance)	Collected public social media posts mentioning 118 products analysed them to determine whether this approach can aid monitoring drug safety.

Clinical trials - improved design and process

Project title	Description of result(s)
AETIONOMY (Alzheimer's disease and Parkinson's disease)	A total of 165 individuals (124 Parkinson's disease (PD) patients and 41 controls) have been already recruited in the PD part of the clinical study, while recruitment for the Alzheimer's disease part is now leveraged with EPAD with 31 research participants already recruited.
COMBACTE-CARE (antimicrobial	Initiated the EURECA study, a prospective observational studies to assess the risk factors, clinical management and outcomes of patients with multidrug-resistant

Project title	Description of result(s)
resistance)	Gram-negative bacteria infections, and to inform the development programmes for new antibiotics. The first patient was enrolled at the end of April 2016, and more than 200 patients (out of the 2 000 planned) have now been recruited in over 20 sites, mainly in Central and Eastern Europe.
COMBACTE-CARE (antimicrobial resistance)	Initiated the REJUVENATE study, with the first patient enrolled in May 2016. REJUVENATE is a prospective, open-label, multicentre, phase IIa study to determine the pharmacokinetics, safety and tolerability of the combined compound aztreonam-avibactam (ATM-AVI) in hospitalised adults with complicated intra-abdominal infections . Selected a partner in the consortium to become the academic research organisation (ARO), for providing support to study operations of the REJUVENATE study, which is a premiere across the ND4BB programme and innovative for industry-sponsored studies using experimental drugs.
COMBACTE-MAGNET (antimicrobial resistance)	Completed the recruitment phase of the RESCUING study, a retrospective observational study to assess the clinical management and outcomes of hospitalised patients with complicated urinary tract infections (cUTI) in European countries with a high prevalence of multidrug resistant Gram-negative bacteria (the first patients were enrolled in late December 2015). The analysis is now ongoing on a total of 1 009 evaluable cases collected from 20 sites across 8 countries (i.e. Bulgaria, Greece, Hungary, Israel, Italy, Romania, Spain and Turkey). Published the study protocol in the BMJ on 29 July 2016: BMJ Open 6:e011500 doi:10.1136/bmjopen-2016-011500.
COMBACTE-MAGNET (antimicrobial resistance)	Enrolled the first patients in the EVADE study, a phase 2 proof-of-concept safety and efficacy of MED13902, a monoclonal antibody in mechanically ventilated subjects at high risk of developing *Pseudomonas aeruginosa* pneumonia. Over 10 patients already randomised and dosed.
COMBACTE-MAGNET (antimicrobial resistance)	Launched the activities of EPI-NET, the epidemiological network, with first engagement with experts from academia, public health experts, and health research foundations as well as ND4BB leads to discuss the development of an effective, coherent epidemiology strategy, and organise pertinent expertise and available data sources in Europe and across ND4BB in support of public health and drug development priorities related to antimicrobials. Three systematic reviews completed and results under analysis: EMBARGO (*EpideMiology of outBreaks due to Antibiotic-Resistant orGanisms in EurOpe*), examining outbreaks of antibiotic resistance within Europe (in collaboration with DRIVE-AB). SURVAIL (*SURVeillance of Antimicrobial resistance in anImal and food*) describing national and supra-national surveillance programmes and networks that collect data regarding antimicrobial resistance of bacterial isolates from livestock, and their meat in slaughterhouses and at retail outlets in Europe. SUSPIRE (*SUrveillance Systems from Public health Institutions and scientific societies for Antimicrobial resistance and healthcare-associated infections in Europe*) assessing active surveillance activities endorsed by national or transnational health organisations and scientific societies in EU/EAA, that provide regular data on frequency and/or distribution and/or determinants (contextual, patient, molecular/pathogen) of HAI and AMR outside the ND4BB programme.
COMBACTE-NET (antimicrobial resistance)	Completed the open call procedure launched in March 2015 to identify potential replacement antimicrobial agents or approaches developed by EFPIA companies further to the early termination of development of GSK1322322. As a result, three proposals were selected and included in the project, two of them from new companies that have joined the consortium, Da Volterra and The Medicines Company. The third proposal concerns an additional clinical study with the MedImmune agent MEDI4893.

Project title	Description of result(s)
COMBACTE-NET (antimicrobial resistance)	Enrolled the firsts patients in the ANTICIPATE study, an observational study that aims to determine the incidence of *Clostridium difficile* infections in hospitalised patients on antibiotic treatment. For this study, 30 qualified clinical sites in 6 European countries have been selected and the project plans to enrol a total of 1 000 hospitalised patients aged ≥50 years old and undergoing predefined antibiotic treatment. This study will be used to design phase III randomised controlled trials (RCT) of DAV132, a product developed by Da Volterra, a new partner in COMBACTE-NET.
COMBACTE-NET (antimicrobial resistance)	First patient first visit for the ASPIRE-SSI study. This is a prospective, observational, multicentre cohort study to assess the incidence of *Staphylococcus aureus* infections and its associated risk factors in the surgical patient population, particularly surgical site infections caused by *S. aureus*. More than half of the sites have already been selected (planned in approximately 20 sites across 10 European countries in a total of 5 000 patients of 18 years of age and older undergoing pre-selected surgical procedures).
COMBACTE-NET (antimicrobial resistance)	Ongoing active enrolment of patients in the ASPIRE-ICU study, a prospective, observational, multicentre, cohort study nested within routine surveillance among ICU patients in Europe aimed at estimating the incidence of *S. aureus* and *P. aeruginosa* ICU-acquired pneumonia and assessing its association with patient-related and contextual factors (out of the 2 000 patients planned more than 15 % already recruited). More than 25 sites across over 10 European countries have been selected to participate in the ASPIRE-ICU study.
COMBACTE-NET (antimicrobial resistance)	More than 100 patients (out of the 450 planned) already randomised in the SAATELLITE study, a phase 2A randomised, double-blind, placebo-controlled, single-dose, dose-ranging study of the efficacy and safety of MEDI4893, a human monoclonal antibody against *S. aureus* toxin alpha in mechanically ventilated adult patients. Out of 93 sites selected in 9 countries (Belgium, Germany, France, Spain, Greece, Hungary, Czech Republic, United Kingdom, Switzerland), more than half are already opened and are randomising patients.
COMBACTE-NET (antimicrobial resistance)	Ongoing setting up of CLIN-NET and LAB-NET networks, including meetings with sites/investigators/national coordinators to further consolidate the local network and role of National Coordinators 5 country visits (including a general programme with the national coordinator(s), CLIN-Net and LAB-Net investigators followed by visit of the clinics and lab sites) (Greece, Bulgaria, Italy, Portugal and Hungary) 2 meetings of the CLIN-Net national coordinators ▪ 1 face to face Good Clinical Practices (GCP) training of the investigators in addition to availability of the online GCP courses (training developed in collaboration with EFGCP and PharmaTrain accredited and Transcelerate compliant). 1 LAB-NET workshop with microbiologists organised in Albania ▪ 1st meeting organised with the LAB-NET national coordinators
EHR4CR (knowledge management)	Developed a robust and scalable platform that can utilise de-identified data from hospital EHR systems to plan clinical trials and facilitate on-time recruitment, in full compliance with the ethical, regulatory and data protection policies and requirements of each participating country. Platform has been implemented in 11 hospital sites
EPAD (Alzheimer's disease)	In less than 6 months, the Longitudinal Cohort Study (LCS) has already screened 76 and enrolled 71 research participants over four sites in Europe. This result shows that the recruitment system for the LCS drastically reduces time to recruit and screening failures leading to a significant reduction in the costs for trials in pre-clinical Alzheimer's disease.

Project title	Description of result(s)
EU-AIMS (autism spectrum disorders)	Enrolled 341 high-risk (HR) and 155 low-risk (LR) infants in Eurosibs, which exceeds the target of 300 HR and 100 LR infants. A subgroup of more than 40 infants has been scanned (foetal, neonatal, and/ or infant magnetic resonance imaging (MRI) scan).
EU-AIMS (autism spectrum disorders)	The Longitudinal European Autism Project (LEAP) has completed recruitment and assessment of the baseline cohort reaching/ exceeding the target number with an overall N of 756 (target: 727).
EU-AIMS (autism spectrum disorders)	Significantly expanded the clinical network, which currently includes 93 sites across 37 European countries. The database compiles clinical data of over 7 000 individuals with Autism Spectrum Disorder. Sites that are equipped to conduct clinical trials have been identified and information on patient characteristics, measures used etc. has been compiled.
EUROPAIN (pain)	Analysed the project clinical database of neuropathic pain patients (the largest available) including sensory phenotypes supports sensory clusters have more in common than aetiologies. The results provide segmentation and stratification tools useful for clinical trials.
EUROPAIN (pain)	Based on the analysis of placebo data from 9 industry phase III trials in 2017 adult patients suffering from chronic pain, determined that patients' perception of treatment allocation and expectations toward treatment efficacy could potently predict outcomes of randomised clinical trials. These results are valuable for the optimisation of clinical trial design in order to minimise and understand placebo effects
GetReal (relative effectiveness)	Published the final case study reports, performed in 5 disease areas (multiple sclerosis, non-small cell lung cancer, rheumatoid arthritis, chronic obstructive pulmonary disease, metastatic melanoma). The final reports incorporate outcomes of workshops that were held bringing together stakeholders to discuss the use of real-world evidence for demonstrating the effectiveness of new drugs.
GetReal (relative effectiveness)	Prepared research and policy recommendations on the use of real world evidence (RWE) in drug development and stakeholder decision making in addition to recommendations around the use of the research tools, key outputs of simulation studies and methodological recommendations generated by the consortium.
GetReal (relative effectiveness)	Developed a framework as a web-based navigator tool online platform designed to: ▪ guide medicine development strategy/ evidence of relative effectiveness generation strategy; ▪ provide a methodological platform to provide options for study designs and analytical approaches; ▪ guide users towards more detailed material and case studies reported by each GetReal work packages; ▪ direct users to authoritative external guidance and sources.
GetReal (relative effectiveness)	Developed the pilot PragMagic tool as a decision support tool that helps in the design and planning of pragmatic trials, giving insights to the consequences of design choices and allowing users to visualise the interplay between the various design options, operational challenges and implications.
GetReal (relative effectiveness)	Developed a toolbox of methodological guidance and best practice recommendations for (aggregate and individual patients' data) evidence synthesis and predictive modelling of effectiveness methods for network meta-analysis. Also released a new version of the software tool ADDIS - an evidence-based decision support system for conducting evidence synthesis and predictive modelling of effectiveness
iABC (antimicrobial	FDA and EMA have agreed on a revised study design proposed by the iABC Trial Steering Committee for the Phase 2 clinical study with the Novartis Tobramycin

Project title	Description of result(s)
resistance)	inhaled powder (TIP) in bronchiectasis patients. All clinical sites have been selected and health authority and ethics committee approvals were received as planned in 7 out of 8 countries.

'Big data' solutions & data standards to leverage knowledge

Project title	Description of result(s)
DDMoRe (knowledge management)	Interoperability framework: 3 DDMoRe standards – MDL, PharmML and the SO provide a consistent environment in which researchers can work, using modelling tools they know, while opening up their work to others through a standard language for describing models. New open source platform that allows researchers to simply and reliably share drug and disease models with one another launched.
DRIVE-AB (antimicrobial resistance)	Achieved international and multidisciplinary consensus on a global definition of responsible antibiotic use; consensus also achieved on quality indicators and quantity metrics for the inpatient and outpatient setting. Largest existing database of antimicrobial resistance spanning 22 years and 68 countries has allowed completion of two systematic reviews on spread and impact of antimicrobial resistance, and informed the design of two agent-based models, one of transmission of resistant bacteria in hospitals and one of regional resistant bacterial spread.
EHR4CR (knowledge management)	The EHR4CR Common Information Model (CIM) standard has allowed the searching of 11 hospital sites to recruit patients for clinical research.
EMIF (knowledge management)	TranSMART improvements: cross-cohort analysis, omics data analysis pipelines integration and further analytical tools developed that can interact with it to support cohort work from the research topics
EMIF (knowledge management)	Mapped a selection of data sources into the OMOP Common Data Model to evaluate feasibility and further integration of OHDSI tools into the Platform
EMIF-AD (Alzheimer's disease)	Harmonised 6 cohorts that are now available in tranSMART, with 60 priority variables defined for which cross-cohort analyses can be performed, thus providing means for large-scale pooled analyses.
EMIF-AD (Alzheimer's disease)	Included the first 124 cognitively normal subjects in the preclinical Alzheimer's disease (AD) cohort study, with subjects undergoing deep phenotyping of a range of cognitive and clinical biomarkers. A sub-group of subjects are monozygotic twins, and this is the first cohort study on AD biomarkers in twins.
eTOX (drug safety)	Data from over 7 000 previously unused industry animal toxicology studies were combined and analysed to produce 80 models that help predict the toxicity of a drug candidate based on its chemical structure.
eTOX (drug safety)	OntoBrowser provides an online collaborative solution for expert curators to map code list terms (sourced from multiple systems/databases) to preferred ontology terms. freely available under the Apache v2.0 license
eTRIKS (knowledge management)	eTRIKS is currently engaging 40 projects and exploring immediate engagement opportunities with a further 8 projects.
eTRIKS (knowledge	Standardised 80 studies pertinent to IMI research interests and stored them on the eTRIKS servers.

Project title	Description of result(s)
management)	
EU-AIMS (autism spectrum disorders)	Collected and bio-banked patient and control hair samples (currently exceeding 400 samples) for future reprogramming to inducible pluripotent stem cells (iPSCs).
EUROPAIN (pain)	Created the largest available clinical database of human volunteers and neuropathic pain patients – 3 500 individuals, with linked DNA blood sample bank and skin biopsies.
iABC (antimicrobial resistance)	Established data coordinating centre to support the EMBARC (European Multicentre Bronchiectasis Audit and Research Collaboration) European Bronchiectasis Registry. Achieved aligned set of data fields agreed between EMBARC, the US COPD foundation and the Lung Foundation of Australia. All European collaborators of EMBARC will use same electronic case report form, which was successfully deployed to stakeholders. The target recruitment of the European Bronchiectasis Registry rate was exceeded, with more than 4 000 patients enrolled into the study from 25 countries.
Open PHACTS (knowledge management)	An updated version of the Open PHACTS application programming interface (API) was released in May which added standardised patent data, as well as completely refreshing chemistry data, thereby allowing researchers free access to a large, rich pharmacology data set.
PREDECT (cancer)	ClustVis is a publicly available web tool for exploratory data analysis / a web tool for visualising clustering of multivariate data (BETA).
PreDiCT-TB (infectious diseases)	PreDiCT-TB collaborated with eTRIKS to curate their data into the tranSMART knowledge management platform, thereby ensuring their data is in a standardised format for reuse.
StemBANCC (stem cells)	Collaborated with the International Society for Stem Cell Research (ISSCR) and contributed to the Research Guidelines for Stem Cell Research and Clinical Translation, which was announced in May 2016.
SUMMIT (diabetes)	Delivered the largest dataset of optical coherence tomography (OCT) measurements with longitudinal follow-up to date (multi-centre study, 1 320 study subjects completed) for the study of diabetic retinopathy.
WEB-RADR (pharmacovigilance)	Developed / applied English, French and Spanish dictionaries to map colloquial phrases commonly used in social media to 500 MedDRA preferred terms (PTs).

Impact on regulatory framework

Project title	Description of result(s)
ADVANCE (vaccines)	Finalised the ADVANCE code of conduct for benefit-risk monitoring of vaccines and submitted it for publication.
DDMoRe (knowledge management)	Held 2.5-day training courses on some of the new tools developed within DDMoRe were held for FDA regulators in Washington DC on Oct 7-9, 2015 and for EMA/EU regulators in Uppsala, March 1-3, 2016. In conjunction with the latter course, a separate meeting between DDMoRe members and regulators took place.
DRIVE-AB (antimicrobial resistance)	Completed a detailed review of health technology assessment (HTA) for antibiotics across Europe and presented the results at the Society for Medical Decision Making.

Project title	Description of result(s)
EBiSC (stem cells)	Approved cell line process workflow procedures and policies according to Quality Management system (DIN EN ISO 9001:2015).
EPAD (Alzheimer's disease)	Submitted for Scientific Advice to the European Medicines Agency (EMA) the Longitudinal Cohort Study (LCS) protocol and briefing document. Positive, constructive feedback has been received and used to fine tune the study.
EUROPAIN (pain)	Provided comments and inputs that have been integrated into the new EMA Guideline for the development of new treatments for pain (approved 15 December 2016)
OrBiTo (drug delivery)	Collaborating with regulatory agencies in Europe and the US on how the new tools being investigated in OrBiTo could be applied in future regulations.
PROactive (respiratory disease)	The EMA qualification of novel methodologies of medicines development procedure is ongoing. The consortium has submitted an updated data analysis for the validation of daily and clinical visit PROactive physical activity (PA) in COPD instruments (D- and C-PPAC), which includes 1 083 patients with COPD from clinical trials performed by the academic consortium partners (*Mr PAPP study and Rehabilitation study*) and by EFPIA companies (*ExOS to some extent and PHYSACTO*). Of the 1 083 patients; 723 were used for analyses of the daily patient reported outcomes (PROs), and 636 patients for the clinical visit version. Three studies investigated the responsiveness of the tool: the PHYSACTO study, conducted by Boehringer Ingelheim; the MrPaPP study run by 6 PROactive academic centres; and one single centre study conducted in Greece in the context of pulmonary rehabilitation. Further cross-sectional data were collected from clinical trial run by Chiesi, the COPDMAP consortium ExOS study (supported by GSK) and a trial supported by AstraZeneca. Another set of cross-sectional data (follow-up at one year pending) was provided through a collaboration with CREAL, the PROactive partner in Barcelona. The consortium has determined a total score to capture a single concept: physical activity (PA) experience, constructed as the mean of the amount and difficulty score and scored from 0 to 100, with better scores expressing better PA experience. The data generated confirmed the reliability, validity and responsiveness of the single score that provides insight into the evaluation of the driver of change in PA experience (i.e. either amount or difficulty).
PROactive (respiratory disease)	PROactive tools are already available for use by any sponsor under a formal licensing agreement accompanied with a comprehensive user manual. (Daily Patient Report Outcomes tools (D-PPAC) are available in 62 languages and the clinical visit PRO (C-PPAC) is available in 14 languages).
PROactive (respiratory disease)	A patient panel webinar was organised to get final input on the PROactive tools, ensuring that these tools are indeed capturing domains and items relevant to people suffering from COPD.
SAFE-T (drug safety)	Identified four liver safety biomarkers that can be measured in human serum. Both FDA and EMA acknowledged that higher levels of these biomarkers in patients diagnosed with drug-induced liver injury could indicate a risk for progression towards liver failure. In addition, EMA considered results for four other serum biomarkers promising in terms of possibly improving early prediction of liver injury in clinical trials.
SAFE-T (drug safety)	Among the safety biomarkers studied, 20 showed promising performance. The data on some of these biomarkers has been submitted to the

Project title	Description of result(s)
	European Medicines Agency and the US Food and Drug Administration and the agencies issued a Letter of Support for the biomarkers targeting liver injury. The Letters of Support indicate that the new biomarkers have the potential for use in drug development.
SPRINTT (geriatrics)	Analysed economic burden of frailty based on community-dweller population aged 65 years old or more in 2012 in France. The results indicate that frailty as a progressive condition has an incremental effect on ambulatory health expenditures of roughly €570 additional euros for pre-frail individuals, and €1 270 for frail individuals.
SPRINTT (geriatrics)	Performed the first economic analysis of physical frailty and sarcopenia. This demonstrated that wealthier older people have a lower propensity to become frail than more deprived people, and once frail, the wealthier are less likely to become dependent and more likely to recover.
WEB-RADR (pharmacovigilance)	Launched Dutch and Croatian versions of the WEB-RADR smartphone app that allows patients, carers and healthcare providers can use to report side effects of medicines directly to the national regulators. In addition, users can set up alerts to receive the latest information on specific medicines.

Implementation of project results inside industry

Project title	Description of result(s)
CHEM21 (green chemistry)	Developed a rapid, simple method to synthesise the World Health Organization (WHO) Essential Medicine flucytosine, an anti-fungal. The technology involved has been patented by the project and will be further pursued within industry
DDMoRe (knowledge management)	The Interoperability Framework which allows researchers to collaborate on computer model development has been implemented in 3 companies
DRIVE-AB (antimicrobial resistance)	Developed a preliminary list of the most promising rewards models and presented it to stakeholders representing large and small pharmaceutical companies, product development partnerships, academia, the public health sector and civil society.
EBiSC (stem cells)	White paper versions compiled on business case for self-sustainability on not-for-profit provision to research community of cell lines/data based on surveyed demand. IP landscape reviews. Cell line pricing policies.
EBiSC (stem cells)	Research data on cell line phenotypes used by SME partners for business development.
EHR4CR (knowledge management)	The spin-off organisation, European Institute for Innovation through Health Data (i~HD), maintains the projects results for the industry participants and also aims to expand the hospital network in 2017 and beyond.
eTOX (drug safety)	The toxicology database and models developed within the project have been implemented in all 13 industry partners. According to industry researchers, eTOXsys models can be used to prioritise compounds for further experimental investigations, and the search results have changed the way they communicate about safety hypotheses.
eTRIKS (knowledge management)	An SME specialising in cleaning, filtering, hosting and standardising data in the pharmaceutical sector was built on the knowledge and expertise gained during the eTRIKS project.

Project title	Description of result(s)
ELF (drug discovery)	17/49 EFPIA partner screens have triggered further work. 12/14 of the public target programmes offered to the EFPIA have been invited to provide a dossier for further assessment.
K4DD (drug discovery)	The results of the project are now being integrated in the drug discovery research pipeline, with some EFPIA companies implementing kinetic aspects in the hit finding phase and others in the lead optimisation phase. The project results should have a serious impact on attrition rates in drug discovery and the time to reach clinical proof of concept in the future.
OncoTrack (cancer)	Animal and cell culture models created by the project are in use for drug screening by EFPIA partners. Several EFPIA partners are also using genomic data generated by the consortium in their research organisations.
Open PHACTS (knowledge management)	A 'virtual machine' version of Open PHACTS was developed to allow industry to use the system inside their firewalls without fear of leakage of confidential data. This virtual machine also allows companies to integrate their own data and strengthen its capabilities.
PREDECT (cancer)	Bioreactor-based 3D tumour cell models have been implemented at AbbVie, Boehringer Ingelheim, AstraZeneca and EPFL (tech transfer from iBET of methodologies developed within the scope of PREDECT).
PreDiCT-TB (infectious diseases)	*Mycobacterium tuberculosis* reporter strains have been successfully tech-transferred to an EFPIA company
StemBANCC (stem cells)	A spin out from Newcastle University has been created (Newcells Biotech). It provides services and products based on iPSC technology for drug discovery and toxicity testing activities of academic and industrial customers. The company is close to the infrastructure developed under the StemBANCC project for reprogramming.
StemBANCC, EBiSC (stem cells)	Reached agreement over the contract terms on the induced Pluripotent Stem Cells (iPSCs) ownership between StemBANCC and EBiSC to secure the sustainability of StemBANCC lines.
TRANSLOCATION (antimicrobial resistance)	Industry partners are currently using assays to determine whole cell uptake passage through porins or other channels that were developed through the project.
ULTRA-DD (drug development)	At least one of the collaborating pharma companies has launched an effort to generate compounds suitable for clinical trials in glioblastoma (PRMT5 inhibitor program) based on the project results.

Education and training for a new generation of R&D scientists

Project title	Description of result(s)
CANCER ID (cancer)	During the yearly CANCER-ID General Assembly Meetings there is a dedicated session where young scientists are encouraged to present their work to train/enhance their presentation capabilities. Young Scientists are being offered courses and workshops to increase their technical know-how, enable networking and improve project management skills.
CHEM21 (green chemistry)	Launched a new online training platform comprising a range of free, shareable, and interactive educational and training materials created to promote the uptake of green and sustainable methodologies, with a particular focus on the synthesis of pharmaceuticals. CHEM21 partners and external experts edited and wrote a book 'Green

Project title	Description of result(s)
	and Sustainable Medicinal Chemistry: Methods, Tools and Strategies for the 21st Century Pharmaceutical Industry', which was published by the Royal Society of Chemistry (RSC). The book addresses current challenges in modern green chemical technologies and sustainability thinking, and encompasses a broad range of topics covered by the CHEM21 project. Held a themed workshop and symposium on 'Practical Aspects of Green Chemistry in the Pharmaceutical Industry'.
DDMoRe (knowledge management)	8 tutorials on building and uploading models. Six one-week face-to-face courses were held for participants from academia and industry. One day workshops have been held at three conferences. On-line training material has been made available.
DRIVE-AB (antimicrobial resistance)	Held a train-the-trainer workshop on indicators and metrics of responsible antibiotic use in inpatient and outpatient settings. Workshop targeted antimicrobial stewardship experts from 20 different European countries and was filmed. Podcasts freely available online as an educational resource.
EBiSC (stem cells)	Training course on 'Differentiation of iPS cells into neuron and cardiomyocyte lineages' organised in the high quality EBiSC central stem cell laboratory facilities on 23-25 November 2016 at Roslin BioCentre in the UK. The event brought together the extensive expertise of the EBiSC project partnership from across Europe. It provided hands on training and workshop activities in stem cell technology relating to the culture and differentiation of pluripotent stem cell lines into cardiac and neural cell types and their functional characterisation.
EBiSC (stem cells)	The EBiSC 'Derivation and culture of human induced pluripotent stem cells' practical training course and workshop took place on 23 – 25 May 2016 at the University of Hertfordshire, UK. The course comprised lectures and 'wet lab'.
EHR4CR (knowledge management)	The inaugural conference of the European Institute for Innovation through Health Data (i~HD) was held.
ELF (drug discovery)	>75 academic postdoctoral fellows trained in industry methods and approaches. 2 PhD theses enhanced with ELF target programme assay development and screening results.
EMTRAIN (education and training)	The on-course resource centre now has approximately 7 700 entries with 3 627 masters Programmes, 3 787 continuing professional development (CPD) courses and 1 157 PhD programmes (www.on-course.eu).
EMTRAIN (education and training)	Use of the on-course resource centre has increased and now exceeds 1 500 visits per week (equates to more than 75 000 per year). The on-course database was expanded to include courses on transferable skills, e.g. leadership, management, financial control, project management, change management and negotiating skills. IMI courses from EU2P, SafeSciMET, PharmaTrain, CHEM21 and EUPATI included in on-course
EMTRAIN (education and training)	Published the background and framework documents - LifeTrain: towards a European framework for continuing professional development in biomedical sciences, and LifeTrain driving lifelong learning for biomedical professionals.
EMTRAIN (education and training)	28 students attended the fifth EMTRAIN public-private-partnership PhD workshop. The theme was 'innovative approaches to address unmet needs in common and rare diseases'.

Project title	Description of result(s)
EMTRAIN (education and training)	The Horizon 2020-funded projects RItrain, CORBEL and BioExcel are all developing competency profiles based on the initial LifeTrain principles.
ENABLE (antimicrobial resistance)	Implemented earlier stage education and consultative support to owners of potential new discovery programmes, particularly from academic groups, via webinars and consultative exchanges to support programmes with limited data gaps for entry into the project.
eTRIKS (knowledge management)	eTRIKS provided training to over 30 scientists across 5 projects with a recorded webinar on data security widely used in new projects before access is granted to project data. Training topics included eTRIKS data curation, data standards, ETL procedures and upload as well as information security, data analysis and tranSMART training. eTRIKS engaged over 40 patients and patient advocates, including physicians and politicians, during two conference events using a specially developed multi-stakeholder scenario-based interactive game (Play/Decide) to encourage better understanding, discussion and feedback regarding the use of patient data for subsequent medical research.
EU2P (education and training)	Masters courses 17 candidates selected for the fourth Master year 1 intake. 38 candidates selected for the fifth Master year 2 intake. 9 Master year 2 trainees awarded the joint EU2P Master of Science in Pharmacovigilance and Pharmacoepidemiology.
EU2P (education and training)	Certificates 59 candidates selected for certificate intake. 55 Certificate trainees awarded the joint Eu2P Certificate in Pharmacovigilance and Pharmacoepidemiology.
EU2P (education and training)	281 students submitted an online application to participate in courses.
EU2P (education and training)	PhD 7 trainees pursued their PhD curriculum on their 3rd year of research and study.
EU2P (education and training)	Increased proportion of students from outside the EU to 47% of total intake. 15% of trainees come from countries such as defined as low and low-middle income by the World Bank.
EU2P (education and training)	9 partners (5 academic and 4 pharmaceutical companies) have signed a MoU to continue their cooperation beyond the lifetime of the IMI funding and continue to deliver the Masters, Certificate and Short courses.
EUPATI (education and training)	Trained 98 patient experts in its Patient Expert Training Course, and has reached out to more than 65 000 individuals through its online EUPATI Toolbox on Medicines R&D.
EUPATI (education and training)	Generated educational resources for the lay public, patients and patient advocates in six key areas: ▪ Discovery of Medicines & Planning of Medicine Development ▪ Non-Clinical Testing and Pharmaceutical Development ▪ Exploratory and Confirmatory Clinical Development ▪ Clinical Trials ▪ Regulatory Affairs, Medicinal Product Safety, Pharmacovigilance and Pharmaco-epidemiology ▪ HTA principles and practices Material has been developed in English, German, Spanish, Polish, French, Russian and Italian, and the resources are also being translated into

Project title	Description of result(s)
	Danish, Dutch and Romanian. There are national platforms in 18 European countries (AT, FR, DE, IE, IT, LU, MT, PL, ES, CH, UK, DK, SK, PT) with additional platform initiatives ongoing in NO, GR, RU, SRB, BE. The project addresses three audiences. The 'Expert Level' has been served with two EUPATI Patient Expert Training Courses for patient experts, patient ambassadors and patient journalists. Advocacy leaders from patients' organisations have been addressed on the 'Education Level' through EUPATI Toolbox (available via open access via www.eupati.eu). This will include a diverse range of cutting-edge resources such as texts, illustrations, webinars, videos, slide shows in more than 3500 content items. Finally, all patients and the wider public have access to the EUPATI Internet Library, which guides patients, including those with relatively low health literacy, through the complexities of the pharmaceutical R&D process.
EUPATI (education and training)	Developed guidance documents on the interactions of patient organisations with (1) industry (2) regulators (3) HTA bodies and (4) ethics Committees. www.eupati.eu/guidance-patient-involvement/
EUROPAIN (pain)	Investigators were trained and laboratories certified to perform standardised quantitative sensory testing (QST) assessments, 284 investigators since 2008, ready to be involved in drug development programs. Homogeneity of results across laboratories was demonstrated.
GetReal (relative effectiveness)	Series of 4 webinars organised by the consortium around the themes of relative effectiveness and how it can best be integrated into drug development. Presentation to stakeholders on the key outputs of the different work packages of GetReal with the purpose of educating but also receiving feedback and stakeholder perspectives to further align outputs with the needs of final users.
GetReal (relative effectiveness)	Release of the updated glossaries with definitions of key terms related to real-world both for the purpose of GetReal, and also with the aim of providing clarity to external stakeholders around these terms.
GetReal (relative effectiveness)	Initial pilot of an online training course intended to increase knowledge and skills of participants around real-world evidence, with a particular emphasis on the connection between methodology development and practical applications within companies, regulatory agencies and HTA bodies.
K4DD (drug discovery)	K4DD has offered multiple full PhD positions and multi-year positions for Post docs. The education program which has run during the whole K4DD project has offered a wide range of additional training experiences ranging from Career Workshops, multi day drug discovery course, cross partner internships, networking workshops and a scientific writing course. 25 PhDs and Post-Docs
OncoTrack (cancer)	Postdoctoral fellows, graduate students enrolled in PhD programmes and students enrolled in Masters programmes are trained in the frame of this project
Open PHACTS (knowledge management)	Held a series of public webinars including: ▪ Integrating private and public data with Open PHACTS Open source software components for chemistry standardisation
PREDECT (cancer)	PhD students were trained in the frame of this project
SafeSciMET (education and training)	Completed the final 7 courses to complete the third course cycle of SafeSciMET. 84 participants attended attend these courses (a total of 230 people

Project title	Description of result(s)
	participated in the third course cycle completed in 2016 with 52% of attendees coming from industry, 37% from academia and 9% from regulatory agencies). The geographical distribution of attendees increased in the third cycle courses with attendees coming from 34 different countries.
SafeSciMET (education and training)	Developed 2 new pilot courses using blended learning and e-learning facilities in collaboration with the IMI project EU2P.
TRANSLOCATION (antimicrobial resistance)	Roughly 15 PhD and 30 post-docs are involved in the TRANSLOCATION project. This is an excellent training setup due to the multidisciplinary nature of the project and the opportunity to interact with researchers at different institutions, including big pharma.
U-BIOPRED (respiratory disease)	Published a short guide to successful patient involvement in EU-funded research.

IMI2 projects

Identification and validation of new drug targets and novel hit and lead discovery

Project title	Description of result(s)
INNODIA (diabetes)	Discovered novel beta cell targets of the early autoimmune attack in diabetes (citrullinated proteins and splice variants).

Establishment of robust, validated tools for preclinical drug development

Project title	Description of result(s)
INNODIA (diabetes)	Developed a robust method for large-scale production of 3-dimensional islet-like aggregates from human pluripotent stem cells. These have a high content of insulin- and glucagon-positive cells and are able to respond to physiological and pharmacological stimuli.

Development of biomarkers and tools predictive of clinical outcomes (efficacy and safety)

Project title	Description of result(s)
EbolaMoDRAD (Ebola and related diseases)	Developed a way to inactivate the Ebola virus in blood samples so they can be safely processed in the field or easily transported to other centres without the need for high containment facilities.
FILODIAG (Ebola and related diseases)	Patent application covering superparamagnetic particles which are used to speed up the diagnosis of Ebola.
INNODIA (diabetes)	Discovery of miRNA's that regulate human pancreatic beta cell death in diabetes.
INNODIA (diabetes)	Identified Interferon-alpha as a key regulator of early markers of beta-cell dysfunction/death in human diabetes, suggesting this inflammatory cytokine could be a target for novel clinical interventions to prevent diabetes.
INNODIA (diabetes)	Developed and progressing with validation of an oral vaccination strategy for type 1 diabetes prevention.
INNODIA (diabetes)	Development of a dry blood spot method for C-peptide measurement in the home setting.
MOFINA (Ebola and related diseases)	Device designed to test for the Ebola virus and other related Filo viruses has been successfully tested in three European reference labs and has also passed initial field studies in Sierra Leone. The device is now ready for product registration and the data obtained from lab and field tests is being submitted to the regulatory authorities
VSV-EBOVAC (Ebola and related diseases)	A series of new biomarkers of VSV-ZEBOV vaccination were identified.

Clinical trials - improved design and process

Project title	Description of result(s)
EBODAC (Ebola and related diseases)	Supporting the EBOVAC-Salone trial in Kambia, Sierra Leone. 9326 individuals were engaged using public meetings, house visits, drama and radio. Biometric Identification tools collected iris scans and fingerprints for nearly 900 volunteers to ensure that trial participants receive both vaccines. Mobile messaging has supported 419 rural participants to vaccinate on time.
EBOMAN (Ebola and related diseases)	The investment by the contract development and manufacturing organisation (CDMO) extends its aseptic fill and finish capability by around 300% and reinforces its ability to support early phase biologic supply needs for Phase I and II clinical trials.
EBOVAC1 (Ebola and related diseases)	Data from the Phase 1 clinical trial in the UK (87 trial participants) with the Janssen prime-boost Ebola vaccine regimen showed the regimen is safe, well tolerated, and induces durable antigen-specific antibody and cellular immune responses. Results published in the Journal of the American Medical Association. Phase 1 clinical trials in Kenya, Uganda, and Tanzania have completed 12 months follow up with 144 subjects enrolled. In the northern Kambia District of Sierra Leone, staged trial gathering immunogenicity and safety data is ongoing with 443 adults currently randomised. Across the different EBOVAC trials (including EBOVAC2), 1653 subjects have been enrolled to date.
EBOVAC2 (Ebola and related diseases)	Implementation of the Phase 2 trials with Janssen prime-boost vaccine regimen in Europe and Africa progressing. To date, 423 trial participants (out of 630) have been enrolled in the Phase 2 trial in the UK and France. In Africa, 556 subjects (out of 1188) have been randomised across sites in Burkina Faso, Uganda, Kenya and Cote d'Ivoire. Across the different EBOVAC trials (including EBOVAC1), 1653 subjects have been enrolled to date.

Impact on regulatory framework

Project title	Description of result(s)
ADAPT-SMART	Publication of a discussion paper on engagement criteria for MAPPs (medicines adaptive pathways to patients) to aid in debates on how and when a MAPPs approach should be used and for which medicines and diseases/conditions. The paper proposes a set of six questions that will trigger discussions initially at the company level (i.e. medicine developer) and subsequently at interaction meetings between the company and the other stakeholders and will help to drive selection or de-selection of a product for MAPPs. These questions were designed on the basis of input gathered from a wide range of stakeholders, including regulators, payers, HTA bodies, prescribers, patients and companies. The paper is intended to inform and drive future discussions on MAPPs, both within the ADAPT-SMART consortium and in the wider scientific and healthcare communities.
EBOVAC1 (Ebola and related diseases)	Pioneering regulatory pathways, adapting to a post-epidemic situation, through numerous interactions with regulatory agencies on potential way forward to licensure for novel Ebola vaccine.

Education and training for a new generation of R&D scientists

Project title	Description of result(s)
ADAPT-SMART (MAPPs)	Glossary developed providing working definitions including references of standardised terms relevant in MAPPs (working document to be updated during the lifespan of the project). Publication of an animated lay explanation note of the MAPPs concept to explain what is early access and how Medicines Adaptive Pathways to Patients (MAPPs) seek to foster access to beneficial treatments for the right patient groups at the earliest appropriate time and in a sustainable fashion
EBODAC (Ebola and related diseases)	Capacity building in Kambia, remote area of Sierra Leone. Local staff trained in clinical trials, community engagement, data entry, use of biometric identification and other technological tools: 122 clinic-based research staff trained on communications and engagement skills (1 half-day workshop per month), 11 community liaison staff have received 4 formal 2-day workshops on community engagement, with refresher training performed on weekly basis.
EbolaMoDRAD (Ebola and related diseases)	Workshop in Dakar entitled 'ModRAD workshop on Mobile Laboratory' on 4 –5 February 2016
EBOVAC1 (Ebola and related diseases)	Training of local staff in Sierra Leone. Capacity-building in remote area of Kambia in Sierra Leone. Built an emergency room, research laboratory and vaccine depot.
EBOVAC2 (Ebola and related diseases)	Providing training on blood sample handling and extracting a special cell preparation (PBMC) and helping to reduce existing gap between East African sites which have this capacity already well established and West African trial sites not yet familiar with these techniques. Participating trial site in Burkina Faso fully qualified by the Sponsor according to strict quality control guidelines and currently preparing PBMC for the Janssen vaccine trial.
VSV-EBOVAC (Ebola and related diseases)	Postdoctoral fellows, PhD students and students enrolled in Masters programmes are trained in the frame of this project

Annex 4 – Publications from projects

Hot papers from 2016

- Aliberti, Stefano; Masefield, Sarah; Polverino, Eva; De Soyza, Anthony; Loebinger, Michael R. (2016) Research priorities in bronchiectasis: a consensus statement from the EMBARC Clinical Research Collaboration, EUROPEAN RESPIRATORY JOURNAL 48:632-647, 10.1183/13993003.01888-2015
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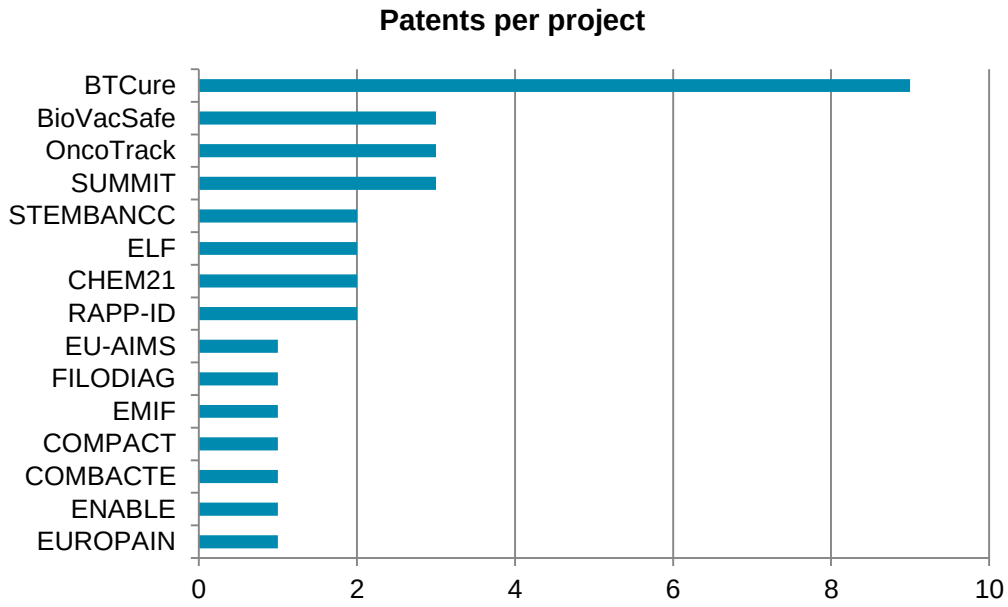
Annex 5 – Patents from projects

IMI projects are already patenting developed technologies. The statistics below encompass 33 patent applications filed from the beginning of IMI until December 31 2016. Interestingly, patent applications are mostly filed by public participants in IMI consortia, such as academia, SMEs, and research organisations. Pharmaceutical industry partners have filed or co-filed only 3 out of 33 patents. The graph below shows the breakdown of patents by project.



The patents filed and/or already awarded covered the following areas:

ENABLE

- novel inhibitors of bacterial DNA enzymes with a potential to treat bacterial infections.

SUMMIT

- imaging technology for non-invasive atherosclerosis assessment;
- animal model for diabetic vascular complications;
- predictors of rapid decline in renal function in diabetes.

BTCURE

- novel peptides for the treatment of rheumatoid arthritis and other forms of arthritis;
- novel stable scaffolds enabling modulation of immune responses;
- novel compound for treating diseases mediated by inhibition of tumour necrosis factor (TNF), such as inflammatory or autoimmune diseases;
- novel effective inhibitor of TNF for the treatment of autoimmune diseases, such as rheumatoid arthritis;
- methods for inhibiting the trimerisation of ligands belonging to the TNF superfamily, to treat disorders related to bone loss;
- quinolinone derivatives for use in the treatment of an autoimmune disease and/or an inflammatory disease;
- method for diagnosing Immunoglobulin G4 related diseases;
- method for diagnosing rheumatoid arthritis in the pre-clinical phase;
- compositions and methods relating to C5L2.

BioVacSafe

- diagnosis of systemic lupus erythematosus using protein, peptide and oligonucleotide antigens.

OncoTrack

- *in vitro* assay for miRNA.

RAPP-ID

- system for coupling radiation into a waveguide;
- patent for OprM approach to *P. aeruginosa*-specific diagnostic.

CHEM21

- green fluorination - process for producing fluorocytosine and fluorocytosine derivatives;
- synthetic biology - compact and optimised metabolic pathway design in *P. pastoris*.

ELF

- potential drug target for multidrug resistance in bacterial infections;
- chemical matter of potential use in cancer research.

EUROPAIN

- mouse model.

COMBACTE

- procedure for the rapid determination of bacterial susceptibility to antibiotics that inhibit protein synthesis PCT/US2016/013835.

COMPACT

- poly(lactic-co-glycolic acid) (PLGA) polymeric nanoparticles.

EU-AIMS

- bicyclic heteroaryl derivatives as mnk1 and mnk2 modulators and uses thereof US0150038506 A1.

FILODAG

- superparamagnetic particles

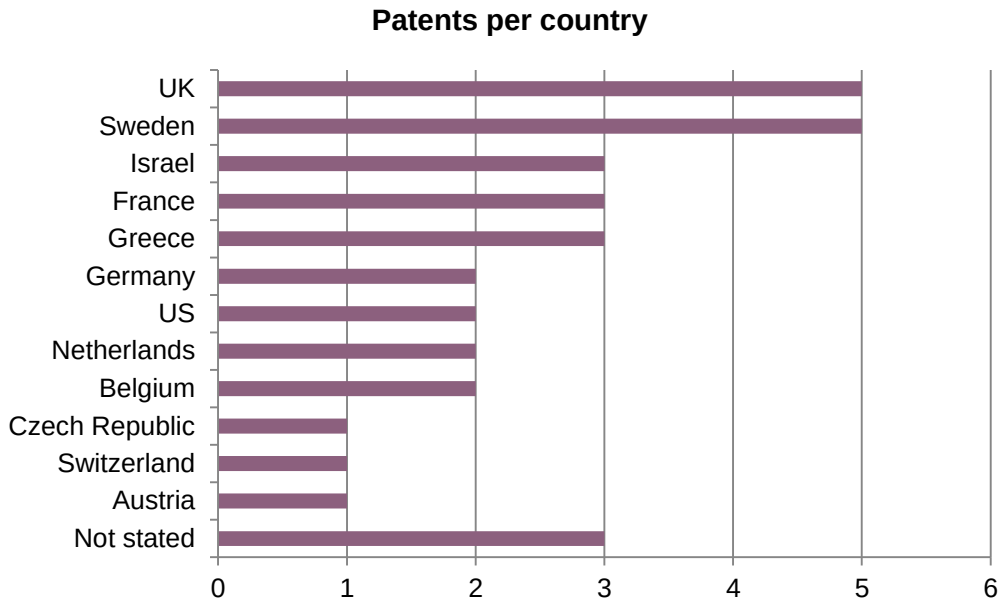
OncoTrack

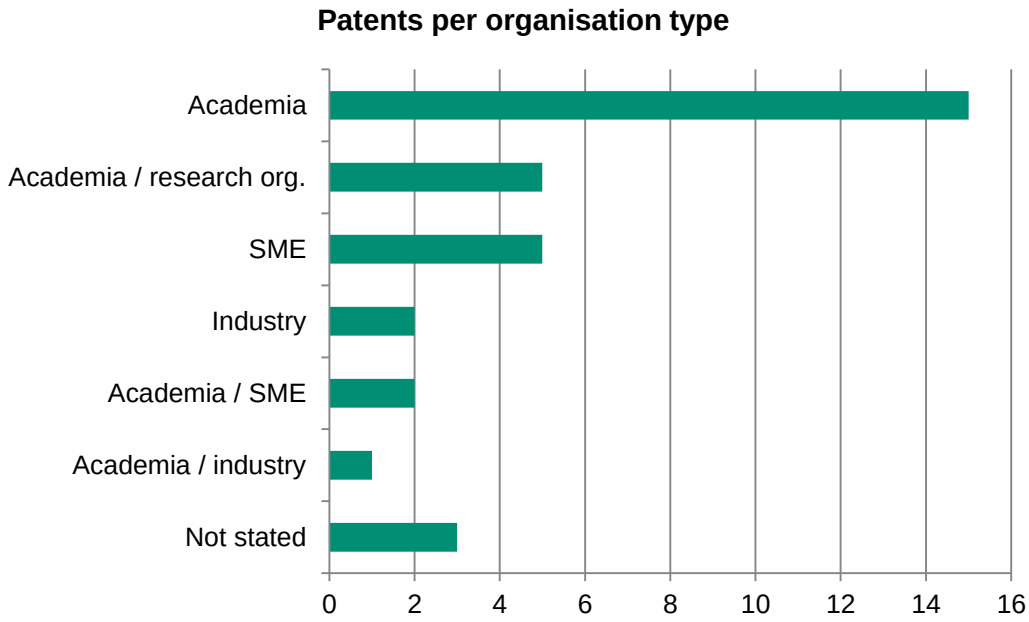
- transcriptional classifiers for the response of colon cancers to the therapeutic agents cetuximab and 5-fuorouracil

StemBANCC

- method for generating mature cardiomyocytes and their applications;
- step by step protocol of myocardial differentiation from pluripotent stem cells.

The graphs below show the breakdown of patents by country, and organisation type.





NB: some projects were unable to provide details of patents filed (country, organisation type) for confidentiality reasons.

Annex 6 – Scoreboard of H2020 common KPIs

Table I[49] - Horizon 2020 Key Performance Indicators common to all JTI JUs

	Correspondence to general Annex 1	Key Performance Indicator	Definition/Responding to question	Type of data required	Target at the end of H2020	Results in 2016
INDUSTRIAL LEADERSHIP	12	SME - Share of participating SMEs introducing innovations new to the company or the market (covering the period of the project plus three years)	Based on Community Innovation Survey (?). Number and % of participating SMEs that have introduced innovations to the company or to the market	Number of SMEs that have introduced innovations	50 %	n/a
	13	SME - Growth and job creation in participating SMEs	Turnover of company, number of employees	Turnover of company, number of employees	To be developed based on FP7 ex-post evaluation and /or first H2020 project results	n/a

[49] Table I shows the H2020 KPIs which apply to JTI JUs, both under Industrial Leadership and Societal Challenges (H2020 Key Performance Indicators ,Annex II - Council Decision 2013/743/EU). In tables I and II, the numbers attributed to the indicators correspond with those in the H2020 indicators approved by the RTD Director-General and agreed by all the research family DGs (according to Annexes II and III - Council Decision 2013/743/EU). The missing numbers correspond to KPIs not applicable to the JUs.

KPIs and indicators that correspond to those approved by the RTD Director-General are presented with a white background in the tables. They are aligned to what has been discussed between the Common Support Centre and the JUs. KPIs and monitoring indicators in tables I and II which do not correspond to those approved by the RTD Director-General are presented with a green background in the tables.

	Correspondence to general Annex 1	Key Performance Indicator	Definition/Responding to question	Type of data required	Target at the end of H2020	Results in 2016
SOCIETAL CHALLENGES	14	Publications in peer-reviewed high impact journals	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.	[On average, 20 publications per EUR 10 million funding (for all societal challenges)]	9 out of 16 papers (56.25 %) published in top 10 % journals.
	15	Patent applications and patents awarded in the area of the JTI	Number of patent applications by theme; Number of awarded patents by theme	Patent application number	On average, 2 per EUR10 million funding (2014 - 2020) RTD A6	1
	16	Number of prototypes testing activities and clinical trials[50]	Number of prototypes, testing (feasibility/demo) activities, clinical trials	Reports on prototypes, and testing activities, clinical trials	[To be developed on the basis of first Horizon 2020 results]	0
	17	Number of joint public-private publications in projects	Number and share of joint public-private publications out of all relevant publications	Properly flagged publications data (DOI) from relevant funded projects	[To be developed on the basis of first Horizon 2020 results]	5 out of 16 papers (31.25 %) with public-private authorship.

[50] Clinical trials are IMI specific

	Correspondence to general Annex 1	Key Performance Indicator	Definition/Responding to question	Type of data required	Target at the end of H2020	Results in 2016
	18*	New products, processes, and methods launched into the market	Number of projects with new innovative products, processes, and methods	Project count and drop down list allowing to choose the type processes, products, methods	[To be developed on the basis of first Horizon 2020 results]	n/a
EVALUATION	**NA**	Time to inform (TTI) all applicants of the outcome of the evaluation of their application from the final date for submission of completed proposals	To provide applicants with high quality and timely evaluation results and feedback after each evaluation step by implementing and monitoring a high scientific level peer reviewed process	Number and % of information letters sent to applicants within target Average TTI (calendar days) Maximum TTI (calendar days)	153 calendar days	No. of Short Proposal information letters: 60 (100% on time) No. information letters for Full Proposals: 21 (100% on time) Average TTI: 76 days
	NA	Redress after evaluations	To provide applicants with high quality and timely evaluation results and feedback after each evaluation step by implementing and monitoring a high scientific level peer reviewed process	Number of redresses requested		0
GRANTS	**NA**	Time to grant (TTG) measured (average) from call deadline to signature of grants	To minimise the duration of the granting process aiming at ensuring a prompt implementation of the Grant Agreements through a simple and transparent grant preparation process	Number and % of grants signed within target Average TTG in calendar days Maximum TTG in calendar days	TTG < 243 days (as % of GAs signed)	9 out of 14 grants (64%) were signed within the target Average TTG: 232 days Maximum TTG: 307 days

	Correspondence to general Annex 1	Key Performance Indicator	Definition/Responding to question	Type of data required	Target at the end of H2020	Results in 2016
	NA	Time to sign (TTS) grant agreements from the date of informing successful applicants (information letters)		Number and % of grants signed within target Average TTG in calendar days Maximum TTG in calendar days	TTS 92 calendar days	0 out of 14 grants (0%) were signed within the target Average TTS: 164 days Maximum TTS: 241 days
PAYMENTS	**NA**	Time to pay (TTP) (% made on time) Pre-financing Interim payment Final payment	To optimise the operational payments circuits	Average number of days for Grants pre-financing, interim payments and final payments	Pre-financing: 30 days Interim payment: 90 days Final payment: 90days	Pre-financing: 12 days 16 out of 16 (100%)paid on time Interim payment: 95 days 25 out of 44 (57%)paid on time Final payment: 62 days 6 out of 8 (75%)paid on time
HR	**NA**	Vacancy rate (%)		% of post filled in, composition of the JU staff		Vacancy rate: 21.15 % (10.53% TA, 50% CA)
JU EFFICIENCY	**NA**	Budget implementation / execution:	Realistic yearly budget proposal, possibility to monitor and report on its execution, both in commitment (CA) and payments (PA), in line with sound financial management principle	% of CA and PA	100 % in CA and PA	94.08 % CA to total budget 69.60 % PA to total budget
	NA	Administrative Budget: Number and % of total of late payments	realistic yearly budget proposal, possibility to monitor and report on its execution in line with sound financial	Number of delayed payments % of delayed payments (of the total)		1 241 payments of which 34% were late

	Correspondence to general Annex 1	Key Performance Indicator	Definition/Responding to question	Type of data required	Target at the end of H2020	Results in 2016
			management principle			

Notes:

18* This indicator is not legally compulsory, but it covers several additional specific indicators requested for more societal challenges by the EC services in charge.

Annex 7 – Indicators for monitoring cross-cutting issues

Table II[51] - Indicators for monitoring H2020 Cross-Cutting Issues common to all JTI JUs

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2016
2	Widening the participation	2.1 Total number of participations by EU-28 Member State	Nationality of H2020 applicants & beneficiaries (number of)	YES	Applicants: 847 Beneficiaries: 342 (cumulative figures up until 31/12/2016)
		2.2 Total amount of EU financial contribution requested by EU-28 Member State (EUR millions)	Nationality of H2020 beneficiaries and corresponding EU financial contribution	YES	263 088 183
NA		Total number of participations by Associated Countries	Nationality of H2020 applicants & beneficiaries (number of)	YES	Applicants: 29[52] Beneficiaries: 1, Norway (cumulative figures up till 31/12/2016)
NA		Total amount of EU financial contribution requested by Associated Country (EUR millions)	Nationality of H2020 beneficiaries and corresponding EU financial contribution	YES	362 000

[51] Table II presents all indicators for monitoring of cross-cutting issues which apply to JTI JUs (Annex III - Council Decision 2013/743/EU).

In tables I and II, the numbers attributed to the indicators correspond with those in the H2020 indicators approved by the RTD Director-General and agreed by all the Research family DGs (according to Annexes II and III - Council Decision 2013/743/EU). The missing numbers correspond to KPIs not applicable to the JUs.

KPIs and Indicators that correspond to those approved by the RTD Director-General are presented with a white background in the tables. They are aligned to what has been discussed between the Common Support Centre and the JUs. KPIs and monitoring indicators in tables I and II, which do not correspond to those approved by the RTD Director-General, are presented with a green background in the tables.

[52] From: Former Yugoslav Republic of Macedonia, Iceland, Israel, Norway, Turkey, Ukraine.

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2016
3	SMEs participation	3.1 Share of EU financial contribution going to SMEs (Enabling & industrial tech and Part III of Horizon 2020)	Number of H2020 beneficiaries flagged as SME % of EU contribution going to beneficiaries flagged as SME		43 out of 365 (11.78%) participations are SMEs EUR 28 483 427.50 (10.33%) of EU contribution (EUR 275 839 842) goes to beneficiaries flagged as SMEs
6	Gender	6.1 Percentage of women participants in H2020 projects	Gender of participants in H2020 projects	YES	n/a
		6.2 Percentage of women project coordinators in H2020	Gender of MSC fellows, ERC principle investigators and scientific coordinators in other H2020 activities	YES	n/a
		6.3 Percentage of women in EC advisory groups, expert groups, evaluation panels, individual experts, etc.	Gender of memberships in advisory groups, panels, etc.	YES	SRG: 20 out of 35 appointed nominees (57 %) SC: 6 out of 10 full members (60 %) Expert evaluators: 89 out of 219 (41 %) Interim review experts: 14 out of 35 (40 %)
7	International cooperation	7.1 Share of third-country participants in Horizon 2020	Nationality of H2020 beneficiaries	YES	21 out of total 249 participants (8%) From: Burkina Faso, Gabon, Senegal, Sierra Leone, Switzerland, United States
		7.2 Percentage of EU financial contribution attributed to third country participants	Nationality of H2020 beneficiaries and corresponding EU financial contribution	YES	4.5% (EUR 12 389 659 out of EUR 275 839 842)

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2016
9	Bridging from discovery to market [53]	9.1 Share of projects and EU financial contribution allocated to Innovation Actions (IAs)	Number of IA proposals and projects properly flagged in the WP; follow up at grant level.		n/a
		9.2 Within the innovation actions, share of EU financial contribution focused on demonstration and first-of-a-kind activities	Topics properly flagged in the WP; follow-up at grant level		n/a
NA		Scale of impact of projects (High Technology Readiness Level)	Number of projects addressing TRL[54] between (4-6, 5-7)?		n/a
11	Private sector participation	11.1 Percentage of H2020 beneficiaries from the private for profit sector	Number of and % of the total H2020 beneficiaries classified by type of activity and legal status		n/a subject to transition to H2020 IT tools
		11.2 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		n/a subject to transition to H2020 IT tools
12	Funding for PPPs	12.1 EU financial contribution for PPP (Art 187)	EU contribution to PPP (Art 187)		EUR 275.8 million
		12.2 PPPs leverage: total amount of funds leveraged through Art. 187 initiatives,	Total funding made by private actors involved in PPPs		IMI1: EUR 953.1 million IMI2: EUR 249.1 million

[53] This indicator (9.2) is initially intended to monitor the Digital Agenda (its applicability could be only partial)

[54] TRL: Technology Readiness Level

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2016
		including additional activities, divided by the EU contribution	- in-kind contribution already committed by private members in project selected for funding - additional activities (i.e. research expenditures/investment of industry in the sector, compared to previous year)		(EFPIA) + 14.4 million (Associated Partners)
13	Communication and dissemination	13.3 Dissemination and outreach activities other than peer-reviewed publications - [Conferences, workshops, press releases, publications, flyers, exhibitions, trainings, social media, web-sites, communication campaigns (e.g. radio, TV)]	A drop down list allows to choose the type of dissemination activity. Number of events, funding amount and number of persons reached thanks to the dissemination activities	YES	See dissemination section of report.
14	Participation patterns of independent experts	14.2 Proposal evaluators by country	Nationality of proposal evaluators		33 different countries[55] (148 experts)
		14.3 Proposal evaluators by organisations' type of activity	Type of activity of evaluators' organisations	YES	102 - academia and research institutes 20 - consultants 3 - regulators 4 - governmental or non-governmental organisations (NGOs)

[55] Argentina (1), Austria (3), Belgium (8), Bulgaria (1), Canada (3), Croatia (1), Cyprus (1), Czech Republic (4), Denmark (3), Estonia (1), Finland (4), France (9), Germany (10), Greece (4), Hungary (2), Ireland (5), Israel (2), Italy (11), Malaysia (1), Netherlands (9), Nigeria (1), Norway (2), Philippines (1), Poland (3), Portugal (1), Romania (3), Spain (13), Slovenia (3), Slovakia (1), Sweden (8), Turkey (1), United Kingdom (19), United States (9)

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2016
					19 - private (non-EFPIA)
NA	Participation of RTOs and Universities	Participation of RTO[56]s and Universities in PPPs (Art 187 initiatives)	Number of participations of RTOs to funded projects and % of the total Number of participations of Universities to funded projects and % of the total % of budget allocated to RTOs and to Universities	YES	Participations in funded projects and % of all beneficiaries: RTOs: 71 (27.8 %) Universities: 123 (48.2 %) % budget allocated: RTOs: 23.5 % Universities: 56.7 %
NA	Ethics	The objective is ensuring that research projects funded are compliant with provisions on ethics efficiently	% of proposals not granted because non-compliance with ethical rules/proposals invited to grant (target 0%); time to ethics clearance (target 45 days)[57]		0 %
NA	Audit	Error rates	% of common representative error; % residual error		See section 4.3 First audits of IMI2 projects are ongoing
NA		Implementation	Number of cases implemented; in total EUR million; ´of cases implemented/total cases		

[56] RTO: Research and Technology Organisation

[57] Data relates to pre-granting ethics review. This time span runs in parallel to granting process.

Annex 8 – Scoreboard of KPIs specific to IMI

Table III[58] - KPIs specific to each single JU

#	Key Performance Indicator	Objective	2016 target	Results in 2016
1	**IMI2 KPI 1:** Target number of priority areas defined in IMI2 JU's annual scientific priorities for year n that are addressed by IMI's Calls for proposals launched in year n	Measure the IMI2 portfolio	Annual target: ≥4 priority areas from IMI2 JU's annual scientific priorities	7
2	**IMI2 KPI 2:** Percentage of IMI projects that are assessed by the Programme Office as having achieved at least 90 % of pre-set deliverables by the last reviewed reporting period by the end of the year	Measure the scientific output	Annual target: ≥80 % of IMI JU projects	69 % of projects completed at least 90 % of pre-set deliverables Average deliverable completion rate: 88 %
3	**IMI2 KPI 3:** Average number of IMI publications per EUR 10 million of total IMI funding requested by the projects	Measure the scientific output	≥20 publications	2 690 publications for EUR 424.1 million of funding. 63.43 publications per EUR 10 million of IMI funding
4	**IMI2 KPI 4:** Extent to which the IMI's average impact factor of journals in which IMI publications have been published is higher than the EU average	Measure the scientific output	Annual target: ≥10 % higher than EU average	IMI = 5.968 EU = 3.478 IMI is 72 % higher

[58] Table III presents the KPI specific for each JU, as transmitted by the Programme Offices or the operational services.

#	Key Performance Indicator	Objective	2016 target	Results in 2016
5	**IMI2 KPI 5:** Extent to which the citation impact of IMI publications is higher than the EU average	Measure the scientific output	Annual target: ≥20 % higher than EU average	IMI = 2.03 EU = 1.14 IMI is 77 % higher
6	**IMI2 KPI 6.1**: Compare the citation impact of IMI publications with the one of other international funding bodies	Measure the scientific output	Annual target: ≥15 % higher than the average of sampled institutions	IMI = 2.03 Medical Research Council (MRC) = 2.08 MRC is 2 % higher
7	**IMI2 KPI 6.2**: Compare the percentage of highly cited papers of IMI programme with the one of other international funding bodies	Measure the scientific output	Annual target: ≥5 % higher than the average of sampled institutions	IMI = 26.1 % MRC = 24.7 % IMI is 6 % higher
8	**IMI2 KPI 7:** Number of scientific advice and qualified opinions initiated by IMI projects at the EMA and FDA	Measure impact on regulatory framework and standardisation	Target to measure the number of scientific advice and qualified opinions initiated/or completed by the IMI projects at the EMA and FDA: ≥ 5	5
9	**IMI2 KPI 8:** Number of regulatory guidelines derived from IMI projects	Measure impact on regulatory framework and standardisation	N/A	Not possible to report on. IMI project might only inform regulatory guideline development.
10	**IMI2 KPI 9**:Number of new standards and best practices derived from IMI projects	Measure impact on regulatory framework and standardisation	N/A	55
11	**IMI2 KPI 10:** Number of patent applications filed and/or awarded to those IMI projects which have been reimbursed at least for the third year of implementation	Measure business development and sustainability	≥2 patent applications per EUR 10 million of costs accepted and reimbursed by IMI2 JU	12 patent applications in 2016 1.18 patent applications per €10 million cost accepted and reimbursed by IMI JU

#	Key Performance Indicator	Objective	2016 target	Results in 2016
12	**IMI2 KPI 11:** Impact on EU competitiveness	Measure business development and sustainability	N/A	KPI under revision
13	**IMI2 KPI 12:** Creation of spin-off companies or foundations created as a result of IMI projects	Measure business development and sustainability	Annual target: 25 % of finalised projects	43% of finalised projects
14	**IMI2 KPI 13:** Estimated number of reported Full-Time Equivalents (FTEs) based in the EU that can be considered as directly related to the IMI programme	Measure business development and sustainability	Annual target: ≥ 1 500	2 768 (cumulative since beginning of IMI, based on person months listed in description of work)
15	**IMI2 KPI 14:** Percentage of participants in signed Grant Agreements that are SMEs	Measure business development and sustainability	20 %	IMI2: 38 out of 284 participants (13.4 %) are SMEs IMI1: 164 out of 652 (25.2 %) are SMEs
16	**IMI2 KPI 15:** Percentage of overall budget for projects that has been allocated to SMEs	Measure business development and sustainability	20 %	IMI2: EUR 28 483 427.50 (10.33%) of EU contribution (EUR 275 839 842) goes to SMEs IMI1: EUR 127 994 480 (13.25%) of EU contribution (EUR 965 730 983) goes to SMEs
17	**IMI2 KPI 16:** Percentage of projects involving patient organisations as consortium partners, members of advisory boards, ethical advisory boards or on consultancy basis for topics of relevance	Measure patient participation	Annual target: 100 %	75 %
18	**IMI2 KPI 17**: Impact for patients	Measure patient participation	N/A	KPI under revision

#	Key Performance Indicator	Objective	2016 target	Results in 2016
19	**IMI2 KPI 18:** Additional impact on society	Measure impact on society	N/A	KPI under revision
20	**IMI2 KPI 19:** Number of average monthly visitors to the IMI website	Measure information, communication and dissemination	Target: ≥10 000	11 546
21	**IMI2 KPI 20:** Performance of communication activities	Measure information, communication and dissemination	N/A	KPI under revision

Annex 9 – Final annual accounts

In accordance with the IMI2 JU Financial Rules Article 20 paragraph 1 information on the accounts and the report on budgetary and financial management should be included in the annual activity report.

The following tables have been extracted from the IMI2 JU final accounts 2016.

Balance sheet

EUR '000

	Note	31.12.2016	31.12.2015
NON-CURRENT ASSETS			
Intangible assets		–	*31*
Property, plant and equipment	*2.1*	*123*	*131*
Pre-financing	*2.2*	*182 426*	*200 748*
		182 549	**200 910**
CURRENT ASSETS			
Pre-financing	*2.2*	*62 204*	*50 939*
Exchange receivables and non-exchange recoverables	*2.3*	*95 389*	*69 090*
		157 592	**120 029**
TOTAL ASSETS		**340 141**	**320 939**
CURRENT LIABILITIES			
Payables and other liabilities	*2.4*	*(203 696)*	*(260 042)*
Accrued charges and deferred income	*2.5*	*(103 887)*	*(135 950)*
		(307 582)	**(395 992)**
TOTAL LIABILITIES		**(307 582)**	**(395 992)**
NET ASSETS			
Contribution from Members	*2.6*	*1 323 107*	*985 676*
Accumulated deficit		*(1 060 729)*	*(681 256)*
Economic result of the year		*(229 819)*	*(379 473)*
NET ASSETS		**32 559**	**(75 053)**

Statement of financial performance

EUR '000

	Note	2016	2015
REVENUE			
Revenue from non-exchange transactions			
Recovery of expenses	*3.1*	*34*	*461*
Other		*0*	*1*
		34	**462**
Revenue from exchange transactions			
Financial income		*10*	*65*
Other exchange revenue		*25*	*99*
		35	**164**
Total revenue		**70**	**626**
EXPENSES			
Operating costs	*3.2*	*(221 209)*	*(372 202)*
Staff costs	*3.3*	*(4 168)*	*(3 551)*
Finance costs		*(91)*	*(53)*
Other expenses	*3.4*	*(4 421)*	*(4 293)*
Total expenses		**(229 889)**	**(380 099)**
ECONOMIC RESULT OF THE YEAR		**(229 819)**	**(379 473)**

Cash flow statement[59]

EUR '000

	2016	2015
Economic result of the year	*(229 819)*	*(379 473)*
Operating activities		
Depreciation and amortization	*86*	*101*
(Increase)/decrease in pre-financing	*7 058*	*8 479*
(Increase)/decrease in exchange receivables and non-exchange recoverables	*(26 298)*	*(67 676)*
Increase/(decrease) in payables	*(56 347)*	*260 031*
Increase/(decrease) in accrued charges and deferred income	*(32 063)*	*(87 438)*
Increase/(decrease) in cash contributions	*209 265*	*149 797*
Increase/(decrease) in in-kind contributions	*128 166*	*65 432*
Investing activities		
(Increase)/decrease in intangible assets and property, plant and equipment	*(48)*	*(73)*
NET CASHFLOW	-	**(50 819)**
Net increase/(decrease) in cash and cash equivalents	–	*(50 819)*
Cash and cash equivalents at the beginning of the year	–	*50 819*
Cash and cash equivalents at year-end	–	–

[59] Following the appointment of the Accounting Officer of the Commission as the Accounting Officer of IMI JU, the treasury of IMI JU was integrated into the Commission's treasury system. Because of this, IMI JU does not have any bank accounts of its own in 2016. All payments and receipts are processed via the Commission's treasury system and registered on intercompany accounts, which are presented under the heading exchange receivables.

Statement of changes in net assets

EUR '000

	Contribution from Members	Accumulated Surplus/ (Deficit)	Economic result of the year	Net Assets
BALANCE AS AT 31.12.2014	**770 446**	**(452 247)**	**(229 009)**	**89 190**
Allocation 2014 economic result	*–*	*(229 009)*	*229 009*	*–*
Cash contribution	*149 797*	*–*	*–*	*149 797*
Contribution in-kind	*65 432*	*–*	*–*	*65 432*
Economic result of the year	*–*	*–*	*(379 473)*	*(379 473)*
BALANCE AS AT 31.12.2015	**985 676**	**(681 256)**	**(379 473)**	**(75 053)**
Allocation 2015 economic result	*–*	*(379 473)*	*379 473*	*–*
Cash contribution	*209 265*	*–*	*–*	*209 265*
Contribution in-kind	*128 166*	*–*	*–*	*128 166*
Economic result of the year	*–*	*–*	*(229 819)*	*(229 819)*
BALANCE AS AT 31.12.2016	**1 323 107**	**(1 060 729)**	**(229 819)**	**32 559**

Annex 10 – Materiality criteria

The 'materiality' concept provides the Executive Director with a basis for assessing the significance of any weaknesses or risks identified and thus whether those weaknesses should be subject to a formal reservation in the annual declaration of assurance. This annex provides an explanation of the materiality threshold that was applied as a basis for this assessment.

The control objective is to ensure that the residual error rate of payments made to beneficiaries, i.e. the level of errors which remain undetected and uncorrected, does not exceed 2 % by the end of the research programme. The guidance of the European Court of Auditors as well as the applicable European Commission standards were taken in account for defining the 2 % threshold. In addition, a qualitative and quantitative judgment was applied to assess and quantify any significant weaknesses.

- In qualitative terms, the following factors are considered as part of the materiality criteria:
  - the nature and scope of the weakness;
  - the duration of the weakness;
  - the existence of mitigating controls which reduce the impact of the weakness;
  - the existence of effective corrective actions to correct the weaknesses (action plans and financial corrections) which have had a measurable impact.

- In quantitative terms, the potential financial impact is taken into account.

The assessment of weaknesses was made by identifying their potential impact and judging whether any weakness was material enough that its non-disclosure could influence the decisions or conclusions of the users of the declaration of assurance.

The following considerations were, therefore, taken into account.

- Due to its multiannual nature, the effectiveness of IMI's control strategy can only be fully measured and assessed at the final stages in the life of the IMI programme, once the ex-post audit strategy has been fully implemented and systematic errors regarding beneficiaries have been detected and corrected.
- As the control objective is set to be achieved in the future, it is therefore not sufficient to assess the effectiveness of controls only by looking at the error rate determined during the year under review. The analysis must also include an assessment of whether (1) the scope and results of the audits carried out until the end of the reporting year were sufficient and adequate to meet the multi-annual control strategy goals; and (2) whether the preventive and remedial measures in place are deemed to be adequately effective in order lead to the expected reduction in the error rate by the end of the programme.

Effectiveness of controls

The main legality and regularity indicators for payments made to beneficiaries, as defined in the IMI ex-post audit strategy approved by the Governing Board in December 2010, are the representative and residual error rates detected by ex-post audits, measured with respect to the amounts accepted after ex-ante controls.

- The ***representative error rate*** **(RepER)** is the error rate resulting from the representative audits. It provides a reasonable estimate of the level of error in the population relating to the accepted IMI contributions on completion of the audits, but does not take into account the corrections and follow-up undertaken by IMI. It is calculated as the **average error rate (AER)** according to the following formula:

$$AER\% = \frac{\sum (err)}{n} = RepER\%$$

Where:

- ∑ **(err)** = sum of all individual error rates of the sample (in %). Only errors in favour of the JU (i.e. overstated amounts) are taken into consideration;
- **n** = sample size (i.e. number of audited financial statements).
- The ***residual error rate*** (**ResER**) is the level of error remaining in the population after deducting corrections and recoveries made by IMI JU. This includes the extension of audit results to non-audited financial statements of the audited beneficiaries to correct systematic errors. The formula for the residual error rate is:

$$\text{ResER\%} = \frac{\text{(RepER\% * (P-A) – (RepERsys\% * E)}}{\text{P}}$$

Where:

- **ResER%** = residual error rate, expressed as a percentage;
- **RepER%** = representative error rate, or error rate detected in the representative sample, in the form of the Average Error Rate, expressed as a percentage and calculated as described above (AER%);
- **RepERsys%** = systematic portion of the RepER% (the RepER% is composed of complementary portions reflecting the proportion of systematic and non-systematic errors detected) expressed as a percentage;
- **P** = total amount in euros of the auditable population relating to accepted IMI contribution;
- **A** = total value of audited IMI contribution, expressed in euros;
- **E** = total non-audited amounts of IMI contributions of all audited beneficiaries. This will consist of the total JU's share, expressed in euros, of all non-audited cost statements received for all audited beneficiaries.

The calculation of the error rates is performed on a point-in-time basis, i.e. all the figures are provided as of a certain date.

In addition, due to its multiannual nature, the effectiveness of IMI's ex-post audit strategy can only be fully measured and assessed during the final stages of IMI, once the ex-post control strategy has been fully implemented and systematic errors have been detected and corrected in the relevant claims. For this purpose, the weighted average residual error rate for the entire cumulative period covered by ex post audits during the execution of the IMI programme will be applied once sufficient audits from each representative sample have been concluded.

Annex 11 – Media highlights

- The Herald (UK), 17 November 2016
  Beyond Brexit: We need to build upon historic strengths
- Nature (UK), 9 November 2016
  How to defeat dementia
- Science| Business (EU), 2 November 2016
  In the lab: a big data project is trying to improve outcomes for patients
- Euronews - Business Planet (EU), 28 October 2016
  Euronews Deutsch: Europäische Substanz-Bibliothek spart Zeit und Geld in der Medikamentenforschung
  Euronews English: The vital role of SMEs in medical research
  Euronews Español: Una plataforma paneuropéa única para desarrollar medicamentos innovadores
  Euronews Français: Les PME, leviers indispensables de l'innovation pharmaceutique
  Euronews Italiano: Ricerca farmaceutica e Pmi, la rete europea dell'innovazione 'accessibile'
  Euronews Magyar: Kkv-kal gyorsítanák a gyógyszerkutatást
  Euronews Portugues: O European Lead Factory e a Iniciativa sobre Medicamentos Inovadores
- Drug Discovery World (UK), 25 October 2016
  Reconfiguring drug discovery through innovative partnerships
- Science|Business (UK), 20 October 2016
  EU Commission sketches possible directions for FP9
- Huffington Post (UK), 12 October 2016
  Labour's 170 Brexit Questions For The Government And David Davis To Answer
- Financial Times (UK), 14 September 2016
  Europeans are among those most sceptical of vaccine safety
- Scrip (UK), 24 August 2016
  View From The Top of IMI: Heading Up Life Sciences' Biggest Public-Private Partnership
- Bloomberg (US), 18 July 2016
  Shrinking Talent Pool May Bind Biotechs After Brexit
- Nature (UK), 13 July 2016
  Neuropathy: A name for their pain
- Medical Device Daily (US), 24 June 2016
  EU making progress in AMR via research, regulatory efforts
- BioWorld (US), 22 June 2016
  Agencies push bug drug pipeline but development lacks market pull
- The Lancet (UK), 30 May 2016
  Better together for better dementia research and care
- Financial Times (UK), 20 May 2016
  EU exit would lessen the influence of UK scientists
- Financial Times (UK), 19 May 2016
  Big pharma hits back at tax to tackle superbugs
- Science Business (EU), 19 May 2016
  Innovative Medicines Initiative says its early goals being met
- Novi List (Croatia), 19 May 2016
  Nova mobilna aplikacija HALMED-a: Prijave nuspojava lijeka odsad i putem smartphonea (HALMED's new mobile app: from now on it will be possible to report side effects via smartphone)
- T-Portal (Croatia), 18 May 2016
  Kako mobitelom saznati i prijaviti nuspojave lijeka? (How to find out about and report side effects of medicines via smartphone)
- Chronicle.lu (Luxembourg), 11 May 2016
  Strategy on Quality and Partnerships Pays Off for IBBL
- Nature (UK), 11 May 2016
  Competition: Unlikely partnerships
- Nature (UK), 11 May 2016
  Data sharing: Access all areas
- Ärzte Zeitung (Germany), 10 May 2016
  Mobile Geräte sollen vor Anfällen warnen (Mobile devices should warn of attack)
- Navarrainformacion.es (Spain), 3 May 2016
  La European Lead Factory analizará una diana terapéutica emergente del CIMA de la Universidad de

Navarra contra el cancer (The European Lead Factory will analyse an emerging anti-cancer therapeutic target from the University of Navarra)

- Corriere Della Sera (Italy), 29 April 2016
  Uno smartphone anti-depressione (An anti-depression smartphone)
- Science Business (EU), 28 April 2016
  Too much talk of innovation?
- La Marseillaise (France), 27 April 2016
  Marseille s'empare de la lutte contre le virus Ebola (Marseille seizes the fight against the Ebola virus)
- Medical News Today (UK), 26 April 2016
  Genetic barcode could pave way to bespoke liver cancer therapies
- Financial Time (UK), 25 April 2016
  Experimental Ebola vaccines need testing
- Politico Europe (EU), 21 April 2016
  Vaccines need a new business model
- Corriere Della Sera (Italy), 13 April 2016
  L'isolamento sociale ha basi biologiche (Social isolation has a biological basis)
- Science (US), 12 April 2016
  European mental health project targets biological roots of social withdrawal
- Manufacturing Chemist (UK), 11 April 2016
  IMI project recommends caution when assessing medicine impact studies from different databases
- EurActiv (EU), 5 April 2016
  Ebola refuses to let go of West Africa
- The Telegraph (UK), 2 April 2016
  Lord Darzi: Leaving the EU would be 'disastrous' for UK science and health
- Science Business (EU), 30 March 2016
  Despite potential benefits, big data faces resistance in healthcare
- Europa Press (Spain), 18 March 2016
  Reina Sofía de Córdoba e Imibic participan en un proyecto sobre enfermedades autoinmunes (Reina Sofía de Córdoba e Imibic are participating in a project on auto-immune diseases)
- Luxemburger Wort (Luxembourg), 17 March 2016
  Daten sind die Währung der modernen Medizin (Data are the currency of modern medicine)
- Il Sole 24 Ore (Italy), 15 March 2016
  Big data per la salute. L'Europa cerca la cura più efficace (Big data for health. Europe seeks the most effective cure)
- Granada Hoy (Spain), 12 March 2016
  Genyo: el corazón de un proyecto mundial sobre enfermedades raras (Genyo: the heart of a global project on rare diseases)
- Nature Biotechnology (UK), 10 March 2016
  Community crystal gazing
- The Malta Independent (Malta), 14 February 2016
  Explaining the enigma in medicines research & development
- The Parliament Magazine (European), 8 February 2016
  mHealth: New challenges as well as new opportunities
- La Libre (Belgium), 3 February 2016
  Un projet européen pour mieux comprendre le diabète de type 1 (A European project to better understand type 1 diabetes)
- Fierce Biotech (US), 29 January 2016
  Allergan links with AstraZeneca on new antibiotic treatment
- Politico Playbook (European), 27 January 2016
  Bill Gates to EU ministers: love your work, now pay up…
- Science Business (European), 7 January 2016
  UK scientists throw weight behind EU membership

Annex 12 – List of acronyms

Acronym	Meaning
AAR	Annual Activity Report
ABAC	Accrual Based Accounting System
ACS	Acute coronary syndrome
AD	Alzheimer's disease
ADA	Anti-drug antibody
ADPKD	Autosomal dominant polycystic kidney disease
ADR	Adverse drug reaction
AER	Average error rate
AF	Atrial fibrillation
AMP	Accelerating Medicines Partnership
AMR	Antimicrobial resistance
API	Active pharmaceutical ingredients
API	Application Programming Interface
ARLG	Antibacterial Resistance Leadership Group
ARO	Academic research organisation
ASD	Autism spectrum disorder
ATM-AVI	Aztreonam-avibactam
AWP	Annual Work Plan
BaaS	backup-as-a-service
BBSRC	Biotechnology and Biological Sciences Research Council
BD4BO	Big Data for Better Outcomes
BMJ	British Medical Journal
CA	Commitment appropriations
CA	Contract agent
CAS	Common Audit Service
CDA	Confidential Disclosure Agreement
CDMO	Contract development and manufacturing organisation
CFS	Certificates on Financial Statements
CKD	Chronic kidney disease
CNIO	Spanish National Cancer Research Centre
CNS	Central nervous system
CNV	Copy number variation
CO-ADD	Community For Open Antimicrobial Drug Discovery
COMPASS	H2020 workflow tool providing harmonisation between business processes & validation workflows

Acronym	Meaning
COPD	chronic obstructive pulmonary disease
CORDA	Common Research Data Warehouse
C-Path	Critical Path Institute
CPD	Continuing professional development
CSA	Coordination and support action
CSF	Cerebro-spinal fluid
CSO	Chief Scientific Officer
cUTI	complicated urinary tract infection
CVD	Cardiovascular disease
DCGMS	Dahlem Institute for Genome Research and Medical Systems Biology
DDS	Drug delivery system
DG BUDGET	European Commission Directorate-General for Budget
DG CONNECT	European Commission Directorate-General for Communications Networks, Content & Technology
DG HR	European Commission Directorate-General for Human Resources and Security
DG RTD	European Commission Directorate-General for Research and Innovation
DG SANTE	European Commission Directorate-General for Health and Food Safety
DILI	Drug-induced liver injury
DORA	Document Registry Application
DoW	Description of Work
DPO	Data protection officer
DTI	Diffusion tensor imaging
E/I	Excitation-inhibition
EC	European Commission
ECA	European Court of Auditors
EDPS	European Data Protection Supervisor
EEG	Electroencephalograph
EFPIA	European Federation of Pharmaceutical Industries and Associations
EHR	Electronic health record
EMA	European Medicines Agency
eMA	Electronic Missions Application
ENVI	European Parliament's Committee for Environment, Public Health and Food Safety
ERM	Enterprise Risk Management
ESIF	European Structural and Investment Funds
eTOXsys	eTOX in silico toxicology prediction system
EU	European Union
FC	Financial contribution

Acronym	Meaning
FDA	US Food and Drug Administration
FG	Function group
fMRI	functional magnetic resonance imaging
fNIH	Foundation for the National Institutes of Health
FO	Finance officer
FP	Full proposal
FP7	Seventh Framework Programme
FTE	Full-time equivalent
FWC	Framework contract
GA	Grant Agreement
GAP	Grant Agreement preparation
GAP	Global Alzheimer's Platform
GB	Governing Board
GCP	Good Clinical Practice
GFP	Green fluorescent protein
GPCR	G-protein-coupled receptor
GSK	GlaxoSmithKline
GWAS	Genome-wide association study
H2020	Horizon 2020
HBP	Human Brain Project
HF	Heart failure
HR	Human resources
HTA	Health Technology Assessment
HTS	High throughput screening
i~HD	Institute for Innovation through Health Data
IaaS	Infrastructure as a Service
IAS	Internal Audit Service of the European Commission
IB	Imaging biomarker
ICS	Internal Control Standards
ICT	Information and communication technology
ICU	Intensive care unit
IKC	In-kind contribution
ILG	Industry Liaison Group
IMI1 JU	Innovative Medicines Initiative 1 Joint Undertaking
IMI2 JU	Innovative Medicines Initiative 2 Joint Undertaking
IP	Intellectual property

Acronym	Meaning
iPSC	Induced pluripotent stem cell
IR	Insulin resistance
ISA	Information System for Absences
ISSCR	International Society for Stem Cell Research
IT	Information technology
ITRE	European Parliament's Committee on Industry, Research and Energy
ITTM	Information Technology for Translational Medicine
JDRF	Juvenile Diabetes Research Foundation
JECL	Joint European Compound Library
JPIAMR	Joint Programming Initiative on Antimicrobial Resistance
JTI	Joint Technology Initiative
JUs	Joint Undertakings
KPI	Key performance indicator
LCS	Longitudinal Cohort Study
LEAP	Longitudinal European Autism Project
LT	Long-term contract
MAPPs	Medicines adaptive pathways to patients
MEP	Member of the European Parliament
MID3	Model-informed drug discovery & development
MoU	Memorandum of Understanding
MRC	Medical Research Council
MRI	Magnetic resonance imaging
MRS	Magnetic resonance spectroscopy
MS	Multiple sclerosis
NAFLD	Non-alcoholic fatty liver disease
NASH	Non-alcoholic steatohepatitis
NCP	National Contact Point
ND4BB	New Drugs for Bad Bugs
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
NIMH	National Institute of Mental Health
NTDs	Neglected tropical diseases
OCT	Optical coherence tomography
OLAF	European Anti-Fraud Office
ORR	Operating Risk Register
PA	Payment appropriations

Acronym	Meaning
PA	Physical activity
PBPK	Physiologically based pharmacokinetic modelling
PCR	Polymerase chain reaction
PD	Parkinson's disease
PET	Positron emission tomography
PHH	Primary human hepatocyte
POC	Point-of-care
PPP	Public-private partnership
PRACE	Partnership for Advanced Computing
PRO	Patient reported outcome
PTC	Pediatric Trials Consortium
QST	Quantitative system toxicology
QST	Quantitative sensory testing
R&D	Research and development
RAE	Risk assessment exercise
RepER	Representative error rate
ResER	Residual error rate
RIA	Research and Innovation Action
RP	Reporting period
RSC	Royal Society of Chemistry
RSV	Respiratory syncytial virus
RTO	Research and Technology Organisation
RWE	Real world evidence
SC	Scientific Committee
SC	Short-term contract
SEP	H2020 IT tool for submission and evaluation of proposals
SFARI	Simons Foundation Autism Research Initiative
SGC	Structural Genomics Consortium
SGG	Strategic Governing Group
SME	Small and medium-sized enterprise
SO	Scientific officer
SOFIA	Submission of Information Application
SOP	Standard operating procedure
SP	Short proposal
SRA	Strategic Research Agenda
SRG	States Representatives Group

Acronym	Meaning
SRR	Strategic Risk Register
SyGMA	H2020 IT tool for grant management
TA	Temporary agent
TB	Tuberculosis
TTG	Time to Grant
TTI	Time to inform
TTP	Time to Pay
TTS	Time to sign
UCD	University College Dublin
UCSF	University of California at San Francisco
UK	United Kingdom
US	United States
WAT	White adipose tissue
WHO	World Health Organisation

Annex 13 – Table of IMI projects

(as of 31 December 2016)

IMI1 projects

Project acronym	Full project title	Website	Subject area
ABIRISK	Anti-biopharmaceutical immunization: prediction and analysis of clinical relevance to minimize the risk	www.abirisk.eu	drug safety
ADVANCE	Accelerated development of vaccine benefit-risk collaboration in Europe	www.advance-vaccines.eu	vaccines
AETIONOMY	Organising mechanistic knowledge about neurodegenerative diseases for the improvement of drug development and therapy	www.aetionomy.eu	Alzheimer's disease and Parkinson's disease
APPROACH	Applied public-private research enabling osteoarthritis clinical headway	www.approachproject.eu	osteoarthritis
BioVacSafe	Biomarkers for enhanced vaccine safety	www.biovacsafe.eu	vaccines
BTCURE	Be the cure	www.btcure.eu	rheumatoid arthritis
CANCER-ID	Cancer treatment and monitoring through identification of circulating tumour cells and tumour related nucleic acids in blood	www.cancer-id.eu	cancer
CHEM21	Chemical manufacturing methods for the 21st century pharmaceutical industries	www.chem21.eu	green chemistry
COMBACTE-CARE	Combatting bacterial resistance in Europe - carbapenem resistance	www.combacte.com/combacte-care	antimicrobial resistance
COMBACTE-NET	Combatting bacterial resistance in Europe	www.combacte.com/combacte-net	antimicrobial resistance
COMBACTE-MAGNET	Combatting bacterial resistance in Europe - molecules against Gram negative infections	www.combacte.com/combacte-magnet	antimicrobial resistance
COMPACT	Collaboration on the optimisation of macromolecular pharmaceutical access to cellular targets	www.compact-research.org	drug delivery
DDMoRe	Drug disease model resources	www.ddmore.eu	knowledge management
DIRECT	Diabetes research on patient stratification	www.direct-diabetes.org	diabetes
DRIVE-AB	Driving re-investment in R&D and responsible antibiotic use	drive-ab.eu	antimicrobial resistance
EBiSC	European bank for induced	www.ebisc.org	stem cells

Project acronym	Full project title	Website	Subject area
	pluripotent stem cells		
EHR4CR	Electronic health record systems for clinical research	www.ehr4cr.eu	knowledge management
ELF	European Lead Factory	www.europeanleadfactory.eu	drug discovery
EMIF	European medical information framework	www.emif.eu	knowledge management, Alzheimer's disease, metabolic syndromes
EMTRAIN	European medicines research training network	www.emtrain.eu	education and training
ENABLE	European Gram negative antibacterial engine	www.nd4bb-enable.eu	antimicrobial resistance
EPAD	European prevention of Alzheimer's dementia consortium	ep-ad.org	Alzheimer's disease
eTOX	Integrating bioinformatics and chemoinformatics approaches for the development of expert systems allowing the *in silico* prediction of toxicities	www.e-tox.net	knowledge management, drug safety
eTRIKS	Delivering European translational information & knowledge management services	www.etriks.org	knowledge management
EU2P	European programme in pharmacovigilance and pharmacoepidemiology	www.eu2p.org	education and training
EU-AIMS	European autism interventions - a multicentre study for developing new medications	www.eu-aims.eu	autism
EUPATI	European patients' academy on therapeutic innovation	www.eupati.eu	education and training
EUROPAIN	Understanding chronic pain and improving its treatment	www.imieuropain.org	chronic pain
FLUCOP	Standardization and development of assays for assessment of influenza vaccines correlates of protection	www.flucop.eu	vaccines
GetReal	Incorporating real-life clinical data into drug development	www.imi-getreal.eu	relative effectiveness
iABC	Inhaled antibiotics in bronchiectasis and cystic fibrosis	www.iabcproject.com	antimicrobial resistance
IMIDIA	Improving beta-cell function and identification of diagnostic biomarkers for treatment monitoring in diabetes	www.imidia.org	diabetes

Project acronym	Full project title	Website	Subject area
iPiE	Intelligent assessment of pharmaceutical in the environment	i-pie.org	environmental issues
K4DD	Kinetics for drug discovery	www.k4dd.eu	drug discovery
MARCAR	Biomarkers and molecular tumor classification for non-genotoxic carcinogenesis	www.imi-marcar.eu	safety, cancer
MIP-DILI	Mechanism-based integrated systems for the prediction of drug-induced liver injury	no website	drug safety
NEWMEDS	Novel methods leading to new medications in depression and schizophrenia	www.newmeds-europe.com	schizophrenia, depression
OncoTrack	Methods for systematic next generation oncology biomarker development	www.oncotrack.eu	cancer
Open PHACTS	The open pharmacological concepts triple store	www.openphacts.org	knowledge management
OrBiTo	Oral biopharmaceutics tools	www.orbitoproject.eu	drug delivery
PHARMA-COG	Prediction of cognitive properties of new drug candidates for neurodegenerative diseases in the early clinical development	www.alzheimer-europe.org/Research/PharmaCog	Alzheimer's disease
PharmaTrain	Pharmaceutical medicine training programme	www.pharmatrain.eu	education and training
PRECISESADS	Molecular reclassification to find clinically useful biomarkers for systemic autoimmune diseases	http://www.precisesads.eu/	rheumatoid arthritis and lupus
PREDECT	New models for preclinical evaluation of drug efficacy in common solid tumours	www.predect.eu	cancer
PreDiCT-TB	Model-based preclinical development of anti-tuberculosis drug combinations	www.predict-tb.eu	tuberculosis
PROactive	Physical activity as a crucial patient reported outcome in COPD	no website	respiratory disease
PROTECT	Pharmacoepidemiological research on outcomes of therapeutics by a European consortium	www.imi-protect.eu	pharmacovigilance
QUIC-CONCEPT	Quantitative imaging in cancer: connecting cellular processes with therapy	www.quic-concept.eu	cancer
RAPP-ID	Development of rapid point-of-care test platforms for infectious diseases	www.rapp-id.eu	infectious diseases
SafeSciMET	European modular education and training programme in safety	www.safescimet.eu	education and training

Project acronym	Full project title	Website	Subject area
	sciences for medicines		
SAFE-T	Safer and faster evidence-based translation	www.imi-safe-t.eu	drug safety
SPRINTT	Sarcopenia and physical frailty in older people: multi-component treatment strategies	www.mysprintt.eu	geriatrics
StemBANCC	Stem cells for biological assays of novel drugs and predictive toxicology	www.stembancc.org	stem cells
SUMMIT	Surrogate markers for vascular micro- and macrovascular hard endpoints for innovative diabetes tools	www.imi-summit.eu	diabetes
TRANSLOCATION	Molecular basis of the outer membrane permeability	www.translocation.eu	antimicrobial resistance
U-BIOPRED	Unbiased biomarkers for the prediction of respiratory disease outcomes	www.ubiopred.eu	respiratory disease
ULTRA-DD	Unrestricted Leveraging of Targets for Research Advancement and Drug Discovery	www.ultra-dd.org	drug development
WEB-RADR	Recognising adverse drug reactions	web-radr.eu	pharmacovigilance
ZAPI	Zoonotic Anticipation and Preparedness Initiative	zapi-imi.eu	infectious diseases

IMI2 projects

Project acronym	Full project title	Website	Subject area
ADAPTED	Alzheimer's disease apolipoprotein pathology for treatment elucidation and development	www.imi-adapted.eu	Alzheimer's disease
ADAPT-SMART	Accelerated development of appropriate patient therapies: a sustainable, multi stakeholder approach from research to treatment-outcomes	adaptsmart.eu	MAPPs
AMYPAD	Amyloid imaging to prevent Alzheimer's disease	www.amypad.eu	Alzheimer's disease
BEAT-DKD	Biomarker enterprise to attack DKD	no website	diabetes
EBODAC	Communication strategy and tools for optimizing the impact of Ebola vaccination deployment (Compliance with vaccine regimens)	www.ebovac.org/ebodac	Ebola and related diseases
EbolaMoDRAD	Ebola virus: modern approaches for developing bedside rapid diagnostics	www.ebolamodrad.eu	Ebola and related diseases
EBOMAN	Manufacturing and development for rapid access Ebola vaccine	www.ebovac.org/eboman	Ebola and related diseases
EBOVAC1	Development of a prophylactic Ebola vaccine using an heterologous prime-boost regimen	www.ebovac.org	Ebola and related diseases
EBOVAC2	Development of a prophylactic Ebola vaccine using an heterologous prime-boost regimen: Phase II	www.ebovac2.com	Ebola and related diseases
FILODIAG	Ultra-fast molecular filovirus diagnostics	www.filodiag.eu	Ebola and related diseases
HARMONY	Healthcare alliance for resourceful medicines offensive against neoplasms in hematology	no website	cancer
INNODIA	Translational approaches to disease modifying therapy of type I diabetes: an innovative approach towards understanding and arresting type I diabetes	innodia.eu	diabetes

Project acronym	Full project title	Website	Subject area
MOFINA	Mobile filovirus nucleic acid test	no website	Ebola and related diseases
MOPEAD	Models of patient engagement for Alzheimer's disease	www.mopead.eu	Alzheimer's disease
PERISCOPE	Pertussis correlates of protection Europe	www.periscope-project.eu	vaccines
PHAGO	Inflammation and AD: modulating microglia function - focussing on TREM2 and CD33	www.phago.eu	Alzheimer's disease
PREFER	Patient preferences in benefit risk assessments during the drug life cycle	www.imi-prefer.eu	patient involvement in R&D
PRISM	Psychiatric ratings using intermediate stratified markers: providing quantitative biological measures to facilitate the discovery and development of new treatments for social and cognitive deficits in AD, SZ and MD	prism-project.eu	neurological disorders
RADAR-CNS	Remote assessment of disease and relapse in central nervous system disorders	www.radar-cns.org	neurological disorders
RESCEU	Respiratory syncytial virus consortium in Europe	www.resc-eu.org	infectious disease
RHAPSODY	Assessing risk and progression of prediabetes and type 2 diabetes to enable disease modification	www.imi-rhapsody.eu	diabetes
ROADMAP	Real world outcomes across the AD spectrum for better care: Multi-modal data Access Platform	www.roadmap-alzheimer.org	Alzheimer's disease
TransQST	Translational quantitative systems toxicology to improve the understanding of the safety of medicines	transqst.org	safety
VAC2VAC	Vaccine lot to vaccine lot comparison by consistancy testing	www.vac2vac.eu	vaccines
VSV-EBOVAC	Vaccine safety and immunogenicity signatures of human responses to VSV-ZEBOV	www.vsv-ebovac.eu	Ebola and related diseases

Annex 14 – Analysis and assessment of the IMI2 JU Annual Activity Report 2016 (AAR2016) by the IMI2 JU Governing Board

Legal basis

Article 20 (1) of the IMI2 JU Financial Rules states that *"The authorizing officer shall report annually to the Governing Board on the performance of his or her duties in the form of a consolidated annual activity report […]* (which) *shall be submitted to the Governing Board for assessment and approval"* (Article 20(1)).

Article 20 (2) of the IMI2 JU Financial Rules further specifies that *"No later than 1 July each year the consolidated annual activity report together with its assessment shall be sent by the Executive Director to the Court of Auditors, to the Commission, to the European Parliament and the Council"* (Article 20(2)).

Analysis

The Innovative Medicines Initiative Annual Activity Report 2016 (Authorising Officer's report) was presented to the IMI2 JU Governing Board at the end of February 2017 and it is planned to have it approved by the Governing Board in June 2017.

The Governing Board is of the opinion that the IMI2 JU AAR 2016 covers well the main activities and achievements of the IMI2 JU in 2016 in relation to the objectives set; clearly identifies the risks associated with the IMI2 JU operations; duly reports on the use made of the IMI JU resources provided; and indicates the efficiency and effectiveness of the IMI2 JU internal control system.

- The Governing Board recognises the progress made by the IMI2 JU towards achieving the objectives set for year 2016 and notes in particular that:
- IMI2 JU officially started on 9 July 2014 and is running in parallel two programs with different rules: actions initiated under Framework Programme 7, and those under Horizon 2020.
- The Joint Undertaking has its discharge separated from the Commission.
- The Annual Work Plan 2016 together with the draft Budget 2016 was approved by the Governing Board on 13 January 2016 (Decision IMI2-GB-DEC-2016-01), first amended by the Governing Board on 19 April 2016 (Decision IMI2-GB-DEC-2016-04), last amended by the Governing Board on 06 December 2016 (Decision IMI2-GB-DEC-2016-30).
- In 2016, the JU implemented the final stages of the IMI2 Calls for proposals 5, 6 and 7, initiated under the Horizon 2020 Framework Programme. The JU also implemented the evaluation steps for the two first cut-off dates of call 8.
- In 2016, the JU launched 2 new Calls under Horizon 2020, IMI2 Calls 9 and 10. Those calls represent the commitment of: €228,218,000 of EU contribution; €181,512,000 of contribution from EFPIA companies (including €4,000,000 as cash contribution to the IMI2 JU for call 9 topic 6); and €55,956,000 of contribution from Associated Partners for Call 10.
- In 2016, the JU signed 14 new grant agreements from IMI2 Calls 3, 5 and 6 initiated under Horizon 2020.
- With an average of 232 days in 2016, the "Time To Grant" is higher than in 2015 (average of 135 days) but remains slightly below the requirement of maximum 240 days for the Horizon 2020 Programme.
- As at 31 December 2016, the IMI portfolio of projects represented a total of 59 projects from the first phase of IMI (initiated under Framework Programme 7, of which 21 finished their activities but are not closed yet), as well as 25 Grant Agreements signed from IMI2 Calls 1 to 6 (initiated under Horizon 2020).
- With these new Calls for proposals and new projects selected, IMI2 JU continued to implement key strategic objectives of its Scientific Research Agenda. This has been possible thanks to efficient collaboration between the European Commission and the European Federation of Pharmaceutical Industries and Associations (EFPIA), with the support from IMI Scientific Committee, the States Representatives Group, and the entire JU Programme Office.

- The IMI2 JU continued to promote SME participation in projects. By the end of 2016 SMEs account for 11.78% of all EU beneficiaries receiving 10.33% of the EU funding in the first 25 IMI2 signed grant agreements.
- The analysis of projects deliverables indicates outstanding scientific performance, with uptake of results in research processes, regulatory and clinical practice. Projects have in particular delivered in: (a) The identification and validation of new drug targets and novel hit and lead discovery; (b) The establishment of robust, validated tools for preclinical drug development; (c) The development of biomarkers and tools predictive of clinical outcomes (efficacy and safety); (d) Improved design and process of clinical trials; (e) 'Big data' solutions to leverage knowledge; (f) The implementation of project results inside industry; (g) Impact on the regulatory framework; (h) Education and training for a new generation of R&D scientists. Considering that only the first projects from the first phase of IMI now come to an end, it is however premature to report on long-term effects (impacts).
- In 2016, IMI started organising meetings with coordinators and key partners of projects that have come to an end. Six such meetings were organised in 2016. This allowed consortia to highlight the most significant results, share lessons learned and discuss impact and legacy of the projects in the longer term.
- By 31 December 2016, IMI projects have led to 33 patents filled, and produced 2690 publications in peer reviewed journals, 30% of which were published in year 2016. The latest biblio-metric analysis demonstrated that the citation impact of papers associated with IMI projects increased to 2.03, more than twice the world average (baseline of 1), and almost twice the EU's average (1.14). Also, more than 55% of the publications are published in top 10 % journals. This confirms, like for previous year 2015, the scientific excellence of IMI projects.
- In 2016, the IMI2 JU States Representatives Group met 3 times. The IMI2 JU Scientific Committee held 3 meetings and 7 new members were appointed to replace members whose mandates were due to expire. A new Strategic Governing Group was established to focus on oncology and the 6 other groups continued their work (in the areas of Immunology; Diabetes and metabolic disorders; Neuro-degeneration; Translational safety; Data and Knowledge management; and Infections control). Strategic Governing Groups regularly met and held teleconferences, each 2 to 4 times. A new SGG charter was adopted, clearly defining the tasks, composition, operations, requirements for confidentiality and reporting to GB.
- In 2016, communication activities were focused on continuing to raise awareness of IMI2 JU, promoting new IMI2 JU Calls for proposals, increasing IMI's outreach to policymakers and increasing engagement of SME in IMI2 JU activities.
- The 2016 edition of the Stakeholders Forum attracted around 500 registrations (375 attendees), compared to 200 in 2014 and 300 in 2015. It was successful in enabling the public assessment of the progress of the IMI2 JU Programme towards its objectives. It was in particular the occasion to present IMI2 Call 10 but also exchange views on new potential IMI2 JU actions in the domains of advanced therapies, bioprepardness, digital health and oncology.
- IMI2 JU continued fostering cross-project interactions and collaboration, in particular in drug discovery platforms, taxonomy of diseases, Alzheimer's disease, autism, antimicrobial resistance, Ebola disease, stem cell research and vaccines, as well as creating new relationships beyond IMI and Europe to achieve global impact in the area of autism and diabetes.
- The execution of projects was adequately followed up, including ex-ante and ex-post financial and scientific verifications. In 2016, as was expected, IMI2 JU conducted 10 interim reviews of projects from the IMI1 Calls 4, 7, 8 and 9 initiated under Framework Programme 7 and from the IMI2 Calls 2 and 3. Overall, the reviewers were satisfied with the progress made by these projects. In 2016, 21 of the 59 IMI1 projects finished their activities and the final scientific and financial reports are being reviewed.
- In total 197 ex-post audits of beneficiaries have been launched since 2011, out of which a total of 187 have been finalised, of which 43 during the year 2016 alone. This represents a very significant progress for year 2016. In addition, by the end of 2016, thirteen ex-post audits on the declared in-kind contribution of EFPIA companies participating in IMI projects had been finalised, and a further three audits were ongoing, altogether covering 95% of total in-kind contributions.
- In 2016, the cumulative residual error rate from the finalised audits was 1.67% and below the materiality threshold of 2%, like in previous year.

- The JU continued implementing preventive and corrective measures to mitigate the risk of errors in financial statements submitted by beneficiaries (e.g. guidance related to financial rules).
- Actions have been taken by the IMI2 JU to address the remarks provided by the European Court of Auditors in its report on the financial year 2015.
- In 2016 IAS issued a final audit report on "Controls over in-kind contributions in IMI2 JU" with four recommendations for improvements (three classified as very important and one as important). IMI2 JU Programme Office prepared an action plan that was approved by IAS and all four recommendations were implemented within agreed deadlines during 2016.
- Migration towards the Horizon 2020 IT tools progressed significantly in 2016. At the end of the year, IMI launched Call 10 using the SEP application, and the use of the SyGMA application is planned to take place in Q1 of 2017 with the preparation of grant agreements from Call 9. In addition, the integration with CORDA is also expected to be completed in 2017.
- In relation to the use of human resources, the IMI2 JU staff assigned to the activities carried out in 2016 has been used for their intended purpose. The Staff Establishment Plan of the IMI2 JU Programme Office was amended by the Governing Board on 10 November 2016, increasing number of positions from 47 to 52. On 31 December 2016, out of 52 positions only 41 were occupied. Twelve positions were filled during 2016 (Head of Scientific Operations; Head of Communication and Institutional Relations; senior scientific project manager; scientific programme officer; three scientific project officers; writer/editor; ex-Post Audit assistant; three administrative assistants).

During 2016 the monitoring tools were fully operational and the IMI2 JU AAR 2016 provides information on the effectiveness of the internal controls implemented and on the main results of monitoring and supervision controls.

Based on the information provided, the key objectives set up for 2016 have been met in compliance with legality, regularity and sound financial management.

The technical and operational information provided in the report reflects the situation at the end of 2016 in a realistic way.

However, the Governing Board considers that the following aspects require improvements:

- IMI2 JU Programme Office is encouraged to step up its efforts in measuring, reporting, and communicating on the outputs, outcomes and future impacts of its projects, notably in view of the preparation of the next Annual Activity Reports.
- In 2016, the budget execution of and payment appropriations decreased to 69.60%, and commitment appropriations increased to 94.08%, from previous year (72.68% and 91.04% respectively).
- The revision of the framework of Key Performance Indicators, which is ongoing, should be finalised as soon as possible and be reported in the next Annual Activity Reports.
- Migration towards the Horizon 2020 IT tools progressed significantly in 2016 but was not fully effective by the end of year 2016, and should be finalised in 2017.
- Measures should be taken to enhance SME participation.

Assessment

The declaration of the Executive Director and the IMI2 JU AAR 2016 gives a good assessment (clear, unambiguous, congruous) of operational and financial management in relation to the achievement of objectives, and the legality and regularity of the financial operations of the IMI2 JU in the year 2016.

The Governing Board notes that the management of the IMI2 JU has reasonable assurance that, overall, suitable controls are in place and working as intended, risks are being properly monitored and mitigated and necessary improvements and reinforcements detected by the auditors are being implemented.

Therefore, the IMI2 JU Governing Board hereby adopts this analysis and assessment of the IMI2 JU AAR 2016 of the authorizing officer. This analysis and assessment will be included into the IMI2 JU AAR 2016.

Brussels, on 27/06/17,

For the Governing Board of the Innovative Medicines Initiative 2

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