Annual Activity Report 2017

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-2018-17 approved by the Governing Board of the Innovative Medicines Initiative 2 Joint Undertaking at the meeting of 26.06.2018

Document reference: IMI2/OUT/2017-03352

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 JU, 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 Commission (EC)** Jack Metthey, Chair of the IMI2 JU Governing Board, Acting Deputy Director-General responsible for Research Programmes within the Directorate-General for Research and Innovation Line Matthiessen, Acting Director responsible for the Health Directorate within the Directorate-General for Research and Innovation Irene Norstedt, Head of Unit responsible for Innovative and Personalised Medicine within the Directorate-General for Research and Innovation Carlo Pettinelli, Director responsible for Consumer, Environmental and Health Technologies within the Directorate-General for Internal Market, Industry, Entrepreneurship and SMEs Andrzej Jan Rys, Director responsible for Health systems, medical products and innovation within the Directorate-General for Health and Food Safety **Representatives of the European Federation of Pharmaceutical Industries and Associations (EFPIA)** Jean-Christophe Tellier, CEO of UCB, member of the EFPIA Board, Chair of the EFPIA Innovation Board Sponsored Committee Nathalie Moll, Director General of EFPIA Salah-Dine Chibout, Global Head of Discovery and Investigational Safety at Novartis, Chairman of the EFPIA Innovative Medicines Strategy Priority Working Group

	Carlo Incerti, Sr Vice President, Head of Global Medical Affairs Sanofi Genzyme Paul Stoffels, Chief Scientific Officer at Johnson & Johnson, Worldwide Chairman of Janssen Pharmaceutical Companies of Johnson & Johnson
Other bodies	States Representatives Group (SRG): 28 European Union (EU) Member States and 16 Associated Countries to the Horizon 2020 Framework Programme Scientific Committee: 12 members including ad hoc members Stakeholder Forum: Over 403 registrations in 2017 Strategic Governing Groups (SGGs): 7 groups
Staff	Total posts: 56 (39 Temporary Agents, 15 Contract Agents, 2 Seconded National Experts) Posts filled: 49 (36 Temporary Agents, 13 Contract Agents, 0 Seconded National Experts)
2017 budget	Commitment appropriations: EUR 322 396 498 Payment appropriations: EUR 206 372 367
2017 budget implementation	Commitment appropriations: EUR 312 941 345 (97.07 %) Payment appropriations: EUR 148 514 294 (71.96 %)
Grants	15 grants signed in 2017 for a total value of EUR 105.9 million
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 2017.
Call implementation in 2017	Calls launched: 3 Proposals submitted under two-stage Calls: ▪ Short proposals submitted: 65 ▪ Eligible proposals submitted: 64 ▪ Full proposals submitted: 14 ▪ Proposals selected for funding: 14 Proposals submitted under single-stage Calls: ▪ Proposals submitted: 7 ▪ Eligible proposals submitted: 4 ▪ Proposals selected for funding: 4 Global project portfolio in 2017: 78 projects running during 2017 (38 under IMI1 of which 11 ended by 31 December 2017; and 40 under IMI2 of which 3 ended by 31 December 2017)[1]
Participation, including SMEs	Beneficiaries receiving EU funding 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. IMI2: SMEs account for 15.6 % of beneficiaries and receive 8.4 % of EU funding. IMI1: SMEs account for 24.8 % of beneficiaries and receive 13.2 % of EU funding

Unless stated otherwise, all data in this factsheet reflects the situation as of 31 December 2017.

[1] In total, 78 projects were active during 2017, including 15 new IMI2 projects. During the year, 14 projects (11 from IMI1 and 3 from IMI2) ended. This means that on 31 /12/2017, there were 64 projects up and running.

Foreword

In 2017, IMI[2] continued to demonstrate that large-scale public-private partnerships (PPPs) are well placed to contribute solutions to some of the biggest challenges in medical research and drug development.

The value of a PPP in healthcare was backed up by the reviews of IMI that were published during the course of 2017. The experts conclude that the IMI programme 'remains relevant and justified' and they recognise that IMI projects are delivering both quality research and resources and tools that are being used by researchers in their daily work. Many of these results are described in these pages and on the IMI website.

The evaluators also issued some valuable recommendations to help us further improve our performance and ensure our projects and activities help us to achieve our ambitious goals. We are now implementing an action plan to address these recommendations and I am convinced that these will help us take the IMI2 programme to the next level.

IMI owes its success to many people. I would first like to thank the vast, diverse community of scientists and experts from hundreds of organisations across Europe and beyond who work on our projects. Many of them go above and beyond the call of duty to make sure our projects deliver results that will make a difference to drug development and, ultimately, patients' lives.

I would also like to thank 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 diverse 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.

Finally, I would like to thank my colleagues at the IMI Programme Office for contributing their skills, hard work and efficiency to IMI throughout what has been a very busy year.

Pierre Meulien

IMI Executive Director

[2] A note on nomenclature: to avoid confusion, we use the term IMI throughout to refer to the organisation (and the Programme Office and governing bodies) in general. We only use the terms 'IMI1' and 'IMI2' when referring to the specific programmes.

Executive summary

In 2017, the Innovative Medicines Initiative (IMI) continued to deliver results that demonstrate the impact and added European value of a public-private partnership in the health research domain. Highlights here include:

CHEM21 project scientists devised a new, more efficient way of producing flucytosine, a medicine used to treat a common and often deadly fungal form of meningitis in people with HIV / AIDS. The new method, which is being scaled up by scientists from universities and the pharmaceutical industry, could drastically decrease costs of production, and so make the medicine more affordable for the many people with HIV / AIDS who live in low income countries.

The **MOFINA** project developed a new, portable diagnostic test that will deliver results in under 75 minutes on whether a patient has Ebola or a related disease such as Marburg virus. The device is designed to work in sites where high-end laboratory infrastructures are not available, and so will help to contain outbreaks and save lives. Thanks to the collaboration between companies, national public health institutes and other public partners, the project was able to validate the device on patient samples collected during the west African Ebola outbreak, and get it quickly approved for placement on the market.

Our **PROactive** project on chronic obstructive pulmonary disease, or COPD, developed the first tools capable of capturing both the amount and intensity of physical activity a patient actually carries out which are indicative of the success of medical interventions. The tools combine a wearable activity monitor with a simple questionnaire and the team has validated them in a number of clinical studies. In December, the European Medicines Agency issued a draft qualification opinion on the tools - if this goes through, it will mean that the EMA believes these tools are good enough to be used in future clinical studies of COPD treatments.

Many other projects reported exciting results during the year, and details of these can be found in the 'projects and results' section of the IMI website, which was revamped in 2017.

In addition to a greater focus on project outputs and successes, the website now includes a **catalogue of project resources** that are accessible to researchers outside the projects. The list, which is still in its infancy and is not exhaustive, currently counts 63 resources.

IMI: taking a mission-oriented approach to major societal challenges

More broadly, IMI continued to demonstrate that through a large-scale PPP, it is possible to work in a mission-oriented way on subjects like dementia and antimicrobial resistance (AMR), where market failures are resulting in major unmet medical needs.

The sheer complexity of the brain means that developing new treatments for diseases like dementia is particularly challenging, and failure rates in clinical trials are high. PPPs like IMI allow organisations to share both the risks and the rewards, and IMI's growing dementia portfolio shows that this approach is increasingly popular.

In 2017 IMI launched two new projects on dementia, bringing the total number of projects in the portfolio to 12. Furthermore, four new Call topics

IMI in 2017 at a glance

New projects

15 Grant Agreements signed launching new projects with a combined budget of **EUR 241 million** from the EU, EFPIA and Associated Partners…

Neurodegenerative disease
IMPRiND
NGN-PET
EQIPD

Antimicrobial resistance
COMBACTE-CDI

Paediatric diseases
ITCC-P4

Eye diseases
MACUSTAR

Ebola and related diseases
PEVIA
VSV-EBOPLUS

Rheumatoid arthritis
RTCure

Liver disease
LITMUS

Big Data for Better Outcomes
BigData@Heart (cardiovascular disease)
DO->IT (coordination and support action)

Vaccines
DRIVE

Medicines safety
TRISTAN
eTRANSAFE

addressing dementia were launched as part of IMI2 – Calls 12 and 13. Between them, the projects cover a wide range of issues, including research into the underlying causes of disease, the design of innovative clinical trials, the use of big data to improve outcomes in dementia, and patient engagement. One of the new Call topics is a coordination and support action; once launched it will help to facilitate the flow of information, results and best practice among the projects.

On AMR, the market failure exists because the use of new antibiotics should be restricted, so as to minimise the risk of bacteria developing resistance to them. This means that the potential return on investment is much lower than in most other medical fields.

Again, the IMI programme on AMR ('New Drugs for Bad Bugs) includes projects addressing a wide range of challenges in the sector, including the need to develop new economic models that incentivise innovation while promoting the sustainable use of new drugs.

In 2017, the programme gained a new project in the form of COMBACTE-CDI, which will focus on scoping the extent and impact of *Clostridium difficile* infection in Europe. In addition, a Call topic on diagnostics, involving many representatives of the sector, was launched as part of IMI2 – Call 13.

The need for a PPP on health research

The year 2017 saw the publication of two evaluation reports on IMI – the final review of the IMI1 programme, and the mid-term review of IMI2.

We were pleased to see that the experts conclude that the IMI programme 'remains relevant and justified' and that 'positive contributions on the drug development process have been realised'.

Positive points recognised in the reports include:

- our role in the creation of collaborative research networks that have enhanced trust between partners from different sectors, and triggered a mind shift as partners came to understand each other's needs;
- the quality of the research emerging from IMI projects;
- the creation of important resources and tools for drug development, some of which are already being used by researchers in their daily work.

The reports also note that 90% of the people who responded to the online survey agreed that the EU should cooperate with industry in the context of a public-private partnership on health.

The reports include valuable recommendations that will help us to further improve our performance in the coming years.

We recognise these issues and in collaboration with our Governing Board, we are already implementing an action plan to address the points raised and some progress has already been made, most notably with regards to reaching out to other sectors; implementing new key performance indicators; and increasing the involvement of SMEs in our projects.

IMI in 2017 at a glance

New Call topics

3 Calls for proposals launched with a total of **23 topics** and a budget of **EUR 185 million** from the EU and **EUR 169 million** from EFPIA & Associated Partners

Big data

Primary Sjögren's syndrome

Vaccines

Drug delivery

European screening centre

Diabetes

Skin disease

Diagnostics for antimicrobial resistance

Neurodegeneration

Induced pluripotent stem cells

Digital assessment of mobility

Cancer

Reproductive toxicology

Medicines safety

Repurposing

Exploitation of IMI project results

Bringing new partners in to the IMI family

The pharmaceutical industry plays a leading role in IMI. However, the legislation creating IMI2 notes that other sectors also need to be brought on board if IMI is to achieve its ambitious goals.

One particular highlight in 2017 was the launch, as part of IMI2 – Call 13, of a topic which aims to understand, demonstrate and quantify the value of diagnostics as tools to optimise antibiotic use and tackle antibiotic resistance. The development of the topic was very much led by companies from the diagnostics sector, but also draws on feedback from a consultation workshop held in June. The resulting industry consortium comprises six diagnostics companies (three of which are already EFPIA members, and three of which joined IMI as Associated Partners), plus the Wellcome Trust (which has also become an Associated Partner). Between them, they are investing a total of EUR 6.8 million in the project, matching the EUR 6.8 million invested by the EU.

In total, the number of IMI Associated Partners almost doubled in 2017, rising from 8 to 15. Other topics launched in 2017, for example in areas such as the remote assessment of disease and mobility, also attracted partners from relevant fields through EFPIA's 'Partners in Research' membership category. During 2017, 7 EFPIA Partners in Research with expertise in fields such as diagnostics, medical technology, pre-clinical and clinical development, imaging, and data analysis, committed EUR 8.9 million to new IMI Call topics. In total, by the end of 2017, 24 EFPIA Partners in Research had committed a total of EUR 28.7 million to IMI2 Call topics. The continuing growth in the numbers of both Associated Partners and EFPIA Partners in Research demonstrates the attractiveness of IMI as a model for investing in research.

Looking to the future, IMI worked intensively with the food industry to explore opportunities for future cooperation on the microbiome. These efforts included the organisation of a dedicated track on the microbiome at the IMI2 Stakeholder Forum 2017.

Measuring progress and performance

IMI started working on a new set of key performance indicators (KPIs) in 2016 and these were endorsed by the Governing Board in November 2017. Based on advice from the European Court of Auditors among others, the new KPIs are based on the RACER ('relevant, accepted, credible, easy, robust') principles. The new KPIs are fully aligned with IMI's objectives and those of the wider Horizon 2020 programme, and are designed to show how short and medium-term results and impacts should eventually deliver long-term impacts. IMI2 will use these KPIs to monitor its performance and progress, as from the Annual Activity Report for 2018.

SME involvement

SMEs bring unique skills, expertise and resources to research and drug development projects and their involvement in IMI is essential. Currently, over 200 SMEs are listed as partners in IMI1 and IMI2 projects. While most are from the biomedical field, they also include those working in IT and knowledge management as well as a few management companies. In 2017, IMI continued to make efforts to increase SME involvement in our projects by flagging up SME opportunities in our Call texts, running dedicated webinars for SMEs, creating a page for SMEs on the new IMI website, and by speaking at events where SMEs are present. The benefits for SMEs are showcased in the 'testimonials' section of the IMI website, where SME participants describe IMI as a positive experience and provide advice to other SMEs who may be interesting in applying.

Aiming for operational excellence

IMI continually seeks to improve the way we run the programme and manage the funds and resources entrusted to us by European taxpayers and our industry and Associated Partners. In this respect, in 2017 IMI notably succeeded in:

- launching three Calls for proposals;
- signing 15 Grant Agreements for new projects;
- further improving time to pay for all categories of payment, with all targets being met;
- on audits, keeping residual error rates below the materiality threshold of 2 %.

Evaluations of IMI1 (2008-2016) and IMI2 (2014-2016)

In October 2017, the European Commission published two evaluation reports on IMI – the final review of the IMI1 programme (2008-2016), and the mid-term review of its successor IMI2 (2014-2016). The reports were written by independent experts and drew on interviews with IMI stakeholders as well as an online consultation and an analysis of IMI's outputs. The experts concluded that IMI programme 'remains relevant and justified' and that 'positive contributions on the drug development process have been realised'. Positive points recognised in the reports include:

- IMI's role in the creation of collaborative research networks that have enhanced trust between partners from different sectors, and triggered a mind shift as partners came to understand each other's needs;
- the quality of the research emerging from IMI projects;
- the creation of important resources and tools for drug development, some of which are already being used by researchers in their daily work.

The reports also note that 90% of the people who responded to the online survey agreed that the EU should cooperate with industry in the context of a public-private partnership on health.

The reports include valuable recommendations that will help IMI to further improve its performance in the coming years. IMI recognises these issues and has already started putting in place systems to address them. For example, IMI's key performance indicators have been updated; a strategy to attract more small and medium-sized enterprises (SMEs) to IMI has been created; and IMI is putting greater efforts into identifying our projects' most important outputs and communicating on them to a wider audience.

The IMI Programme Office and Governing Board have agreed on and are now implementing an action plan that will ensure IMI responds to the expert evaluators' recommendations.

1 Implementation of the Annual Work Plan 2017

1.1 Key objectives in 2017

The key objectives for IMI in 2017 were based on the overall objectives of IMI2 JU as set out in Article 2 of Regulation No 554/2014. A summary of the progress made against them is given below. More information on all points can be found throughout the report.

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

- Launched three Calls for proposals, including one single-stage Call on the exploitation of IMI project results (IMI2 – Call 11), and two two-stage Calls (IMI2 – Calls 12 and 13).
- Achieved optimal budget execution in terms of commitments (97 %).
- Met our targets for time to inform applicants of the outcome of evaluations (100 % on time for short and full proposals).
- Comfortably met our targets for time to pay in all categories (pre-financing, interim, and final payments).

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

- Launched a new IMI website with a modernised look and feel and a stronger focus on IMI projects and results and information for core stakeholder groups such as small and medium-sized enterprises (SMEs) and patients.
- Held close-out meetings for 11 projects; details of key project results and impacts, as well as interviews with project leaders, are published on the IMI website. Links to these can be found in section 2.1 (Communication & events).
- The Governing Board approved the new KPI (key performance indicator) framework, which is designed to track IMI's progress in meeting its ambitious goals.
- Continued working with Clarivate Analytics on a detailed assessment of IMI project publications.

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

- Almost doubled the number of Associated Partners from 8 to 15, with organisations committing to projects in the fields of diagnostics, autism, drug discovery, and neurodegeneration. Included a page dedicated to Associated Partners on the new website, featuring more detailed guidance.
- Held two workshops to explore ways of cooperating on smart health with ECSEL, the joint undertaking on electronic components and systems.
- Held workshops to explore opportunities for other (non-pharmaceutical) sectors to get involved in IMI. In the case of the diagnostics sector, this resulted in the launch of a Call topic as part of IMI2 – Call 13.

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

- The IMI Programme Office is now almost fully staffed; at the end of 2017, 49 out of 56 positions were filled and further recruitments were ongoing.
- Achieved process improvements by adopting a project-based management approach to key initiatives within the office.
- Successfully managed the transition to all H2020 tools that will enable projects to report under the new tools from 2018.

1.2 Research and innovation activities

The overarching goal of IMI1 was to significantly improve '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:

- 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;
- develop diagnostic and treatment biomarkers for diseases clearly linked to clinical relevance and approved by regulators;
- where possible, reduce the time to reach clinical proof of concept in medicine development, such as for cancer, immunological, respiratory, neurological and neurodegenerative diseases;
- increase the success rate in clinical trials of priority medicines identified by the World Health Organisation;
- 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;
- reduce the failure rate of vaccine candidates in phase III clinical trials through new biomarkers for initial efficacy and safety checks.

In order to track progress against these ambitious goals, IMI categorises project outputs according to the following categories:

- new tools/resources for drug discovery & preclinical drug development;
- biomarkers and tools developed to predict clinical outcomes (efficacy and safety);
- improved protocols for clinical trial design and processes;
- biomarkers for the efficacy and safety of vaccine candidates;
- new taxonomies of diseases and new stratifications of patient sub-populations;
- development and use of cohorts, registries and clinical networks for clinical studies and trials;
- big data solutions to leverage knowledge / implementation of data standards;
- education and training for new and existing R&D scientists and stakeholders;
- impact on regulatory framework;
- implementation of project results inside industry;
- accessibility of resources/outputs beyond consortium.

These categories are aligned with the new IMI KPIs, which were approved by the Governing Board in November 2017 and will be monitored as from the next Annual Activity Report for the year 2018. They were selected due to their alignment with the goals of IMI, and because they allow IMI to assess projects' actual impact on drug development.

The following sections provide a snapshot of some of the successes generated by IMI1 and IMI2 projects during 2017. A detailed list of achievements for the year can be found in Annex 3 of this report.

1.2.1 Collaborative research and development related outputs from IMI1 projects

New tools/resources for drug discovery & preclinical drug development

IMI projects are adding to our understanding of disease, as well as delivering tools, resources and platforms to make it easier for researchers to study diseases and identify potential treatments.

New Drugs for Bad Bugs projects deliver knowledge to advance the fight against antimicrobial resistance

Bacteria are adept at defending themselves against antibiotics – even if you manage to get an antibiotic into a bug, there is a good chance that the bacteria will expel or destroy the antibiotic before it can take effect and kill the bacteria. Project's in IMI's New Drugs for Bad Bugs (ND4BB) programme are delivering new insights

into bacterial defence mechanisms – knowledge that is key to efforts to develop new antibiotics capable of overcoming these defences.

For example, scientists from IMI's Translocation project have uncovered the workings of a 'molecular vacuum cleaner' in the outer membrane of certain bacteria. The mechanism, described in a paper in the journal Nature Microbiology, helps to keep the outside of the membrane free of clusters of molecules that could weaken it. The system could prove useful as a target for new antibiotics. Gram-negative bacteria like *Escherichia coli* are enclosed by two membranes which form a significant barrier for many antibiotics. The outer membrane is asymmetrical; while the outside of the membrane is coated in sugars that ward off many molecules that could be harmful to the bacteria, the inside is lined with phospholipids. Sometimes, phospholipids from the inside of the membrane accumulate on the outside. These clumps of phospholipids represent weak spots in the membrane, rendering it more vulnerable to compounds like antibiotics that could be toxic to the bacteria. In this study, the scientists identified the system used by bacteria to remove phospholipids that have strayed into the outside of the membrane by sucking them back into the inside of the membrane where they belong. 'Our three-dimensional structures and functional data show that [the system] forms a donut in the inner leaflet of the outer membrane. This binds phospholipids from the outer leaflet and removes these via the central channel, somewhat similar to a vacuum cleaner,' explained Bert van den Berg of Newcastle University in the UK. 'Our study illuminates a fundamental and important process in Gram-negative bacteria and is a starting point to determine whether this system of Gram-negative pathogens could be targeted by drugs to decrease bacterial virulence, and to make various antibiotics more effective.'

Another project that has delivered important findings in this area is ENABLE, which has uncovered a new mechanism to target drug-resistant bacteria, opening up a promising new pathway for further research. The mechanism involves DNA gyrase, a well-known enzyme that is a target of already existing antibiotics. ENABLE scientists found a new way to inhibit this enzyme and kill drug-resistant bacteria in the laboratory. In the study, published in the Proceedings of the National Academy of Sciences, they identified and characterised two new compounds, which have the ability to kill bacteria resistant to quinolones, a family of broad-spectrum antibiotic drugs, in this novel way. Although the work on these specific compounds will not continue within the ENABLE project because the compounds showed toxicity, the new mechanism which was uncovered holds potential for future research. 'This study is very significant, but not because these specific compounds are likely to end up as clinical drugs', said Anthony Maxwell of the John Innes Centre in the UK, one of the ENABLE project partners who played a key role in this study. 'It is significant because it has revealed a novel way of targeting a well validated anti-bacterial target, DNA gyrase, and that new way of targeting this enzyme is not subject to pre-existing resistance to antibiotics. It is very exciting. Eventually this could lead to the development of new antibiotics.'

European Lead Factory compound collection hits 500 000 mark

When it started in 2013, the European Lead Factory's goal was to create a library of half a million compounds gathered from an array of sources. The 7 large pharmaceutical companies in the project quickly contributed over 320 000 compounds from their own collections; these allowed the project to become operational early on. Meanwhile, the project has continued to source thousands of compounds from academic groups and small and medium-sized enterprises across Europe. In December 2017, the compound library hit the 500 000 mark. What's more, a further 20 000 compounds are expected to be added to the library before the end of the project in the first half of 2018.

Analyses of the collection have highlighted the quality and diversity of the collection, which has been used to run over 150 screens for public and private partners. The results of these screens have delivered promising results in a wide range of areas, including Parkinson's disease, diabetes, antimicrobial resistance, depression, motor neuron disease, and cancer.

In some cases, results from the European Lead Factory have triggered further investments. For example, in 2017 Richard Mead of the University of Sheffield turned to the European Lead Factory for help identifying compounds that could prove effective against a drug target involved in oxidative stress, which plays an important role in Parkinson's. The European Lead Factory set up and ran the screens, and the results were so interesting that Parkinson's UK decided to allocate GBP 1 million (approx. EUR 1.2 million) for the creation of a virtual joint venture biotech company with the University of Sheffield to further develop the compounds identified. According to Richard Mead, the results would have been 'absolutely impossible' without the European Lead Factory. 'We made incredible breakthroughs!' he said. 'Many, including ourselves, have screened various commercial and academic libraries, but never found anything useful. The diversity and quality of the Joint European Compound Library is not available anywhere else.'

Biomarkers and tools developed to predict 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.

OncoTrack identifies new biomarkers for colon cancer

Colorectal carcinomas are a very heterogeneous group of cancers and not all of them respond equally to different drugs. Up until now, doctors have decided which drug to use based on the tumour gene mutations. However, the mutation status alone is not specific enough. To be able to predict a tumour's response to certain drugs more accurately, IMI's OncoTrack project set out to produce molecular fingerprints of different tumours and correlate the different fingerprints to how the tumours respond to various drugs. In the process, they identified two new biomarkers for colorectal cancer which could lead to more personalised and effective treatments for patients with this disease.

The study, which was published in the journal Nature Communications, was one of the largest public-private collaborations in this field to date. By bringing together academic institutions, SMEs and the pharmaceutical industry, OncoTrack scientists first collected tumour samples from over 100 colorectal cancer patients at different stages of the disease. They grew these tumours in tissue culture systems, as well as in special mouse strains, and proceeded to analyse them in the lab. In particular, the scientists looked for biomarkers, i.e. molecules that are typical of the different tumour sub-groups. Based on this analysis, they were able to produce molecular fingerprints for all of the tumours. Next, they tested how the tumours respond to different drugs and correlated various tumour fingerprints with their response to the different clinical compounds. Among other things, they discovered two biomarkers that can predict the effectiveness of two drugs commonly used to treat this disease: Cetuximab, which inhibits the receptor for the epidermal growth factor, and the chemotherapy drug 5FU. 'The extensive molecular and drug sensitivity datasets generated within this study are a highly valuable resource,' said Bodo Lange, CEO at Alacris Theranostics, one of the OncoTrack project partners. 'Our findings provide major new insights into the molecular landscape of colorectal cancer and have the potential to guide treatment decisions.'

IMIDIA continues to deliver new insights into diabetes

Although the IMIDIA project finished in 2015, results generated by the project continue to appear in scientific journals. For example, a paper published in the journal Diabetologia in November 2017 explains how the project has identified a novel signature of 19 genes whose activity is faulty in type 2 diabetes. In people with type 2 diabetes, the islet cells in the pancreas do not respond adequately to produce the hormone insulin, leading to elevated blood glucose levels and an inability to keep blood glucose levels stable. The scientists arrived at the signature after analysing and comparing gene activity levels in the largest collection of pancreatic islet cells from diabetic patients, people with pre-diabetes, and non-diabetic healthy individuals. Their work uncovered 19 genes with 'dysregulated' activity levels in the cells taken from people with type 2 diabetes. Of these, 10 had been identified in previous research, but 9 had never been picked up as being dysregulated in pancreatic islets before. Interestingly, the genes are not dysregulated in cells taken from people with pre-diabetes, suggesting that their altered activity levels are the consequence of, rather than the cause of islet cell failure. 'We believe that our data provides novel molecular insights into what is going wrong in diabetic beta cells and sets new standards for how studies in this field shall be carried out in the future,' said Michele Solimena of Dresden University of Technology, one of the leading investigators of the study. 'Ultimately, we are confident that our approach will provide a new view for how exposure of beta cells to nutrient overload wears their function overtime, hence impairing their ability to satisfy the excessive demand of insulin to maintain metabolic homeostasis.' Looking to the future, the researchers are keen to find out which genes are dysregulated before the onset of diabetes; this is a focus on the new IMI project RHAPSODY.

Earlier in the year, a paper in the journal Molecular Metabolism set out the project's work uncovering clues that could help to identify people at risk of developing diabetes. Writing in the journal, the researchers explain how they have identified a gene called Elovl2 that appears to play a key role in insulin secretion. According to the team, Elovl2 codes for an enzyme that makes a poly-unsaturated fatty acid called DHA. The researchers

confirmed its role in insulin secretion in both mice and human cell lines. Another paper, in Cell Reports, demonstrates that the levels of certain lipids (fats) in people's blood plasma appear to be raised up to nine years before diagnosis. Scientists from the Swiss Institute of Bioinformatics (SIB) were involved in both papers. In a press release, they point out that the studies brought together academic teams, pharmaceutical companies, and a small to medium-sized enterprise (SME), and that the results were cross validated through the IMIDIA project. 'The findings therefore highlight the instrumental role of public-private partnerships, such as the IMI, in enabling such advances and improve public health,' they conclude.

EMIF project helps shed light on role of omegas in Alzheimer's

Omega-3 and **omega-6** unsaturated fatty acids play a role in the progression of Alzheimer's disease, according to research published in the journal PLOS Medicine and supported in part by IMI's EMIF project. Currently it is thought that the main reason for developing memory problems in dementia is the presence of two big molecules in the brain called tau and amyloid proteins. These proteins have been extensively studied and have been shown to start accumulating in the brain up to 20 years before the disease onset. In the new study, researchers from King's College London and the National Institute on Aging in the USA looked at concentrations of thousands of metabolites in brain tissue samples of 43 people: 14 people with healthy brains, 15 that had high levels of tau and amyloid but didn't show memory problems, and 14 clinically diagnosed Alzheimer's patients. They found that six unsaturated fatty acids, including omegas, were significantly different in Alzheimer's brains when compared to brains from healthy patients. Overall, their levels were lower than in the healthy patients and one omega, DHA, was increased. As this study was observational, it is not clear whether decreased levels of unsaturated fatty acids drive the progression of Alzheimer's or if they are a result of the disease. As one of the co-leaders of the study, Cristina Legido Quigley of King's College London said: 'While this was a small study, our results show a potentially crucial and unexpected role for fats in the onset of dementia. It is now important for us to build on and replicate these findings in a larger study and see whether it corroborates our findings'.

Improved protocols for clinical trial design and processes

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.

GETREAL tools facilitate use of real world evidence

Incorporating data from 'real life' clinical settings into drug development and associated decision-making represents a serious challenge for pharmaceutical companies, regulators, and health authorities alike. By bringing together all key stakeholder groups (namely industry, academia, regulatory agencies, reimbursement agencies, healthcare budget holders, and patient groups) IMI's GETREAL project has developed a range of practical tools and guides on how best to incorporate real world evidence (RWE) into decision making.

For example, the project developed the PragMagic tool to aid in the design of pragmatic clinical trials. Pragmatic trials aim to capture the true effect of a treatment strategy in the real world. As such, they provide a great opportunity to generate real-world evidence in the early stages of drug development. However, pragmatic trials are still in their early days and designing them is far from easy. PragMagic was developed in collaboration with a gaming company. 'In a user-friendly (and dare we say fun) way, PragMagic gives insight into the possible consequences of more pragmatic trial design choices and operational challenges on generalisability, risk of bias, precision, stakeholder & ethical acceptability, cost and duration,' explained Mira Zuidgeest of the University Medical Centre Utrecht. The project hopes that the new tool will increase the value and feasibility of pragmatic trials by informing stakeholders when designing and assessing pragmatic clinical trials.

Another online educational resource from GETREAL is the Real-World Evidence (RWE) Navigator which, as its name suggests, is designed to help users from a broad range of research and healthcare backgrounds get to grips with RWE. RWE refers to evidence of relative effectiveness - how well medicines work in the real world, as opposed to the controlled experimental settings of clinical trials. Data to generate RWE can come from a range of sources, including patient registries, medical records, pragmatic trials, and other observational studies. The RWE Navigator helps users find out more about potential issues in demonstrating the relative effectiveness of new medicines, and guides users to specific types of analyses or study designs that use RWE to support the development of medicines. Finally, it is a comprehensive directory of resources that support the use of RWE in medicines development. The RWE Navigator has been designed for a wide variety of users. For example, pharmaceutical companies may find it useful to increase awareness about the potential use of RWE among their medicine development teams, or patients may use it to understand concepts related to RWE and the challenges faced when using or generating RWE.

EPAD tackles ethical issues in development of cohorts

A large part of IMI's EPAD project is devoted to building up a cohort of 6 000 people at risk of developing Alzheimer's dementia. Some of these will eventually be invited to participate in clinical trials of treatments to prevent or at least delay the onset of the disease. As the project points out, when designing a study and setting up these cohorts, researchers must make ethically challenging design decisions in at least three areas: re-contacting participants in existing research studies; obtaining informed consent for participation in a readiness cohort; and disclosure of Alzheimer's disease-related biomarkers. The EPAD project set up a dedicated work group comprising representatives of patient groups, universities, and the pharmaceutical industry to address these issues. Their recommendations are published in the Journal of Prevention of Alzheimer's Disease and include the following points:

- Only participants who are willing to learn their AD risk status should participate in a readiness cohort.
- Provide education about biomarkers to participants at an early stage of the research project.
- Biomarker results and their significance should be disclosed by experienced professionals.

New taxonomies of diseases and new stratifications of patient sub-populations

There is growing evidence that while two patients may be classified as having the same disease, the genetic or molecular causes of their symptoms may be very different. This means that a treatment that works in one patient will prove ineffective in another. In other cases, diseases that are currently defined as separate conditions may share a common molecular basis. There is therefore now broad recognition that the way diseases are classified needs to change. Many IMI projects are working to develop new ways of grouping or stratifying patients into more meaningful groups. In the long term, this will allow researchers to develop more targeted medicines, and increase the chances of patients receiving treatments that work for them.

BTCure delivers insights into rheumatoid arthritis

Rheumatoid arthritis (RA) is a chronic disease that affects around 1 % of the population. It occurs when the immune system attacks the joints, which become swollen and painful. Novel treatments can alleviate some of the symptoms, but they only provide relief for around two thirds of patients. IMI's BTCure project set out to broaden our knowledge of the factors that trigger the disease and cause disease progression, information that will pave the way for a personalised medicine approach to the disease. The project has been highly successful. Recent findings include the discovery of biological markers that appear to indicate whether or not someone at risk of RA is likely to develop arthritis within the next three years. This finding is important because the RA is thought to be easier to treat in the very early stages before symptoms appear. Elsewhere, BTCure scientists were part of a team that identified molecules that could block the action of tumour necrosis factor (TNF), a protein that has been implicated in a number of inflammatory diseases, including RA as well as Crohn's disease, psoriasis, and multiple sclerosis (MS). According to the research, which is published in the journal PLoS Computational Biology, the two molecules show low toxicity and 'may be further optimised in drug design […] to develop improved treatments for a range of inflammatory and autoimmune diseases'.

Development and use of cohorts, registries and clinical networks for clinical studies and trials

Behind every clinical trial is a cohort of participants who are selected on the basis of a range of criteria. However, for many disease areas, finding the right number of appropriate patients is far from easy. IMI projects are setting up cohorts and networks of trial sites to facilitate the running of clinical trials in challenging areas such as dementia and antimicrobial resistance.

COMBACTE projects continue to deliver clinical studies on antimicrobial resistance

In 2017, IMI's COMBACTE family of projects gained a new member in the form of COMBACTE-CDI, which is dedicated to increasing our understanding of the extent and impact of *Clostridium difficile* infection in Europe. *C. difficile* is one of the most common healthcare-associated infections, with 172 000 cases annually, many of them in the elderly, in Europe alone. Symptoms include diarrhoea and abdominal pain, and it can prove fatal. Meanwhile, the existing projects (COMBACTE-NET, COMBACTE-CARE and COMBACTE-MAGNET) continued to develop the projects' networks and run clinical studies. Highlights from 2017 include:

- ASPIRE-SSI: Over 400 patients enrolled in a study that aims to increase our understanding of *Staphylococcus aureus* surgical site infections (SSIs) in Europe.
- ASPIRE-ICU: Over 1 200 patients enrolled in study to advance understanding of *S. aureus* and *Pseudomonas aeruginosa* ICU (intensive care unit) pneumonia, especially ventilator-associated pneumonia (VAP).
- ANTICIPATE: Completed enrolment of over 1 000 patients in 30 centres across Europe to detect occurrence of *C. difficile* infection following antibiotic treatment, with a view to identifying risk factors for infection.
- RESCUING: Completed gathering data on the treatment of some 1 000 patients with complicated urinary tract infections. Analysis is now ongoing.
- EURECA: Over 1 300 patients enrolled in this study on the risk factors, clinical management and outcomes of patients with multidrug-resistant Gram-negative bacteria infections.
- SAATELLITE: Over 600 patients at risk of developing VAP in an ICU have been enrolled into this Phase II clinical trial of MEDI4893. COMBACTE-NET is working with the Antibacterial Resistance Leadership Group (ARLG) in the US to select additional sites in the US to participate in the study.
- EVADE: Over 350 ICU patients have been enrolled in this Phase II study of MEDI3902, on the prevention of ventilator-associated pneumonia in adult ICU patients.
- REJUVENATE: Patient recruitment completed for this Phase IIa study of aztreonam-avibactam (ATM-AVI) in patients with complicated intra-abdominal infections.
- Phase 3 ATM-AVI study: final preparations are underway through the global collaboration between the consortium, Pfizer and BARDA (Biomedical Advanced Research and Development Authority).
- Good clinical practice (GCP) training: the project ran face-to-face GCP courses for 131 investigators in Bulgaria, Montenegro, Portugal and Romania as well as online courses for 181 investigators.

EPAD a game-changer in clinical trials for the prevention of dementia

In 2017, the EPAD project continued to build its cohort of people who could be invited to take part in a clinical trial of treatments to prevent or slow the onset of dementia. By the end of the year, the number of clinical sites recruiting volunteers had risen to 10; between them, they had screened 422 research participants. The project partners recognised the research participants as the core of the project, and have set up a participant panel to facilitate their involvement in the running of the project. Cohort volunteers are also represented in one of the key decision-making bodies within the project. The project ultimately plans to recruit 6 000 people into the cohort.

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.

EMIF opens up catalogue to research community

In January 2017, the EMIF project announced that it was extending access to the EMIF Data Catalogue to the wider research community. At the time, the online catalogue included 14 population-based data sources (e.g. electronic health records, regional databases) and 46 cohorts (mainly in the Alzheimer's field) where the project partners had consented to providing information to bona fide researchers who want to explore potential data partners for their own work. The catalogue provides basic information to help users investigate the data sources, and further developments are planned. 'This is the first tool of the EMIF platform to have wider access, and in the coming final year we plan to have deployed platforms for researchers to be able to go beyond the Catalogue phase right through suitability evaluation and ultimately conducting studies with data source collaborators,' the project leaders write. 'On behalf of EMIF we hope that this wider access to the first tool of the EMIF platform will be a significant asset to the EU research community, and very much look forward to its continued development and use, eventually within a broader research platform and communities.'

Education and training for new and existing R&D scientists and stakeholders

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.

IMI's first education & training projects still going strong

Four of the projects resulting from the very first IMI Call for proposals in 2008 focused on improving education and training. Although the projects have finished, their legacy lives on.

Drug safety is an extremely important part of the drug development process. Yet, prior to the launch of SafeSciMET, educational and training programmes in drug safety science in Europe were scarce. By bringing together 16 academic institutions and 14 pharmaceutical companies, the project developed a curriculum of 20 courses covering topics along the whole trajectory of drug safety sciences, from developing a drug candidate, through testing it in laboratory studies, and all the way to bringing it to the patient. Professionals can follow single courses in safety sciences or selected subsets of courses, and be accredited for continuing professional development. More than 800 scientists have already been trained through the programme, with around 40% of students coming from the pharmaceutical industry, 35% from academia and 10% from regulatory offices. After the end of the project, the project partners managed to set up a short-term sustainability plan, thanks to which a fourth course can run in 2017 and 2018. This and future course cycles are coordinated and managed by the University of Konstanz.

By bringing together 20 university training programmes, 10 learned societies (e.g. academies of science), 3 competent authorities, several partner training organisations and 15 pharmaceutical companies, PharmaTrain succeeded in developing shared standards and guidelines for the development of post-graduate diploma and master courses in medicines development and related fields. Matthias Gottwald of Bayer commented: 'One of the big achievements is that we now have a relatively big group of key universities running programmes in a joint way, with both the academic and industry experts involved in the development and delivery of the courses. I think we can also be proud of the fact that the quality of these programmes has been recognised by universities in Asia and Latin America, who have decided to join the PharmaTrain family.' After the end of the project, the partners agreed to donate project outcomes to the new PharmaTrain Federation, a non-profit organisation established to continue some of the project's work. The federation is self-sustaining through

membership fees, and among other things, it continues to assess courses offered in the medicines development field.

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.

During 2017, 18 tools/technologies/solutions (e.g. tools for preclinical drug development, biomarkers and tools developed that are predictive of clinical outcomes, improved design and process of clinical trials, knowledge reflected in regulatory guidelines, etc.) developed by IMI projects received regulatory acceptance.

PROactive patient reported outcomes assessed by EMA

Chronic obstructive pulmonary disease (COPD) affects 10 % of people over the age of 50. Symptoms of include shortness of breath, excessive sputum production, and a chronic cough. Because of these symptoms, patients with COPD tend to reduce their physical activity (PA) levels. Even though a lack of physical activity is one of the most common predictors of mortality, before PROactive there were no valid tests to measure the impact of the disease on physical activity levels in patients' daily lives.

By following guidelines outlined by the regulatory authorities, the PROactive project developed innovative patient reported outcome (PRO) tools to measure patients' experience of physical activity in terms of 'amount' of activity and 'difficulty'. They did this in an innovative way by merging questions about patients' experience of physical activity with information obtained through wearable physical activity monitors. A number of organisations, including some from outside the PROactive consortium, have used the tools in their own research. One of the PRO tools, D-PPAC is for daily data collection with a recall period of one day, while the second tool, C-PPAC, with a recall period of seven days, is intended to collect PA data during specified clinical study visits.

Now the European Medicines Agency (EMA) has issued a draft qualification opinion on the PROactive tools. If approved, this would mean that the tools could be used to capture information on patients' physical activity during clinical trials of treatments for COPD.

Looking to the future, even though PROactive has officially ended, the project participants signed a memorandum of understanding (MoU) to stay together and continue to develop the PRO tools. The idea is to oversee future uses of the tools, such as translations to other languages and the development of the tools in other chronic disease areas.

EU-AIMS research cited in EMA guidelines on autism

Around 1 % of children are diagnosed with autism spectrum disorders (ASD), yet there are currently no treatments designed specifically to treat their main symptoms, and appropriate guidance about the safety and efficacy of interventions for these disorders is just being developed. Since its launch in 2012, the EU-AIMS project has worked to generate tools that will enhance our understanding of ASD, and ultimately pave the way for the development of new, safe and effective treatments for use in both children and adults. Now, work by the project is cited in new EMA guidelines on the clinical development of medicinal products for the treatment of ASD, which were issued in November 2017. Most notably, it highlights ongoing EU-AIMS research efforts to identify markers that could potentially be used to diagnose ASD or assess how well new treatments work. In the document, the EMA encourages clinical trial sponsors to engage in the development and validation of biomarkers and use them as 'exploratory efficacy measures' in clinical trials.

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.

CHEM21 method could cut production costs of essential anti-fungal medicine

Scientists from the CHEM21 project have developed a new, more efficient way of producing flucytosine, a medicine used to treat a common and often deadly fungal form of meningitis in people with HIV / AIDS. The method, which is described in a paper in Organic Process Research & Development (OPR&D), is expected to decrease drastically costs of production, and so make the medicine more affordable for the many people with HIV / AIDS who live in low income countries. Flucytosine is very expensive, as its patented manufacture involves carrying out a sequence of four chemical reactions. In the paper, CHEM21 scientists from the University of Durham in the UK explain how they cut the number of reactions needed from four to one. Because it involves just one selective reaction instead of four, the new method uses significantly less energy and raw materials and produces less waste than conventional techniques to manufacture flucytosine. It is also less expensive. Pharmaceutical company Sanofi, which is also part of CHEM21, contracted MEPI, a French non-profit association, to investigate ways to scale up the process. With input from scientists from Durham and Sanofi, MEPI succeeded in setting up a small reactor capable of producing 1 kg per day of raw material. The next step would be for the team at Sanofi to transform the raw material into an active medicine that meets international standards. Meanwhile, the University of Durham has applied for a patent for the technique. The hopes of the team are summed up in the closing paragraph of the OPR&D paper: 'We envisage that this one-step low cost synthesis of flucytosine will help to raise awareness of the neglected [cryptococcal meningitis] health epidemic and ultimately contribute to meeting the urgent requirement for large quantities of flucytosine for low income nations.'

Accessibility of resources/outputs beyond consortium

Many IMI projects have made their outputs available to researchers outside the consortium, thereby increasing their potential impact on drug development. Results include databases, tools, educational materials, glossaries, compound collections, and cell lines. The new IMI website includes a catalogue of accessible results, including a brief description of each resource and a link for more information.

iPiE releases ECOdrug database

The iPiE project released ECOdrug, a new database that connects drugs to their protein targets across different species. The team hopes the tool, which is freely accessible at www.ecodrug.org, will help industrial, academic and regulatory scientists to assess and manage the risks associated with pharmaceuticals in the environment. Medicines are designed to interact with specific targets (e.g. proteins) in the human body. Very often, these targets have equivalents in other species, especially those that are closely related to humans.

The ECOdrug database draws on data from multiple sources and has information on over 600 species, including other primates, rodents, birds, fish, microscopic animals, fungi, and plants. The user-friendly interface has two tabs – one for drug-related information and one for drug targets. A search of a drug name brings up a table showing the targets of the drug and how well they are conserved across different species. Similarly, a search by drug target uncovers links to all drugs that target that protein, and the interface shows an evolutionary tree showing the numbers of species in different groups that have an equivalent to the drug target.

Looking to the future, the project plans to improve ECOdrug further by integrating it with other platforms. The tool is described in detail in a paper in the journal Nucleic Acids Research. The authors conclude: 'Through integration with the systems outlined above, the addition of new features and regular updating, we aim to ensure ECOdrug is maintained as a valuable and contemporary research tool for the communities in drug discovery, comparative and evolutionary biology and (eco)toxicology.'

First batches of ULTRA-DD patient-based assay data released - ahead of publication

The ULTRA-DD project made good on its promise to make its data open source with the publication online of datasets from experiments on autoimmune diseases such as lupus and myositis. Through the experiments, the ULTRA-DD team has identified potential new targets that could inspire the development of new treatments for these diseases. The project hopes that if other researchers probe and use the data, they may uncover further insights that will add to our knowledge of autoimmune diseases and accelerate the development of medicines for these patients, many of whom do not respond well to existing treatments. Currently, additional follow-up studies are ongoing to verify and validate the results.

The data published by ULTRA-DD comes from experiments using technically advanced tests developed by the project partners. In this case, the ULTRA-DD team studied so-called 'B cells' – immune cells which are known to play a central role in lupus and myositis. The project's Scientific Director, Michael Sundström of the Karolinska Institutet says: 'These are the first of a series of related datasets to be released, and we believe that our approach of pre-publication access to such data is truly unique.'

AstraZeneca opens up preclinical safety data to scientific community

Part of AstraZeneca's contribution to the IMI project eTOX was in the form of extensive data on the safety / toxicity profiles of (potential) medicines. In September 2017, the company announced its decision to make the data provided to eTOX available to the wider scientific community through the company's Open Innovation portal. 'Following on from the success of the eTOX project, we are keen to further broaden access to our preclinical safety data in order to help advance the mechanistic understanding and prediction of drug safety and bring safer medicines to patients faster,' said AstraZeneca's Nigel Greene. In a statement on the project website, the eTOX team notes that the project 'has signified a paradigm change in the pharmaceutical industry's willingness to openly share legacy data for the benefit of the wider toxicology community'. The eTOX project resulted in a number of tools for toxicologists, many of which have been made available to the wider scientific community.

WEB-RADR apps launched in Africa

In 2017, new versions of the mobile application for reporting suspected adverse drug reactions (ADRs) developed by the WEB-RADR project were launched in Burkina Faso and Zambia. The WEB-RADR team worked with ZAMRA (the Zambia Medicines Regulatory Authority) and the Burkina Faso medicines agency DGPML (Direction Générale de la Pharmacie, du médicament et des laboratoires) to adapt and tailor the app for each country's specific needs and for localised branding and language. Both apps were launched at ceremonies involving representatives of the countries' ministries of health as well as other core stakeholders. Commenting on the launch, the Burkina Faso Minister of Health Professor Nicolas Méda said that the application was welcome in his country's healthcare system and that he was 'committed to providing all necessary support for a better use of this application and to monitor its impact on the proper use of health products in Burkina Faso'.

1.2.2 Collaborative research and development related outputs from IMI2 projects

IMI's Ebola+ projects continued to deliver and in some cases finalise results in 2017. All of these will help to ensure that the world will be better prepared for the next Ebola outbreak. Furthermore, many of the results have relevance for other diseases.

MOFINA develops device for faster testing of deadly Ebola

IMI's MOFINA project developed a new, portable diagnostic test that will deliver results in under 75 minutes on whether a patient has Ebola or a related disease such as Marburg virus. The device, which is designed to work in sites where high-end laboratory infrastructures are not available, has been validated, CE-IVD marked and is already commercially available. This is the first commercially available test that is both portable and can test for all known Ebola virus strains. It is anticipated that potential buyers could include public health institutes, diagnostic services, the WHO and non-governmental organisations tackling outbreaks. The project partners would like to develop the device further, making it possible to test for a range of other infectious diseases, which are on the list of WHO priority pathogens, such as the Zika virus, dengue and Lassa fever.

Ebola vaccine immune response lasts at least 1 year

Vaccines are another important tool in the effort to contain an outbreak, and here the EBOVAC1 project reported in March 2017 that the immune response triggered by Johnson & Johnson's two-part 'prime boost' Ebola vaccine regimen appears to last at least one year. The finding was published in in the Journal of the American Medical Association (JAMA). The vaccine regimen consists of an initial vaccine dose to prime the immune system, followed by a boost dose of another vaccine which is intended to enhance the immune response over time. Trials of the regimen are taking place in Europe, Africa, and the US. This study focuses on a Phase I trial in Oxford, UK, in which 75 healthy volunteers received the vaccine regimen. Of the 64 people who attended the one-year follow-up, all had high levels in their blood of Ebola virus glycoprotein-specific antibodies; these antibodies appear to play an important role in immunity to the disease.

VSV-EBOVAC identifies signature of promising Ebola vaccine

How exactly does our immune system respond to vaccination? In the first study of its kind, scientists from IMI's VSV-EBOVAC project, studying a promising Ebola vaccine, set out to find out which immune cells get activated early on, which inflammatory markers are released after that, and how this early activity later impacts the production of antibodies against the Ebola virus. In the process, they discovered a unique signature of a promising Ebola vaccine candidate which could not only help predict adverse reactions and the effectiveness of this vaccine, but also inform the development of vaccines for other diseases as well. 'These findings are important and indeed ground-breaking,' said Claire-Anne Siegrist of the University of Geneva, the project's scientific coordinator. 'No signature for this vaccine or any other Ebola vaccine has been previously identified. On a clinical level, this plasma signature can serve as a biological clue (biomarker) to anticipate and determine common side effects and the ability of our bodies to produce protective antibodies against the Ebola virus.' The findings, which were published in the prestigious journal Science Translational Medicine, wouldn't have been possible without IMI, she added. 'The public-private nature of the project was tremendously important in achieving these results. In addition to academic partners, representatives of the vaccine manufacturers played a very important role in the study.'

INNODIA delivers tools to better study diabetes

The goal of INNODIA is to advance our understanding of type 1 diabetes and address the lack of tools and technologies that will allow clinicians to predict, evaluate and prevent the onset and progression of type 1 diabetes. Diabetes arises when the beta cells of the pancreas fail to produce enough of the hormone insulin to regulate blood sugar levels correctly. There are currently no reliable ways to gauge the 'endocrine cell mass' (ECM), i.e. the level of hormone producing cells in the pancreas of patients. This is a problem because scientists need to understand when and how beta cells are lost in people with diabetes, including in people who have received a transplant of these cells. Now, INNODIA scientists have come up with a non-invasive imaging technique that would allow scientists to assess the ECM with relative ease. They identified a gene called DPP6 which is 25 times more active in insulin-producing cells compared to surrounding tissues. The team then generated an antibody that targets the DPP6 protein, and this antibody was tagged so that it would show up in scans. Initial tests using single-photon computed tomography (CT) imaging proved successful. The technique should also prove valuable in drug research, as it will allow scientists to evaluate the impact of new medicines designed to prevent the loss of beta cells in diabetes.

1.2.3 Collaboration among consortia and with external bodies and other sectors

Collaboration in Alzheimer's disease & beyond: the present and the future of IMI initiatives in neurodegeneration

On 15 March 2017, IMI hosted an event on Alzheimer's disease, bringing together all IMI projects involved in this area and other key organisations and initiatives, with the goal of discussing existing collaboration and exploring future opportunities to work together to advance Alzheimer's research.

This gathering was a unique opportunity for all IMI projects in the Alzheimer's field to learn about other projects' activities and complementarities, and to share their plans and results with the IMI SGG Neurodegeneration, EFPIA, the European Commission, the IMI Scientific Committee, and key stakeholders and partners in the Alzheimer's field. A lecture on Alzheimer's disease was organised for all event participants, IMI Programme Office staff and IMI partners.

Outreach and engagement on the microbiome

A preparatory workshop on the microbiome was organised on 30 May 2017 with the aim of identifying gaps and common objectives (pharma vs food / feed & nutrition vs diagnostics) in the microbiome space that could be addressed by a private-public partnership.

IMI staff, EFPIA companies, European Commission representatives, representatives of the food / feed & nutrition (Danone, Lesaffre, Zoetis) and diagnostic (Biocrates, Biofortis, bioMérieux, Insitut Mérieux) industries attended the event.

Priority themes in the microbiome space which would be likely to have industry commitment were identified as well as industry working groups and industrial leaders for the further elaboration of the priority themes to be discussed at the IMI Stakeholder Forum 2017.

Mobilisation of the diagnostics sector

During 2017, IMI made an important effort to mobilise major Europe-based diagnostics companies to explore their willingness to collaborate with each other, and with non-industry partners, to address the potential diagnostics can bring in the fight against antimicrobial resistance (AMR). A first workshop involving more than 10 representatives of the major diagnostics companies active in Europe as well as the Wellcome Trust was held in March 2017, and led to the agreement to further pursue the development of a programme under IMI. This was then followed with a conference entitled 'Diagnostics for reducing antimicrobial resistance', open to all stakeholders, to consult on a first draft of a Call topic. The objectives of the conference were:

- to consult with the relevant stakeholders on a potential Call for proposals under IMI2 addressing the topic 'diagnostics for reducing AMR' that would aim to establish a framework for value-based translation of innovative diagnostics into routine use to reduce AMR;
- to better understand the challenges and hurdles faced by diagnostic innovators for translation of early-stage products into validation, and value demonstration in primary and clinical healthcare practice;
- to obtain a better understanding of what evidence is needed from regulators, health technology assessment bodies and payers for implementation and adoption by healthcare systems.

More than 80 attendees from academia, SMEs, regulators and public health attended and provided important recommendations to the Call topic writing team. As a result, a Call text was finalised in Q3 2017 and the topic 'The value of diagnostics to combat antimicrobial resistance by optimising antibiotic use' was included in IMI2 – Call 13.

Synergies with ECSEL JU

Considering the health dimension of the ECSEL Research Agenda, initial steps were taken in 2017 to explore possibilities for cooperation between ECSEL and IMI in the domain of smart health.

Following discussion between the JUs, a first workshop for project participants on 5 July 2017 focused on three thematic areas:

- sensors and diagnostics;
- imaging hardware & software;
- patient monitoring platforms.

In total, 25 participants from IMI and ECSEL projects attended the workshop. The main outcomes of the workshop were to facilitate focused interactions between specific projects on sensors and diagnostics, identify potential common priority topics for further developments (mid or long-term), and perform an analysis of the gaps for optimising ECSEL and IMI synergies.

To implement the first of these outcomes, a second workshop was held on 8 December 2017 with the aims of facilitating synergies between existing projects with respect to sensors & related platforms, data security and standards; identifying solutions to some of the common challenges; preparing a roadmap for future activities, especially remote sensing & facilitating remote clinical trials. Some 20 participants from IMI and ECSEL projects in the field attended the workshop. The main outcomes were to:

- increase interactions between IMI and ECSEL at a strategic level, such as facilitating participation in respective Governing Board meetings and also ensuring topic developers are aware of the activities of each JU;
- identify and provide early communication on the key technology requirements of future IMI topics to the ECSEL community to allow time to answer these needs;
- facilitate interactions at project level; or example, IMI and ECSEL projects are working on brain activity monitoring and technologies for use in cancer detection.

A follow-up meeting is planned for 2018.

Bio preparedness

In light of recent epidemics of new and old infectious diseases, there is a strong willingness by different organisations to develop a comprehensive preparedness strategy. In an effort to align strategies and ensure complementarities with EU and non-EU organisations, discussions have taken place with the Coalition for Epidemic Preparedness Innovations (CEPI) to explore to what extent IMI could play a role in the EC's commitment to contribute to CEPI's goals. Different kinds of partnerships have been explored (e.g. a formal partnership between CEPI and IMI, an alignment of funding opportunities, a loose relationship with mutual recognition between IMI and CEPI of who is doing what in bio preparedness). As a first step, in 2017 IMI and CEPI agreed to refer to each other's activities on their websites and engage in discussions with the SGG Infections Control on potential topics for future Calls for proposals.

1.3 Stakeholder engagement

1.3.1 SME involvement

The IMI SME engagement strategy developed in 2016 was further implemented in 2017. This strategy focuses on three pillars of explicitly embedding expected SME participation in Call topics, preparing tailored SME communications for different stakeholders, and then disseminating these communications as widely as possible.

- **Call topics**
  In 2017, all Call texts were reviewed to ensure expected SME participation was highlighted. All SGGs were also informed of the importance of embedding SME participation in all IMI topics.
- **Communications**
  Dedicated SME participation communications were developed for each Call launched in 2017. The importance of SME participation was also emphasised during the topic webinars accompanying each Call launch.
- **Outreach**
  The programme of outreach established in 2016 was continued and enhanced. This included preparing a dedicated SME webpage, giving presentations at SME events, and involving the IMI States Representatives Group, Scientific Committee & European SME clusters / umbrella organisations. In 2017, specific webinars for SME participants were held for the first time for IMI2 - Call 13. The first webinar was oversubscribed so a second webinar was organised for early 2018. Following the webinars, a list of SMEs interested in each topic was disseminated via the IMI website. These webinars will also be organised for Call launches in 2018.

In addition to the direct involvement of SMEs as IMI beneficiaries, several IMI projects support the activities of other SMEs. For example, the European Lead Factory (ELF) and ENABLE projects provide open platforms that allow SMEs to progress interesting drug targets and candidate molecules. In the ELF, there are 10 SMEs among the public target owners and one chemistry SME has received the highest monetary reward for submitting a library proposal in 2017. In addition, one spin-off was founded in 2017 based on ELF results: Keapstone Therapeutics, which is researching a potential Parkinson's disease drug in partnership with Parkinson's UK. For ENABLE, in 2017, a further three expressions of interest were submitted by SMEs. Therefore, since 2014, 35 different European SMEs have submitted 43 out of a total 72 expressions of interest to ENABLE.

For the IMI2 programme, SMEs account for 19.1% of 2017 stage 1 applications, 15.6 % of EU funding beneficiaries and receive 8.4 % of EU funding so far.

1.3.2 Patient involvement

Patients remain a key stakeholder group for IMI. A survey of projects showed that as of the end 2017, approximately half of IMI projects have patient organisations either as partners in the consortium or represented in advisory boards, ethics advisory boards, or being consulted for topics of relevance. Among the 78 IMI projects up and running in 2017, 16 (20.5 %) have patients organisations represented in the consortium as full partners, and 21 (26.9 %) projects have patient organisations represented in advisory boards or have consulted with patient groups on specific topics.

IMI teamed up with the DIA (Drug Information Association) to organise a roundtable discussion entitled 'Patient centricity: What is it and how can we make it meaningful?' during the 29th DIA Annual EuroMeeting in Glasgow, UK. The session, which attracted around 100 participants, focused on patient engagement during research & clinical development. Panellists presented case studies, lessons learned and examples of best practices, with a view to demonstrating the value of patient involvement in medicines R&D. The debate triggered a rich discussion on how to ensure patient perspectives are truly captured and implemented.

Patients were also the focus of IMI's Stakeholder Forum, where one of the two tracks was a 'Patient Forum', co-developed with the European Patient Forum (EPF). The event featured discussions on how to achieve real and meaningful patient engagement; how to measure and demonstrate its value; and how to secure willingness to collaborate. The goal of the event was to further the discussion on what are the most

meaningful models of patient collaboration in order for patients' voices to be heard. The results of the event will feed in to further developments of IMI's patient engagement strategy.

Finally, in 2017 IMI launched the recruitment of a seconded national expert (SNE) to work full time on patient engagement.

1.3.3 Interactions and involvement with regulatory authorities

As the scientific knowledge derived from 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 (US Food and Drug Administration), since its creation. In December 2017, the 5th IMI-EMA-FDA Regulatory Science Summit took place.

The meeting, organised by IMI in collaboration with the EMA and FDA, focused on getting the regulators' input on the 'Think Big' programme - the transformative strategic research priorities planned for the second half of the IMI2 programme (2018-2020), in particular the topics proposed for the first Call of 2018. This was an opportunity to discuss:

(1) what the focus of the proposed topic(s) should be to be transformative for drug development, regulatory science and patients' access to innovation;
(2) how they should be shaped to ensure maximal impact of the deliverables and concrete outputs in both the short and medium term;
(3) what other scientific gaps the regulatory authorities would consider important to be tackled in these areas.

This was also an opportunity to get an overview of the progress made on action points agreed at the last IMI-EMA-FDA regulatory science summit held at the end of 2014.

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. In this respect, IMI organised in December 2017 for the project coordinators and SGG members a webinar entitled 'How to engage with regulators (EMA/FDA)'. During this webinar, a recording of which is available online, representatives of the EMA and FDA stressed the importance of early engagement with the regulatory authorities and explained in a practical way the various ways of engaging with the EMA (e.g. innovation task force, qualification advice etc.) and the FDA.

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. This resulted in the EMA issuing Letters of Support to the project SAFE-T on biomarkers for drug-induced vascular injury (DIVI).

Regular teleconferences throughout the year with the EMA and FDA provided an opportunity to exchange information on activities relevant for IMI, and discuss topics and projects under development.

Dialogue with other healthcare decision makers such as health technology assessment bodies and payers has continued through informal meetings, with a view to developing a framework for interactions.

Meanwhile a survey of projects revealed that by the end of 2017, approximately 30 % of IMI projects had regulatory bodies involved either as partners of the consortium (around a third of cases) or via a project advisory board (around two thirds of cases). Of the 78 projects active in 2017, 26 (33.3 %) reported that regulatory bodies were involved either as partners of the consortium (8) or via a project's advisory board (18).

Approximately 10% of IMI projects have submitted at least one request for scientific advice or qualification opinion of innovative development methods to the EMA or FDA. In 2017, of the 78 IMI projects up and running throughout part or the whole of the year, 8 projects (10.3%) have submitted a total of 9 new requests for scientific or qualification advice to the EMA or FDA. During the course of 2017, 18 tools/technologies/solutions (e.g. tools for preclinical drug development, biomarkers and tools developed that are predictive of clinical outcomes, improved design and process of clinical trials, knowledge reflected in regulatory guidelines, etc.) developed by IMI projects received regulatory acceptance.

1.4 Calls for proposals and grant information

1.4.1 Launch and management of IMI2 JU Calls in 2017

In 2017, three Calls for proposals were launched (IMI2 - Calls 11, 12 and 13) and six Calls were at various stages of the evaluation and granting process (IMI2 - Calls 7, 8, 9, 10, 11 and 12). The evaluation stages for IMI2 - Calls 7 and 8 (first cut-off date) had been completed in 2016 but grant preparation and Grant Agreement signature were completed in 2017.

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 2017 (AWP2017) were addressed through Calls launched in 2017.

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

- 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 SRG and the Scientific Committee), as well as the EC. There were no redress procedures after evaluation in 2017.

Chart showing overview of Call processes in 2017

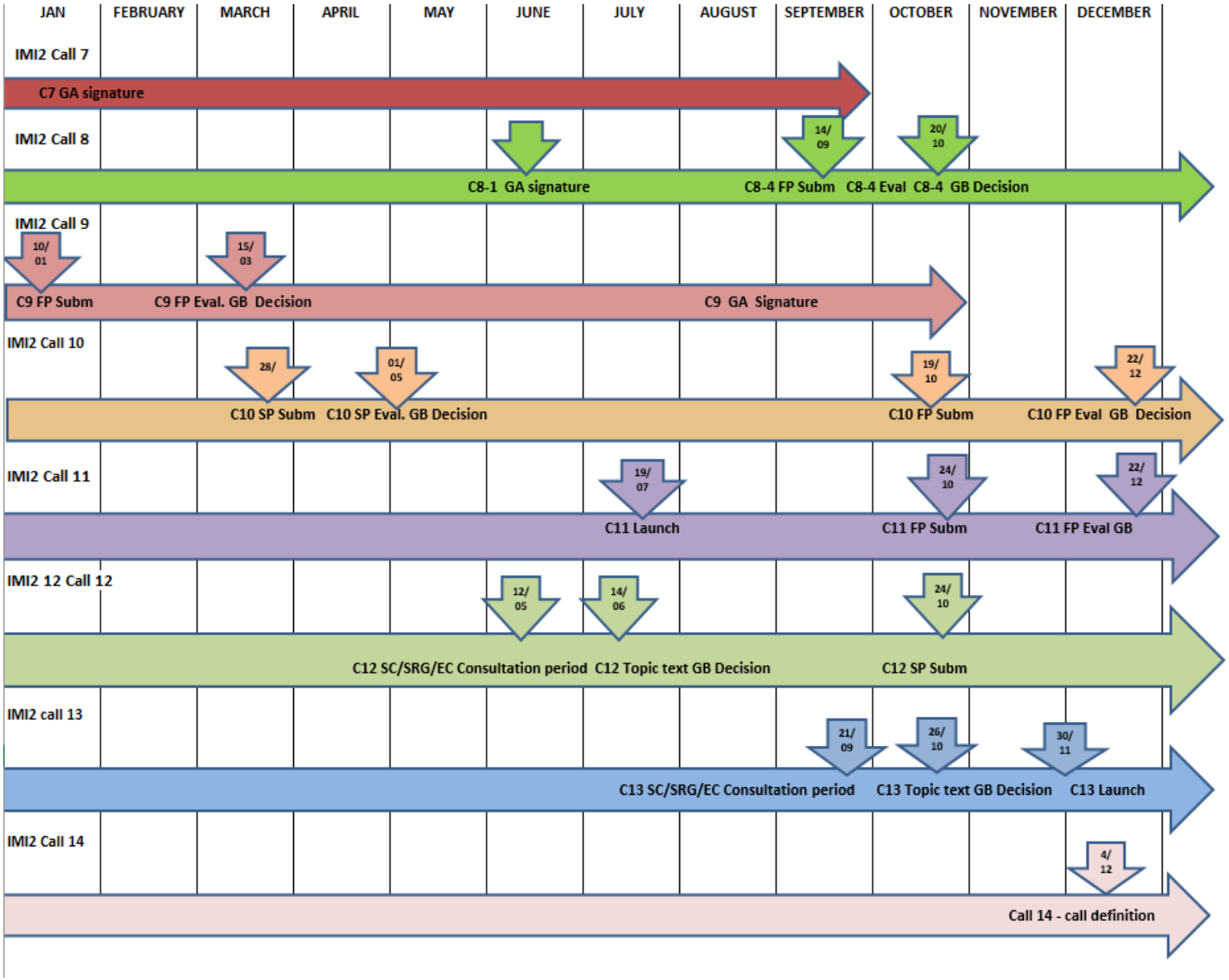


Table summarising key information related to IMI Call launches, submission deadlines and Grant Agreements signed in 2017[3]

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 2017
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 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	two-stage	18/12/2015	17/03/2016	32	317	7	7	7

[3] Note: all topics are research and innovation actions (RIAs), with the exception of one coordination and support action (CSA) in IMI2 - Call 7 and IMI 2 - Call 13; these are 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 2017
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	2
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 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	Third cut-off date: 16/03/2017	0	0	0	0	0
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	Fourth cut-off date: 14/09/2017	1	5	1	1	open
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) ▪ 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	two-stage	27/04/2016	26/07/2016	17	253	6	6	6

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 2017
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 ▪ Unlocking the solute carrier gene-family for effective new therapies (unlock SLCs) ▪ Patient perspectives in medicines lifecycle ▪ Personalised medicine approaches in autism spectrum disorders	two-stage	21/12/2016	28/03/2017	36	406	8	8	open
IMI2 Call 11	▪ Exploitation of IMI project results	single-stage	19/07/2017	24/10/2017	6	39	3	3	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 2017
IMI2 Call 12	▪ Development and validation of technology enabled, quantitative and sensitive measures of functional decline in people with early stage Alzheimer's disease (RADAR-AD) ▪ FAIRification of IMI and EFPIA data ▪ Development of sensitive and validated clinical endpoints in primary Sjögren's Syndrome (pSS) ▪ European Health Data Network (EHDN) ▪ Analysing the infectious disease burden and the use of vaccines to improve healthy years in aging populations ▪ Discovery and characterisation of blood-brain barrier targets and transport mechanisms for brain delivery of therapeutics to treat neurodegenerative & metabolic diseases ▪ European Screening Centre: unique library for attractive biology (ESCulab)	two-stage	19/07/2017	24/10/2017	29	389	open	open	open
IMI2 Call 13	▪ Assessment of the uniqueness of diabetic cardiomyopathy relative to other forms of heart failure using unbiased pheno-mapping approaches ▪ Genome-Environment Interactions in Inflammatory Skin Disease ▪ The value of diagnostics to combat antimicrobial resistance by optimising antibiotic use ▪ Mitochondrial Dysfunction in Neurodegeneration ▪ Support and coordination action for the projects in the neurodegeneration area of the Innovative Medicines Initiative (CSA) ▪ A sustainable European induced pluripotent stem cell platform	two-stage	30/11/2017	28/02/2018	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 2017
	▪ Linking digital assessment of mobility to clinical endpoints to support regulatory acceptance and clinical practice ▪ Human tumour microenvironment immunoprofiling ▪ ConcePTION – Continuum of Evidence from Pregnancy Exposures, Reproductive Toxicology and Breastfeeding to Improve Outcomes Now ▪ Improving the preclinical prediction of adverse effects of pharmaceuticals on the nervous system ▪ Translational Safety Biomarker Pipeline (TransBioLine): Enabling development and implementation of novel safety biomarkers in clinical trials and diagnosis of disease Pilot programme on a Clinical Compound Bank for Repurposing: ▪ Cardiovascular diseases and diabetes ▪ Respiratory diseases ▪ Neurodegenerative diseases ▪ Rare/orphan diseases								

Table summarising IMI2 Calls for proposals launched in 2017, highlighting the priorities of Annual Work Plan 2017 implemented, the date of Call launch and budget available per Call

Call number	Call type	Number of topics	Annual Work Plan 2017 Priorities implemented	Launch date	Budget		
					EU (in EUR)	EFPIA (in EUR)	Associated Partners (in EUR)
IMI2 Call 11	Single stage	1	▪ Exploitation of IMI Project Results	19 July 2017	5 000 000	0	none
IMI2 Call 12	Two stage	7	▪ Neurodegeneration and other Neuroscience Priorities ▪ Immunology ▪ Infection control including vaccines ▪ Data and Knowledge Management ▪ Other Enablers of innovation	19 July 2017	64 077 000	60 887 000	1 475 000
IMI2 Call 13	Two stage	15	▪ Diabetes/metabolic disorder ▪ Neurodegeneration and other Neuroscience Priorities ▪ Immunology ▪ Infection control including vaccines ▪ Translational safety ▪ Data and Knowledge Management ▪ Oncology ▪ Other Enablers of innovation	30 November 2017	116 421 000	101 462 000	5 167 000

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

Evaluation experts

IMI selects independent experts to evaluate proposals via the relevant Horizon 2020 tool. Experts follow the procedures outlined in the Manual for submission, evaluation and grant award and assess proposals against the evaluation criteria. In 2017, IMI used 120 experts from 29 countries in the evaluation of IMI2 - Calls 8, 9, 10 and 11. Most of the experts (90 %) came from EU and H2020 associated countries. Half of the experts (62) came from academia and research institutes. Other sectors represented are: private sector (18), public sector (5), consultancy firms (12), international organisations (2) and other type of organisations (21).

For each Call in 2017, the breakdown of evaluators is as follows:

Call	Total no. experts	Science evaluation	Ethical screening	Observers	Gender Female	Gender Male
IMI2 - Call 8: 4th cut-off date*	9	5	3	1	4	5
IMI2 - Call 9: stage 2	36	31	3	2	18	18
IMI2 - Call 10: stage 1	58	56	0	2	26	32
IMI2 – Call 10: stage 2	58	50	6	2	26	32
IMI2 - Call 11: single stage	15	10	3	2	7	8

*For IMI2 - Call 8 - third cut-off date, no applications were received.

IMI2 – Call 7

Progress in 2017: Signature of the GAs for 7 projects

In 2017, the GAs of the seven projects resulting from the IMI2 - Call 7 (H2020-JTI-IMI2-2015-07-two-stage) were signed: IB4SD-TRISTAN, DO->IT, IMPRiND, NGN-PET, ITCC-P4, BigData@Heart and MACUSTAR.

IMI2 – Call 8

Progress in 2017: Signature of the GAs for 2 projects (1st cut-off date). From FP submission and evaluation to GAP for 1 project (4th cut-off date)

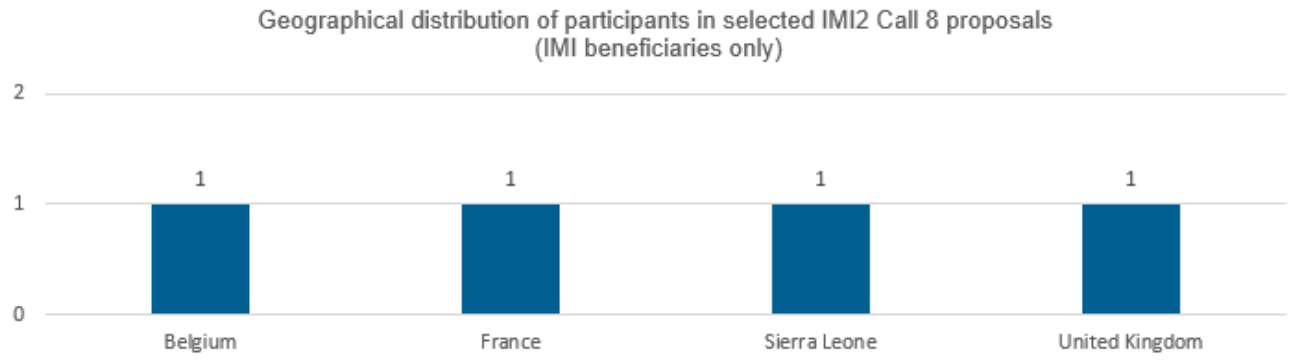
IMI 2 - Call 8 (H2020-JTI-IMI2-2015-08-single-stage) on Ebola and other filoviral haemorrhagic fevers (Ebola +) programmes: future outbreaks consists of a single topic with multiple cut-off dates. The Call was launched on 18 December 2015 with deadlines for submission of FPs of 16 March 2016, 15 September 2016, 17 March 2017, 14 September 2017 and 15 March 2018.

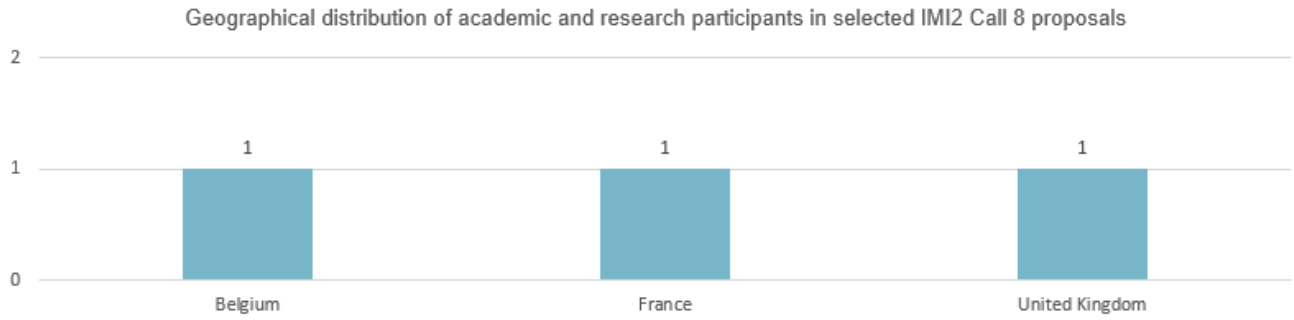
The GAs resulting from the proposals submitted in response to the first cut-off date of 16 March 2016 were signed in the first part of 2017: PEVIA and VSV-EBOPLUS.

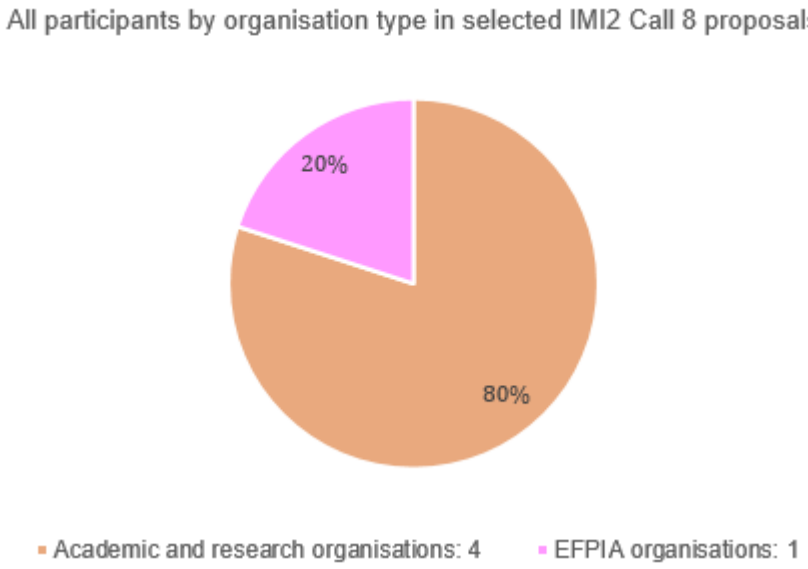
No eligible proposals were received in response to the third cut-off date of 17 March 2017.

The only proposal submitted in response to the fourth cut-off date was evaluated according to the IMI rules and procedures. The Governing Board adopted the evaluation results on 20 October 2017. The winning consortium was invited to start GAP and the GA will be signed in 2018.

IMI2 - Call 8: Participant details[4]







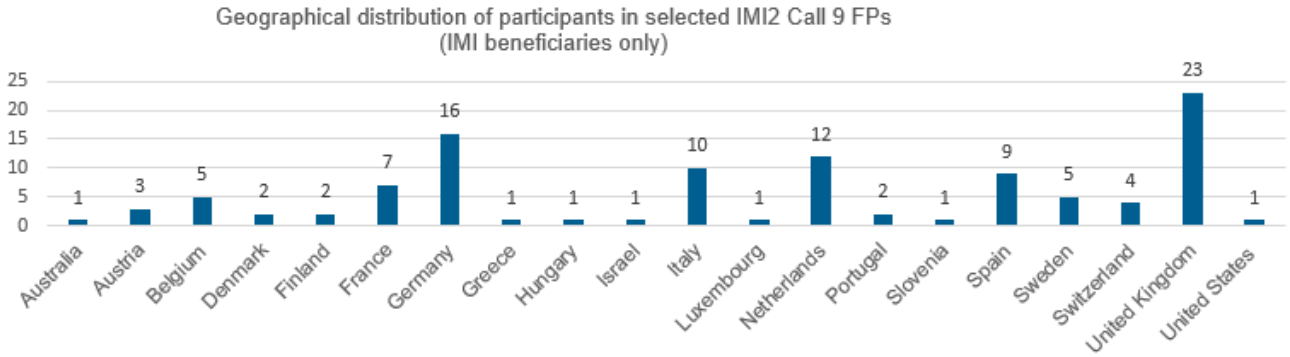
[4] The statistics are based on the information provided by the applicants at the moment of submission. In order to ensure consistency with the information provided at the time of the application and kept into the tool, incorrect information will be corrected at a later stage, during Grant Agreement preparation.

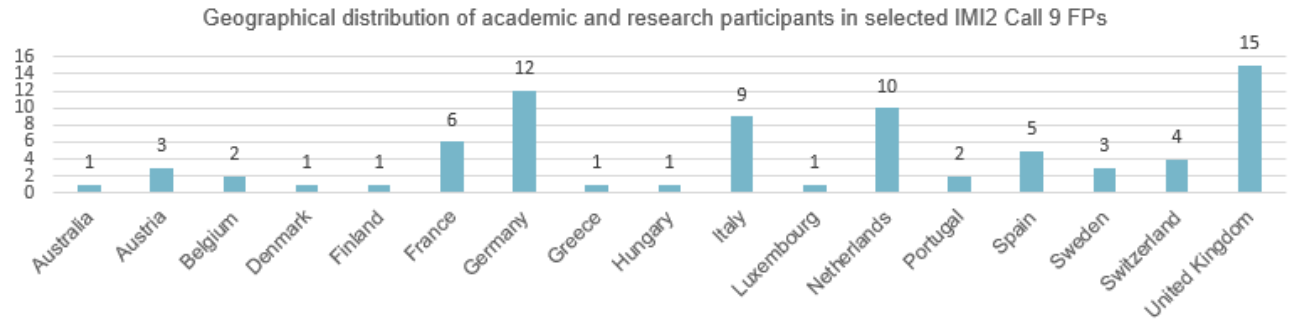
IMI2 – Call 9

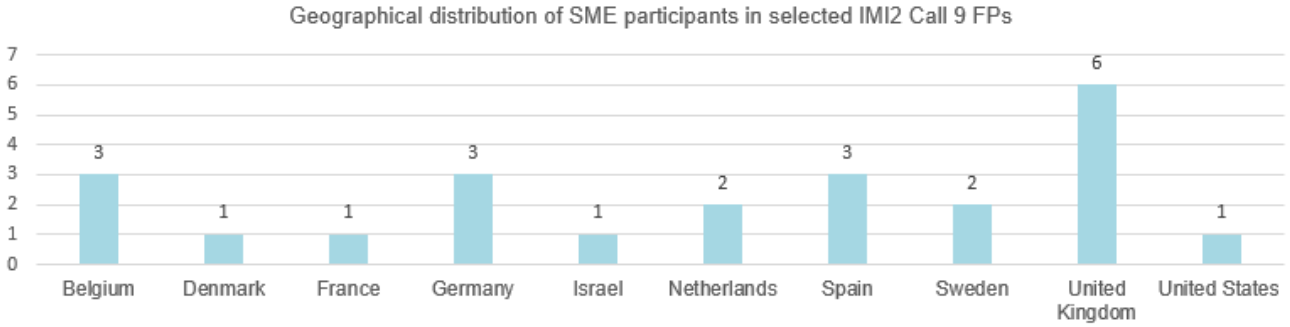
Progress in 2017: From the evaluation of FP to GA signature for 6 projects

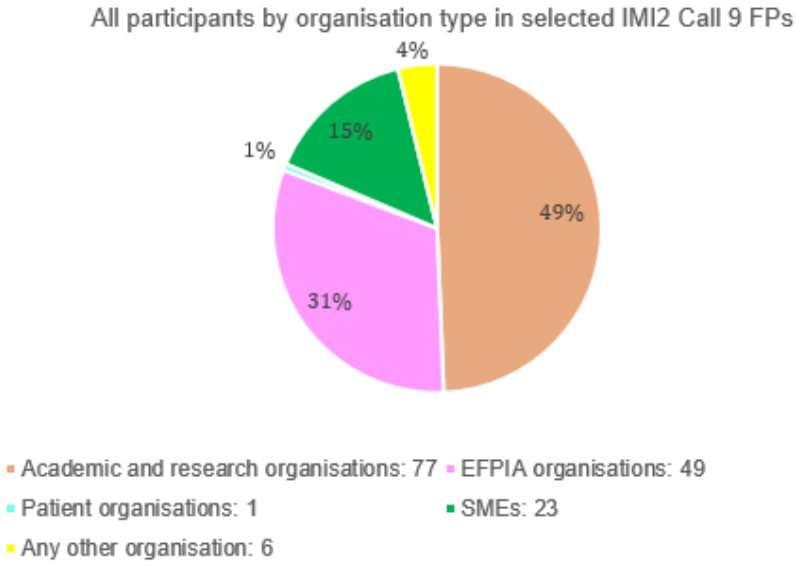
IMI2 - Call 9 (H2020-JTI-IMI2-2016-09-two-stage) was launched on 27 April 2016, with an FP submission deadline of 10 January 2017. The submission of the six FPs and the stage 2 evaluation was completed successfully according to IMI rules and procedures. The Governing Board adopted the outcome on 15 March 2017, and the applicants were invited to start GAP. The GAs were signed in the last part of 2017 for the projects COMBACTE-CDI, DRIVE, EQIPD, eTRANSAFE, RTCure and LITMUS.

IMI2 - Call 9: Full proposal participant details









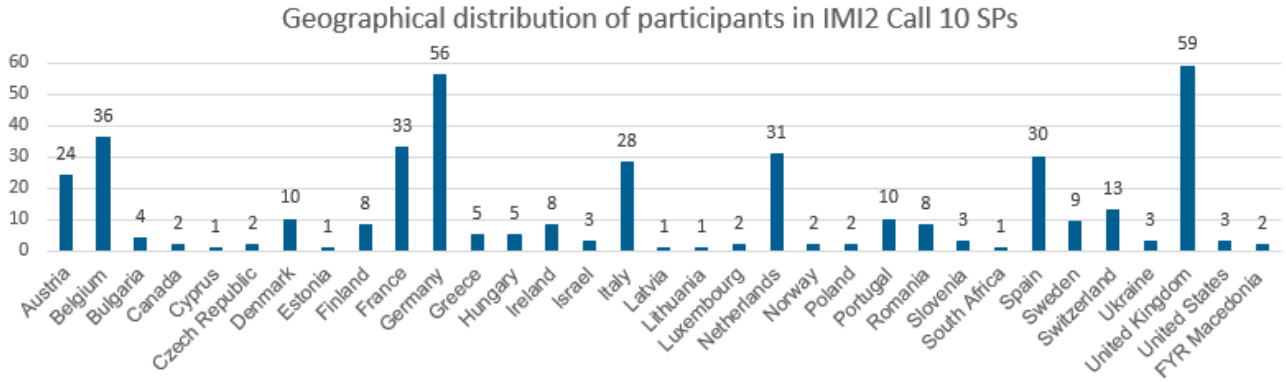
IMI2 – Call 10

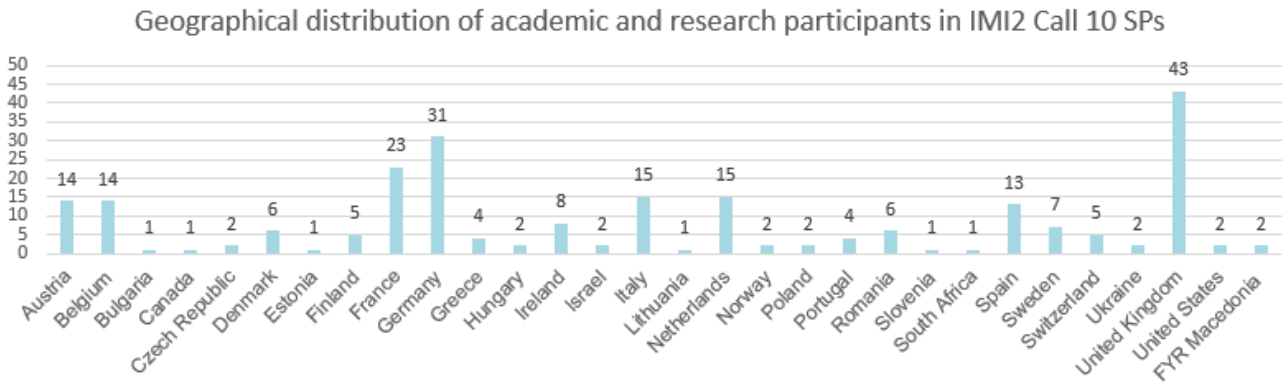
Progress in 2017: from evaluation of SPs to the approval of FP evaluation results

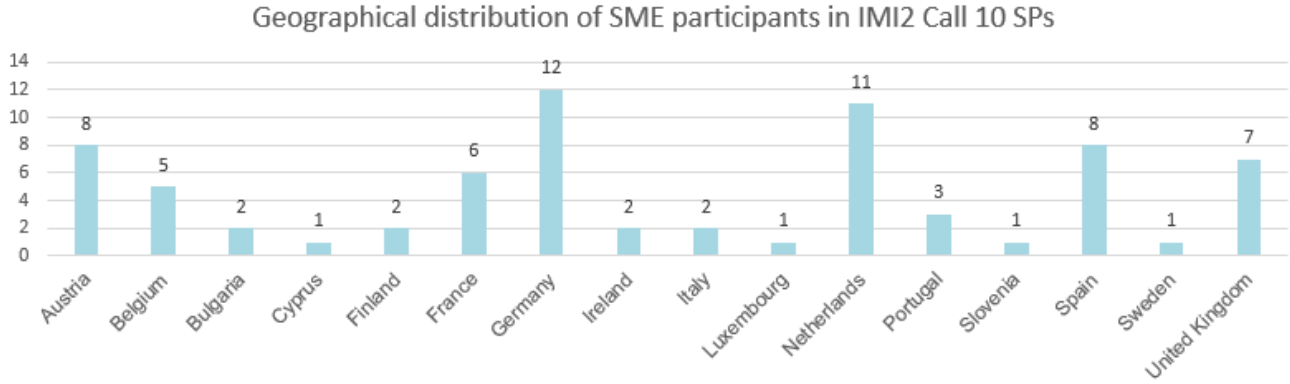
IMI2 - Call 10 (H2020-JTI-IMI2-2016-10-two-stage) was launched on 21 December 2016 with a deadline for submission of SPs of 28 March 2017. The submission of SPs at the stage 1 was completed successfully according to the IMI rules and procedures and the Governing Board adopted the evaluation results on 1 May 2017. The first-ranked SP in each of the eight topics was invited to prepare a FP together with the pre-defined industry consortium, with a deadline for submission of 19 October 2017.

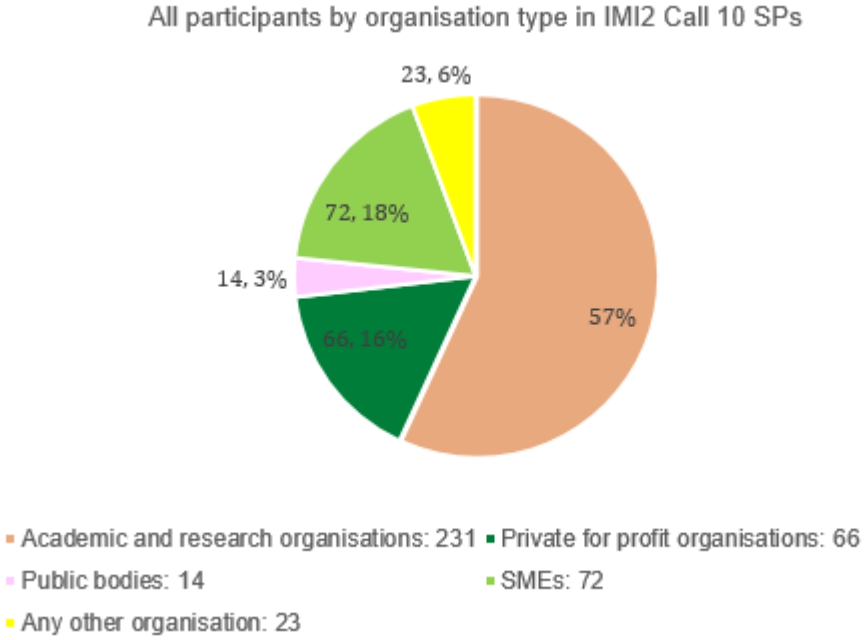
The stage two in-house evaluation was successfully concluded and the IMI Governing Board adopted the evaluation results on 22 December 2017. The applicants will be invited to start the GAP, with the aim of having the GAs signed in the first part of 2018.

IMI2 - Call 10: Short proposal participant details

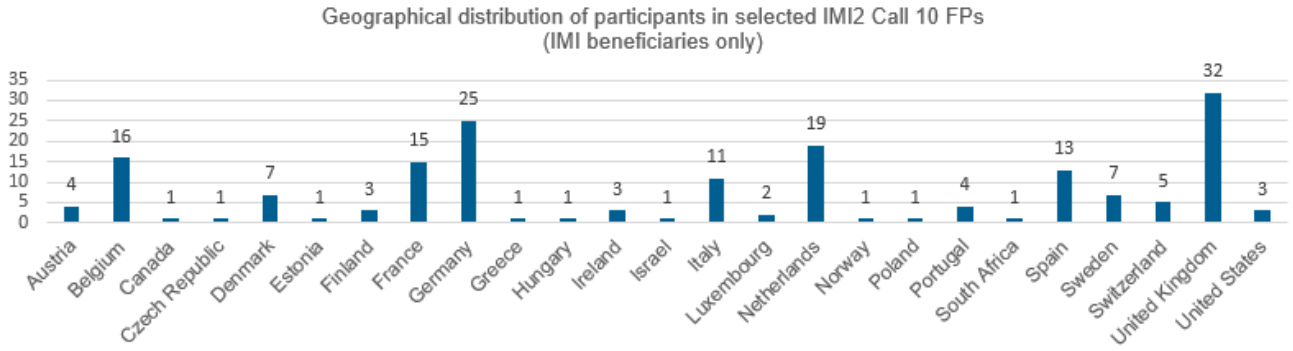


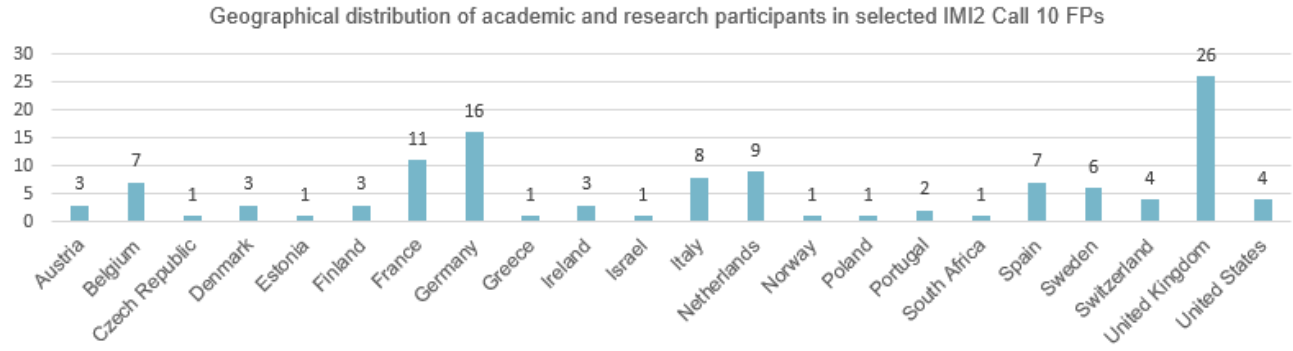

Geographical distribution of academic and research participants in IMI2 Call 10 SPs
50
45
40
35
30
25
20
15
10
5
0
14 14 1 1 2 6 1 5 23 31 4 2 8 2 15 1 15 2 2 4 6 1 1 13 7 5 2 43 2 2
Austria
Belgium
Bulgaria
Canada
Czech Republic
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Ireland
Israel
Italy
Lithuania
Netherlands
Norway
Poland
Portugal
Romania
Slovenia
South Africa
Spain
Sweden
Switzerland
Ukraine
United Kingdom
United States
FYR Macedonia

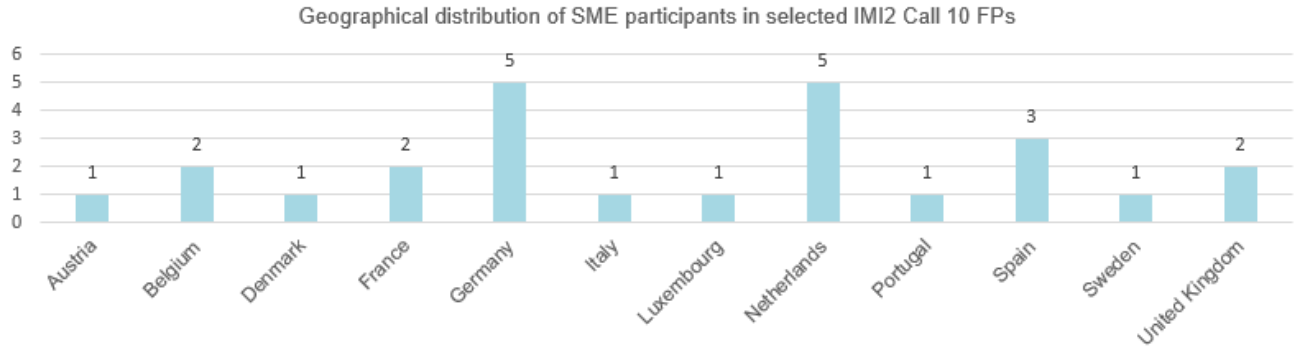

Geographical distribution of SME participants in IMI2 Call 10 SPs
14
12
10
8
6
4
2
0
8 5 2 1 2 6 12 2 2 1 11 3 1 8 1 7
Austria
Belgium
Bulgaria
Cyprus
Finland
France
Germany
Ireland
Italy
Luxembourg
Netherlands
Portugal
Slovenia
Spain
Sweden
United Kingdom

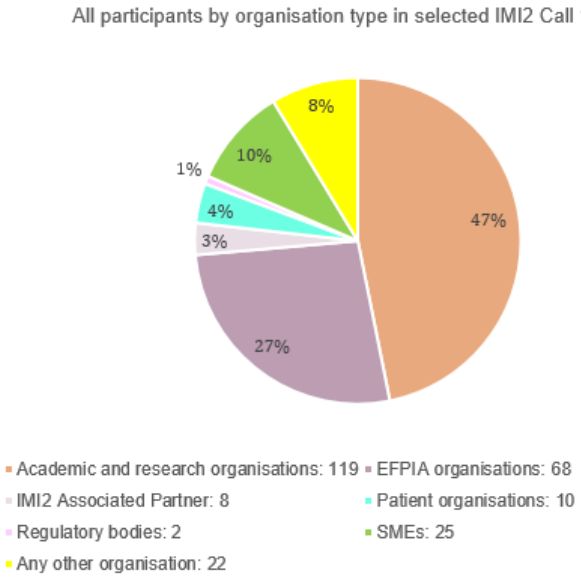

All participants by organisation type in IMI2 Call 10 SPs
23, 6%
72, 18%
14, 3%
57%
66, 16%
Academic and research organisations: 231
Private for profit organisations: 66
Public bodies: 14
SMEs: 72
Any other organisation: 23

IMI2 - Call 10: Full proposal participant details







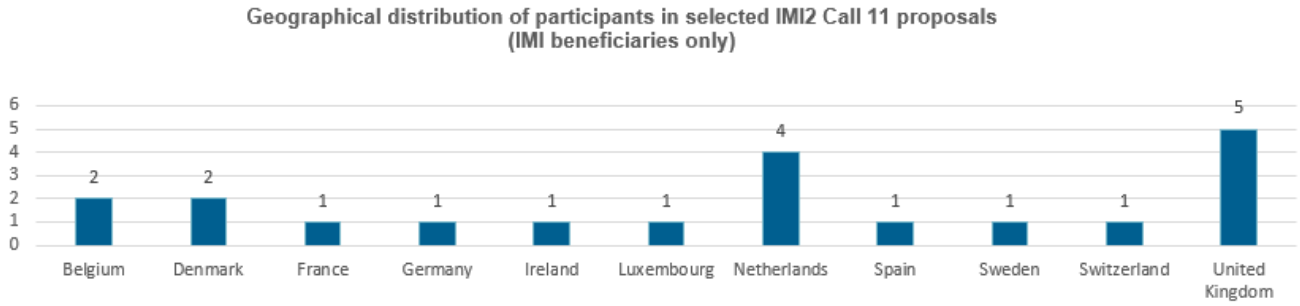


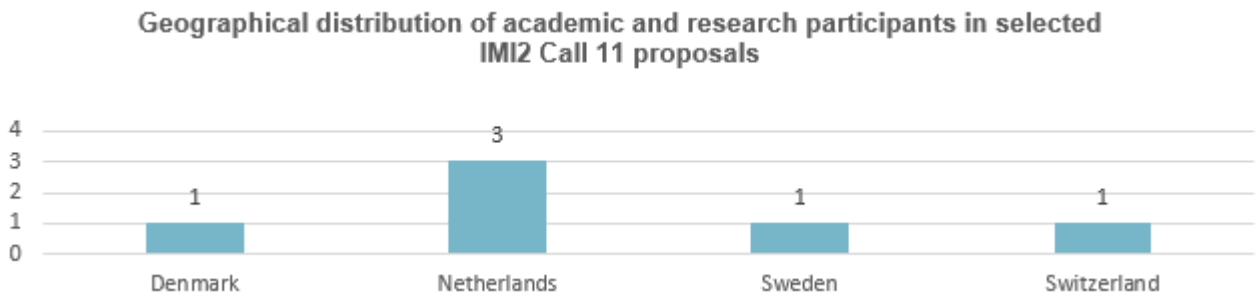
IMI2 – Call 11

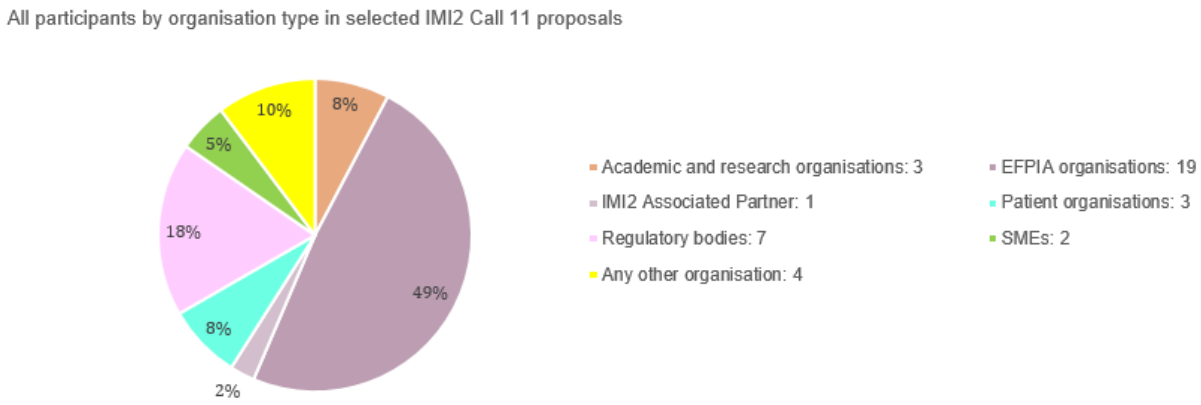
Progress in 2017: from the launch of the Call to the approval of the evaluation results

IMI2 - Call 11 (H2020-JTI-IMI2-2017-11-single-stage), the Call on the exploitation of the results of seven IMI projects, was launched on 19 July 2017, with a submission deadline of 24 October 2017. The evaluation of proposals was done according to the IMI rules and procedures and the Governing Board approved the evaluation results on 22 December 2017. The three winning consortia will be invited to start the GAP and these should be concluded in the first part of 2018.

IMI2 - Call 11: Participant details







IMI2 – Call 12

Progress in 2017: from the launch of the Call to the evaluation of SPs

IMI2 - Call 12 (H2020-JTI-IMI2-2017-12-two-stage) was launched on 19 July 2017, with a submission deadline of 24 October 2017 for SPs. The evaluation of the seven topics' SPs was done according to the IMI rules and procedures. Governing Board decision approving the evaluation results is expected in January 2018.

IMI2 – Call 13

Progress in 2017: launch of the Call

IMI2 - Call 13 (H2020-JTI-IMI2-2017-13-two-stage) was launched on 30 November with a deadline for submission of SPs of 28 February 2018.

Table summarising the number of beneficiaries and budgets for projects with GAs signed in 2017

IMI2 Call	Project acronym	No. IMI beneficiaries	No. EFPIA companies	No. Associated Partners	IMI funding to academic & research orgs. (EUR) (1)	IMI funding to SMEs (EUR) (2)	IMI funding to patient orgs. (EUR) (3)	IMI funding to other orgs. (EUR) (4)	Total IMI contribution to bene-ficiaries (EUR) (1+2+3+4) = (5)	EFPIA in-kind contribution (EUR) (6)	Associated Partners' contribution (EUR) (7)	Total budget (EUR) (= 5+6+7)
7	BigData@Heart	15	5		8 196 420	443 062		1 025 488	9 664 970	9 734 000		19 398 970
7	DO->IT	14	22		2 880 656		221 389	447 788	3 549 833	3 604 817		7 191 755
7	IB4SD-TRISTAN	16	9		8 651 432	3 202 364		146 204	12 000 000	10 448 317		22 641 050
7	IMPRiND	12	6		4 685 000	0		0	4 685 000	6 365 900		11 363 398
7	ITCC-P4	19	6		5 935 212	1 126 850		307 938	7 370 000	8 450 094		16 562 830
7	MACUSTAR	11	4		6 746 579		552 281	726 140	8 025 000	8 067 500		16 092 500
7	NGN-PET	4	2		600 000	900 000		0	1 500 000	1 828 000		3 328 000
8	PEVIA	14	1		5 326 570	863 000		0	6 189 570	6 068 591		17 731 396
8	VSV-EBOPLUS	10	1		7 367 500	485 000	701 250	0	8 553 750	4 828 910		15 430 660
9	COMBACTE-CDI	8	6		2 312 305	0		0	2 312 305	2 312 305		4 624 610
9	DRIVE	11	4		7 643 063	871 813	161 500	323 438	8 999 813 *	1 000 125		9 999 938
9	EQIPD	18	11		3 397 531	910 534		187 458	4 495 523	5 094 138		9 627 162
9	eTRANSAFE	16	12		14 617 000	4 861 125		521 875	20 000 000	18 980 336		40 623 242
9	LITMUS	38	11		12 882 208	2 252 743		662 930	15 797 881	15 045 213		32 507 326
9	RTCure	14	6		5 520 000	480 000		0	6 000 000	6 625 000		13 846 866

* includes EUR 4 million provided by EFPIA directly to IMI

1.4.2 Interim reviews for IMI projects

In 2017, IMI conducted 16 reviews of projects from IMI1 - Calls 3, 6, 8, 10, 11 and IMI2 - Calls 2, 3 and 4. The expert reviewer panels consisted of at least three experts, one from each of the IMI Scientific Committee, the full project proposal evaluation panel, and from suggestions by the consortium.

Interim Reviews for IMI1 - Calls, 3, 6, 8, 10, and 11

IMI project acronym	Call #	Full project name	Interim review
COMBACTE-NET	IMI1 - Call 6	Combatting Bacterial Resistance in Europe	25/01/2017
AETIONOMY	IMI1 - Call 8	Organising mechanistic knowledge about neurodegenerative diseases for the improvement of drug development and therapy	21/03/2017
ENABLE	IMI1 - Call 8	European Gram-negative Antibacterial Engine	26/04/2017
FLUCOP	IMI1 - Call 10	Standardization and development of assays for assessment of influenza vaccines correlates of protection	23/05/2017
iPiE	IMI1 - Call 11	Intelligent Assessment of Pharmaceuticals in the Environment	30/05/2017
iABC Programme	IMI1 - Call 11	Inhaled antibiotics in bronchiectasis and cystic fibrosis	05/07/2017
Cancer ID	IMI1 - Call 11	Cancer treatment and monitoring through identification of circulating tumour cells and tumour related nucleic acids in blood	12/09/2017
EPAD	IMI1 - Call 11	European prevention of Alzheimer's dementia consortium	15/09/2017
DIRECT	IMI1 - Call 3	Diabetes research on patient stratification	20/09/2017
ULTRA-DD	IMI1 - Call 11	Unrestricted leveraging of targets for research advancement and drug discovery	12/10/2017
ZAPI	IMI1 - Call 11	Zoonotic anticipation and preparedness initiative	21/11/2017

COMBACTE-NET

The COMBACTE-NET project aims to give antibiotic drug development a much-needed boost by pioneering new ways of designing and implementing efficient clinical trials for novel antibiotics. The interim review highlighted that overall the COMBACTE-NET project has developed an infrastructure for clinical trials across Europe with a laboratory network and statistical support to aid in trial design. The experts considered that while it was too early to judge the overall impact of this ambitious project, especially considering many delays in milestones and deliverables, notable successes were reported and real progress made. Experts noted that several lessons have been learned about developing a public-private partnership to support a large clinical and laboratory network for surveillance and clinical trials. The experts made several important recommendations going forward in particular to: 1) implement rigorous quality standards and monitor compliance of the clinical sites and labs of the networks; 2) develop clear risk assessment, management and tracking tools; 3) strengthen project management with quality/timely reporting and efficient communication; and 4) develop a pool of backup molecules or products to be included in the consortium especially if any current protocols are withdrawn by sponsors. Sustainability was also an important aspect flagged by the experts. A follow-up review will take place in 2018.

AETIONOMY

The AETIONOMY project is paving the way towards a new approach to the classification of neurodegenerative diseases, particularly Alzheimer's and Parkinson's diseases (AD & PD), thereby improving drug development and increasing patients' chances of receiving a treatment that works for them. The reviewers recognised that the project had made some obvious significant progress, particularly over the last year. Some obstacles have been overcome, and a number of novel observations have been made. The programme has built essential infrastructure and tools including imaging ontologies, BEL (biological expression language) models, the AETIONOMY knowledge base, and ingesting key data sets from ADNI (Alzheimer's Disease Neuroimaging Initiative) and PPMI (Parkinson's Progression Markers Initiative). Individually and in aggregate these all provide important enduring assets for the field. Furthermore, specific mechanistic insights for both AD and PD have been successfully achieved. However, the overall methodology (the type of approach used in this project) and how it can be adapted to other projects in the future is also an important outcome. The reviewers suggested that this should be emphasised, and both the specific findings on AD and PD as well as the overall approach should be further disseminated.

ENABLE

The ENABLE project, within IMI's New Drugs for Bad Bugs (ND4BB) programme, is working to advance the development of potential antibiotics against Gram-negative bacteria, such as *Escherichia coli*. Overall, the reviewers were impressed with what was achieved by the project during the first three reporting periods and with the potentially high impact the project could have. A successful drug discovery platform has been established that has enabled the prosecution of multiple antibacterial programs in parallel. The reviewers confirmed that the project achieved many of its objectives with relatively minor deviations. This speaks to the ENABLE leadership and project organisation, including the Portfolio Management Committee (PMC) as the central decision-making body, allowing timely go / no go decision-making. While its true impact still remains to be seen, ENABLE is on its way to evolving into a consortium model for driving discovery that in itself could prove to be unique. If successful, the ensuing drug discovery / development paradigm could make a substantial impact beyond the delivery of a Phase I compound.

FLUCOP

FLUCOP aims to improve and standardise existing immunological assays and to develop new tools to better evaluate the efficacy of future seasonal human influenza vaccines. The reviewers acknowledged that the FLUCOP consortium successfully established and agreed upon common protocols to perform assays for haemagglutination inhibition (HAI), virus neutralisation (VN), and for the cell preparation procedures to be used in cell-mediated immunity (CMI)-based tests. Because of some delays concerning the standardisation of the VN assay and the start of the training programme on HAI and VN, the reviewers recommended a rapid completion of those outstanding tasks and a careful monitoring of progress towards objectives in the forthcoming year, including a re-evaluation of needs and the feasibility of the chosen approaches (e.g. VN standardisation versus enzyme-linked immunosorbent assay (ELISA) development for neuraminidase (NA) antibodies). The reviewers appreciated the good management structure and the great collaborative spirit in the consortium that have facilitated the achievement of important milestones. Nevertheless, the reviewers flagged the lack of sustainability plans and recommended the consortium address this aspect with the involvement of regulatory and standardisation bodies.

iPiE

Although measures are in place to limit the environmental impact of new medicines, more research is needed in this important area. The iPiE project's goal is to develop a framework that will provide methodologies to prioritise new and existing medicinal compounds for a comprehensive environmental risk assessment. The expert panel found that the project has achieved substantial progress in several areas:

- text mining strategies have been developed that are able to dig through an impressive amount of published information in order to extract important information on toxicity, modes of action, bioaccumulation, etc.;
- a first set of seven active pharmaceutical ingredients (APIs) has been experimentally evaluated for their toxicity;
- a spatially explicit exposure assessment framework has been developed that allows the estimation of environmental concentrations at selectable points in / at European river systems;
- the central database has been designed and populated with the first datasets;
- a substantial amount of work has also been invested to produce an overview of the state of the art.

The review panel made a number of recommendations, for example, developing dedicated strategies to make the project's outputs available to the general public. Currently, a lot of the project's outcome is quite 'fish-centric'. The consortium should consider all three trophic levels (algae, invertebrates, fish) which are equally important for the environmental risk assessment of an API, and even effect assessments for prokaryotes are routinely required. The consortium should also ensure their work is better targeted towards tangible contributions to the regulatory environmental risk assessment process that is outlined in the EMA guideline.

EPAD

EPAD represents a very significant investment in the ability to efficiently capture and test the most promising approaches to preventing Alzheimer's disease (AD). Its parts include:1) a registry from which to recruit subjects; 2) a longitudinal cohort for studies to characterise disease onset and progression using a variety of clinical and biomarker measures; and 3) a research platform that employs adaptive, multi-arm proof-of-concept studies to guide ongoing development of novel interventions. EPAD is creating an infrastructure, both technical and intellectual, to support its overall goals, in which each of the aforementioned elements play a well-defined role(s). The reviewers were impressed with EPAD's opportunities for benefiting AD. Equally, they saw opportunities for enhancing EPAD's programmes. EPAD is a very important step forward in providing a clinical infrastructure to support understanding and prevention of AD. Progress to date is encouraging with no truly significant concerns regarding the overall direction and pace of achievement. Nevertheless, there are still risks that may limit the full success of the project: the consortium has to focus their efforts towards increasing the pace of research participant enrolment, and in investing robustly in securing a suitable pipeline of interventions. The reviewers also encouraged efforts for proactively engaging stakeholders, in particular policy makers and regulators. This will help EPAD to prosper and make EPAD benefits more generally available.

DIRECT

Type 2 diabetes patients are a diverse group; in some, the disease progresses rapidly, while in others it takes a slower course. Similarly, a treatment that works well in one patient may prove less effective in another. This has led researchers to acknowledge that there are actually a number of different subtypes of type 2 diabetes. The goal of the IMI-funded DIRECT project is to identify these subtypes and determine the most appropriate treatments for them. The second interim review of the DIRECT project was held in 2017 and the reviewers pointed out that the DIRECT project has made some important advances since the last review. Importantly, the recommendations of the previous review have been acknowledged and the project direction and priorities have been adjusted accordingly. Within each work package, the consortium has identified and described gaps and key issues relevant to the disease area as well as technical (sample storage matters) and governance issues and has addressed them accordingly.

ULTRA-DD

The ULTRA-DD project's goal is to deliver new tools and resources to speed up the development of truly innovative medicines, especially in the areas of autoimmune and inflammatory diseases, where new treatments are urgently needed. The reviewers found that the project has made impressive progress towards the set goals. The technologies and methods applied are state of the art and the expertise of the team was considered outstanding. Major achievements were made and several target numbers for agreed milestones and deliverables were even exceeded, e.g. the number of purified protein variants and validated antibodies, of new protein structures, including structures of integral membrane proteins, of chemical probes and patient-derived cell assays. For the second half of the project, the reviewers made a number of recommendations to increase the impact and visibility of the project, such as to strengthen the current focus on autoimmune and inflammatory disease and to more clearly differentiate from the Structural Genomics Consortium. The reviewers were convinced that ULTRA-DD is providing an extremely valuable resource for academic researchers and small and major enterprises alike. They stated that there was 'every reason to expect that it will be increasingly used by the scientific/industrial community'.

ZAPI

ZAPI's objective is to design a new manufacturing process (up to large scale) to deliver in a timely manner effective control tools against emerging zoonotic diseases with pandemic potential. The project has achieved major accomplishments in the characterisation, development and expression of immunogens and partially of antibodies against the Middle East respiratory syndrome coronavirus (MERS-CoV), Rift Valley fever (RVFV) and Schmallenberg virus (SBV), in view of the production of vaccines in and neutralising reagents. The reviewers acknowledged the significant and innovative results at small laboratory scale that have been achieved, that yet have to be converted to larger and industrial scale. The reviewers encouraged efforts to seek further contact with regulatory bodies in order to achieve regulatory acceptance of the 'fast track' manufacturing procedure developed in ZAPI and properly respond to pandemic threats.

CANCER-ID

The CANCER-ID consortium aims to evaluate technologies for detection, isolation and analysis of blood based biomarkers (focusing on circulating tumour cells (CTCs), circulating tumour DNA (ctDNA) and circulating microRNAs (miRNA)) and to demonstrate their clinical utility in non-small cell lung cancer (NSCLC) and anti-HER2 treatment resistant metastatic breast cancer (MBC). The reviewers have assessed that overall the consortium has made good progress against its planned objectives and there are no recommendations for major modification of the CANCER-ID project objectives. In order to improve the impact and sustainability of the project the reviewers suggested the consortium should:

1. focus in the clinical validation phase on delivering on 1-3 key studies regarding treatment efficacy in metastatic NSCLC and anti-HER2 treatment resistant MBC;
2. develop plans aiming at facilitating regulatory approval of liquid biopsy technologies.

Interim Reviews for IMI2 - Calls, 3, 6, 8, 10, and 11

IMI project acronym	Call #	Full project name	Interim review
ADAPT-SMART	IMI2 - Call 4	Accelerated development of appropriate patient therapies: a sustainable, multi-stakeholder approach from research to treatment-outcomes	27/02/2017
VSV EBOVAC	IMI2 - Call 2	Vaccine safety and immunogenicity signatures of human responses to VSV-ZEBOV	13 – 14/ 03/2017
EbolaMoDRAD	IMI2 - Call 2	Ebola virus: modern approaches for developing bedside rapid diagnostics	18/05/2017
PRISM (Ethics check)	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 [schizophrenia], and MD [major depression]	18/09/2017
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	22/11/2017

ADAPT-SMART

The ADAPT-SMART project aims to explore how to implement Medicines Adaptive Pathways to Patients (MAPPs) approach i.e. how to make new therapies available to patients with clinical need and lack of a curative therapy at an early stage of development. The experts acknowledged that the activities of this Coordination and Support Action (CSA) are very important in view of the length and cost associated with the development of new medicines, with delays in patient access to new medications, in particular for areas of unmet medical need. They also recognised the challenges and complexity in the CSA due to the multiple stakeholders involved and the sometimes different interests. Overall the experts noted that the project has delivered against the main objectives, despite some delays, considering the complexity of the project, multiple stakeholders and tight timelines and resources. The experts made a number of important recommendations for the remainder of the project, in particular: 1) to focus on key deliverables achievable within the remaining time frame; 2) to strengthen the messages and conclusions of reports produced by the consortium to guide the implementation of MAPPs; and 3) to expand communication activities to a broader public, to stakeholders less involved such as HTA (health technology assessment) and payers, and to some geographical regions like eastern and lower income European Member States which are less represented.

VSV EBOVAC

VSV-EBOVAC builds on existing work to advance the development of the Ebola vaccine candidate VSV-ZEBOV ('vesicular stomatitis virus-vectored Zaire Ebola vaccine'). Clinical trials are underway in Europe and Africa, and the VSV-EBOVAC project is using cutting-edge technologies to carry out in-depth analyses of samples taken from clinical trial participants before and after vaccination. The reviewers assessed that overall the VSV-EBOVAC project progress has been excellent, particularly considering the relatively short time frame since initiation of the three phase 1/2 trials in Europe and Africa, and significant unexpected challenges during the beginning of the first-in-man trial in Geneva. Reviewers said that the results from these trials were central to rapidly paving the way to the first efficacy trial of VSV-ZEBOV during the west African Ebola epidemic that showed 100 % efficiency against the Ebola Zaire strain in humans during a true 'global state-of-emergency'.

EbolaMoDRAD

The EbolaMoDRAD project aims to develop and validate in the field a rapid diagnostic tool that will be both simple and safe to use in low resource settings by people who may not have specialist training. The review panel found that an impressive amount and quality of work had been delivered by the project which will definitely benefit the scientific community involved in this area. For example:

- sampling and inactivation of blood and plasma samples in vacuum blood collection tubes;
- development of a LFD-RPA (recombinase polymerase amplification – lateral flow dipstick) multiplex assay;
- development of a LAMP (loop mediated isothermal amplification) assay;
- Ebola detection in a closed & totally automated system;
- evaluation of EBO RT PCR (Ebola reverse transcriptase—polymerase chain reaction) assays;
- validation of diagnostic tools, field trials of virological and biochemical parameters;
- setting up a decentralised biobank;
- dissemination and knowledge transfer.

The review panel made a number of recommendations to maximise impact with regard to the main ambition of the consortium – i.e. developing bedside rapid diagnostics. These included performing a more detailed assessment of the global landscape and the expected market of comparable diagnostic products in this field in order to establish potential routes for development of the project deliverables. Following this, the review panel recommended the consortium focus their efforts more on those deliverables that are likely to make a difference, and deprioritise less important or less realistic deliverables.

PRISM

The PRISM project aims to study the biological correlates of social withdrawal, a common early symptom in schizophrenia and Alzheimer's disease, in order 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 very much appreciated the efforts the consortium had made to respond to the previous milestone review comments (in 2016). These included addressing the particular issues of clinical and animal protocol harmonisation, knowledge dissemination, stakeholder involvement and clarification of a number of other issues. The consortium has undertaken convincing corrective measures, and all activities are proceeding generally well. Nevertheless, the reviewers flagged the still too slow patient recruitment for the clinical study and recommended the consortium implement further measures to speed up recruitment to ensure a positive outcome of the project.

PRISM – Ethics check

When the PRISM full proposal was at the approval stage, the ethics screening panel concluded that the applicants had provided detailed information on the ethical issues. Nevertheless, there was a list of 18 ethics requirements to be fulfilled by the relevant partners prior to carrying out the research activities. The ethics screening panel also recommended that because of the nature of the patients involved in this research project and their possible vulnerability and incapacity, an ethics check would be prudent at months 12 and 24.

The ethics evaluators were very pleased with the additional information made available for the ethics check at month 12. They concluded that the PRISM consortium had very actively engaged with the ethical issues raised by the research and had conscientiously documented the procedures that have been implemented to mitigate the concerns. The attempts that have been taken to ensure ethical probity of the research merited a score of 'excellent'. In view of the clear engagement by the consortium with the ethical issues raised by the PRISM work plan and the consortium's commitment to mitigate these concerns, together with the establishment of a Scientific and Ethical Advisory Board (SEAB) and appointment of an ethics advisor, the ethics screening panel considered that a further ethics check at month 24 is not necessary.

1.4.3 Progress against key performance indicators (KPIs) and statistics

The 2017 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[5]. 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.

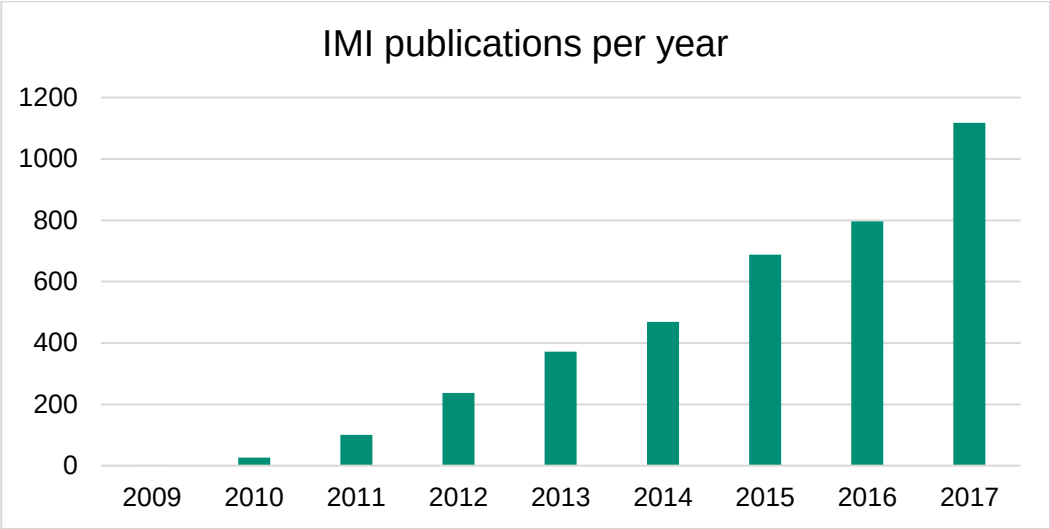
Meanwhile, with the goal of enhancing IMI's performance and accountability measures, in 2017 IMI continued to refine its revised KPIs, and these were endorsed by the IMI Governing Board in November 2017, for use from 2018. The new KPIs are based on a logic model that maps IMI's contribution to the intended 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.

[5] See section 2.2 for details.

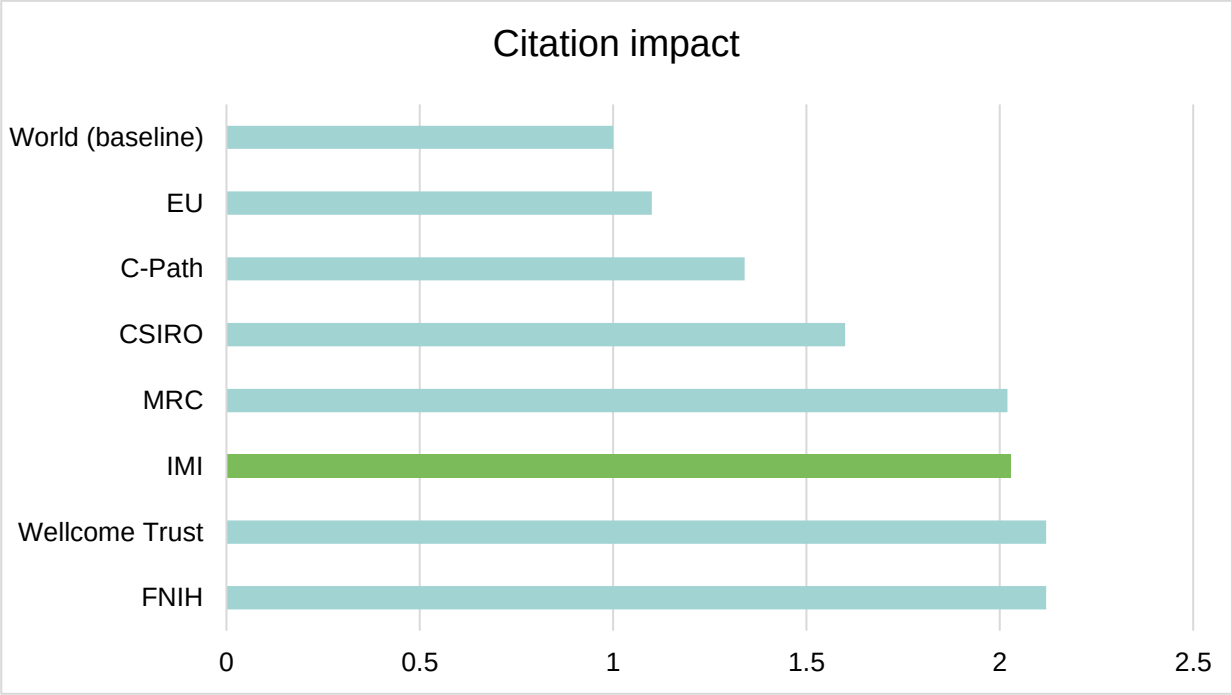
1.5 Dissemination and information about project results

Publications from IMI projects

In 2017, IMI projects continued to publish prolifically in scientific journals; an analysis by Clarivate Analytics (formerly Thomson Reuters) identified 1 118 new articles in 2017, bringing the total number of publications produced by IMI projects to 3 808. As the graph below shows, the number of publications generated per year continues to rise steadily.



The field-normalised citation impact for all IMI papers remains at 2.03 (compared to 1.14 for the EU and the baseline of 1 for the world). IMI also compares favourably with other similar funding bodies, namely the Critical Path Institute (C-Path), Australia's Commonwealth Scientific and Industrial Research Organisation (CSIRO), the Medical Research Council (MRC), the Wellcome Trust, and the Foundation for the National Institutes of Health (FNIH).



The latest Clarivate Analytics analysis also revealed that a quarter of IMI papers are 'highly cited', meaning they are in the top 10% of papers for their field. Again, this compares favourably with similar organisations such as the Wellcome Trust and the MRC (both 25%).

IMI project impacts: spin-offs and commercial exploitation

Spin-offs

In 2017, IMI project results have led to the creation of two new entities, but also have led to the enhancement of many existing businesses:

- As a result of a public programme run in the IMI European Lead Factory project, the spin-out company Keapstone Therapeutics was created. It was founded in partnership between Parkinson's UK and the University of Sheffield.
- The company M4K PHARMA was founded in 2017, receiving support from OICR (Ontario Institute for Cancer Research, Canada). The formation of the company was dependent on research and data generated by the ULTRA-DD partner SGC. M4K PHARMA is built upon an open access model, which is very innovative in the sector.

Follow-on funding

A survey of IMI projects conducted at the end of 2017 shows that approximately 50 % of IMI projects attracted follow-on funding, or leveraged additional funding, from private or public sources, as a result of the initial IMI grant. Examples include:

- The successes of EU-AIMS have fed into a new IMI2 project which is currently under development and will have a total budget of EUR 110 million.
- The European Respiratory Society (ERS) has provided funding for sustainability of the U-BIOPRED project assets during a three year period.
- Partner Karolinska Institute of ULTRA-DD received a grant for a linked study from Takeda Pharmaceuticals amounting to USD 2.5 million. Additional smaller grants have been received as a consequence of the IMI support. In addition, around 20 PhD students are supported by external grants.
- Building upon the results obtained by the VSV-EBOVAC project under the Ebola+ programme, a new project VSV-EBOPLUS was funded under IMI2 - Call 8, building and extending the objectives of the VSV-EBOVAC project to evaluate the Ebola vaccine response in children and adolescents, having a larger number of subjects and studying the long term response (up to 5 years after vaccination). The project received an in-kind contribution of EUR 4 828 910 euros by the industrial partner Merck Sharp & Dohme Corp. Merck was the sponsor of the clinical trial 'Phase 1 randomised, multi-centre, double-blind, placebo-controlled, dose-response study to evaluate the safety and immunogenicity of the BPSC1001 (VSV-ZEBOV) Ebola virus vaccine candidate in healthy adult subjects'. Samples collected in this multicentre study, performed in the US between December 2014 and June 2016, will be analysed in the context of VSV-EBOPLUS project.
- GNA from the IMI project FILODIAG of the Ebola+ programme was able to raise EUR 6 million from venture capital companies, partly thanks to the progress visible in the IMI project.

Commercialisation and exploitation

By 31 December 2017, project results from 9 IMI projects have led to a total of 12 commercialisations. New results include the following:

- A threshold tracking methodology to measure pain signals by electrodes on the skin, developed and further validated by project EUROPAIN, represents a new tool now available for interventional drug trials.
- Rhinovirus-16, developed and tested in a model of exacerbation in a human viral challenge study by U-BIOPRED, is being commercialised for use in clinical trials based on a complete Investigational Medicinal Product Dossier (IMPD) and acceptance by the regulatory authorities (BfArM).
- The results of project EHR4CR have been commercialised into the InSite Platform, an innovative platform that enables the trustworthy re-use of electronic health records (EHR) data for research. The platform is facilitating collaboration between clinicians and researchers and maximising the output of clinical research through new technology.
- Cellular phenomics & oncology Berlin-Buch GmbH ('cpo') is providing drug screening / drug characterisation services using the 3D culture technologies refined by the OncoTrack project. Experimental Pharmacology & Oncology Berlin-Buch GmbH ('EPO') is commercialising OncoTrack's xenograft models.

- As a result of the ABIRISK project, an immunogenicity assay is provided by Eurodiagnostica/Biomonitor.
- BIOVACSAFE supported the development of the SLE-KEY™ rule-out serologic test for the diagnosis of systemic lupus erythematosus (SLE) using the IMMUNARRAY iCHIP®.
- The Sierra Sensors Mass 2 analysis system has been developed in conjunction with the K4DD participants. This system uses surface plasmon resonance (SPR) to measure how long a drug candidate binds to a target molecule.
- An assay to measure the binding kinetics of GPCRs (G-protein-coupled receptors) developed in the project (BRET assay) is commercially available at www.promega.com.
- ULTRA-DD entered a collaborative agreement with MODIQUEST, a Dutch antibody company. MODIQUEST was selected as commercial partner for distribution of ULTRA-DD antibodies to the community.
- The IMI project APPROACH completed the technical validation of the biochemical marker ARGS neoepitope and the assay was made commercially available via partner Nordic Bioscience.
- Finally, results of the IMI2 project FILODIAG were used by GNA, the project's coordinator, as additional input for their first commercial, generic nucleic acid test system, launched in November 2017.

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[6]. 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 2017

The total operational budget approved for 2017 was EUR 312.5 million in commitment appropriations (CA) and EUR 195.1 million in payment appropriations (PA). In 2017, the operational commitment and payment appropriations reached a level of 97.41 % and 71.96 % respectively.

The commitment appropriations related to H2020 were consumed by Grant Agreements implementing IMI2 - Calls 7, 8 and 9 of and by launching IMI2 – Call 8 (the fourth cut-off date), as well as IMI2 – Calls 11, 12 and 13.

The payment appropriations related to H2020 were mainly used by pre-financing for projects of IMI2 - Calls 7, 8 and 9 and by intermediate payments for projects of Call for proposals 1 – 4.

On operational commitment appropriations, IMI is executing its budget well (over 97 %).

As regards operational payment appropriations, the execution is at 71.96 %.

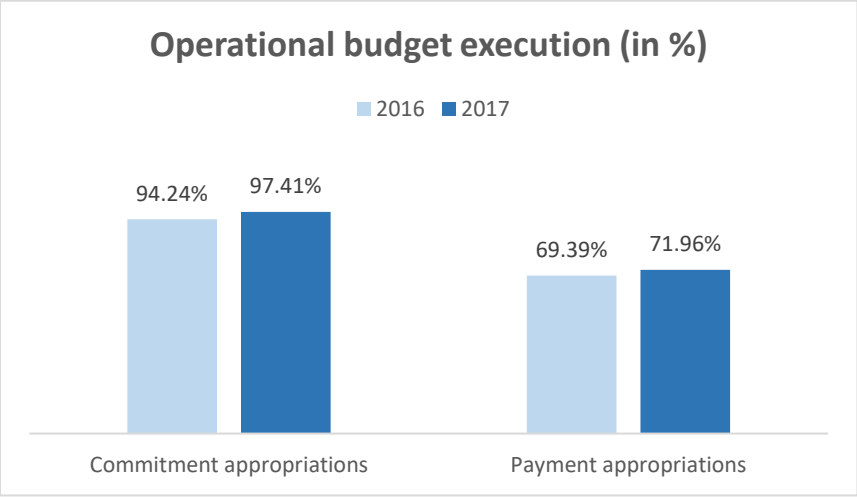
The main reason for this lower execution is the underspending linked to risky late clinical development activities (phases II and/or III), in particular in the areas of antimicrobial resistance (AMR) and Ebola. Projects have claimed fewer funds than planned due to volatility in these high risk projects involving clinical trials that may be significantly reduced or postponed.

Furthermore, the Ebola open call of March 2017 (IMI2 – Call 8) did not result in any eligible applications; as a result, payment of pre-financing planned for 2017 is to be postponed to 2018.

Another reason is the complexity of some public-private consortia that required significant time for Grant Agreement signature, which impacted the ability to pre-finance the projects within the planned budget cycle. Furthermore, the volatility of the pharmaceutical industry (mergers and acquisition, changes of corporate strategies) results in shifting portfolios between companies, therefore adding complications and delays in the execution of IMI projects' tasks.

[6] 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 graph below shows the 2017 operational budget execution compared with 2016.



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

	Execution of commitment appropriations in EUR Total		
	Appropriations	Execution	%
*IMI1 (FP7) **	*25 669*	*-*	*-*
IMI2 (H2020)	*312 505 844*	*304 431 513*	*97.42*
Title 3 Implementing the research agenda of IMI	**312 531 513**	**304 431 513**	**97.41**

**IMI1 (FP7) appropriations - amount recovered during 2017 from projects (assigned revenue)*

	Execution of payment appropriations in EUR Total		
	Appropriations	Execution	%
IMI1 (FP7)	*112 655 669*	*72 020 753*	*63.93*
IMI2 (H2020)	*82 435 003*	*68 360 565*	*82.93*
Title 3 Implementing the research agenda of IMI	**195 090 672**	**140 381 318**	**71.96**

The commitments carried forward from 2016 to 2017 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 amount not consumed, related to IMI2 - Call 10, was de-committed at the end of 2017 and, based on the N+ 3 rule as set out in the IMI2 Financial Rules, the unused appropriations will be carried over to the 2018 budget.

The table below shows the summary of commitments outstanding for operational expenditure per programme at the end of 2017.

Commitments carried forward from previous year 2016	Commitment appropriation in EUR				
	Carry forward	Commitments made during 2017	De-commitments	Payments	Commitments outstanding at the end of 2017
IMI1 (FP7)	*318 102 973*	*-*	*-*	*72 020 753*	*246 082 220*
IMI2 (H2020)	*404 013 173*	*304 431 513*	*174 612 479*	*68 360 565*	*465 471 643*
Total Title 3	**722 116 146**	**304 431 513**	**174 612 479**	**140 381 318**	***711 553 863***

EU funds committed under IMI1 and IMI2

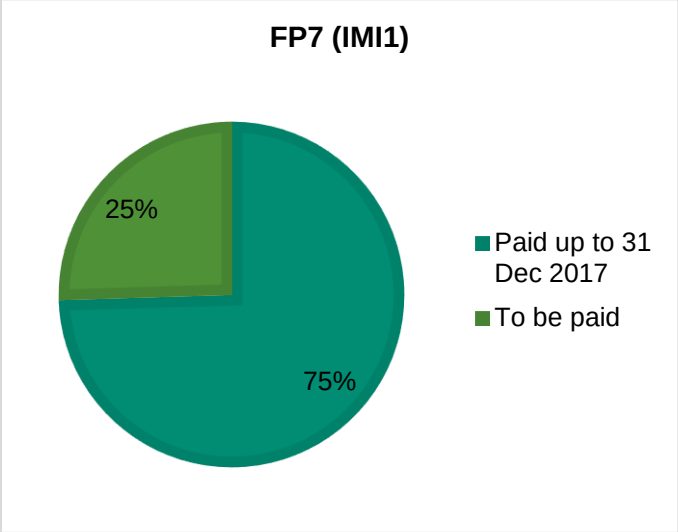
The table below outlines the breakdown per Call of EU committed funds for IMI1 (FP7).

			EUR '000
FP7 (IMI1)	Committed	Paid up to 31 Dec 2017[7]	To be paid
Call 1	116 082	114 364	1 718
Call 2	85 765	85 012	753
Call 3	112 839	104 194	8 645
Call 4	97 943	86 685	11 258
Call 5	79 999	72 011	7 988
Call 6	125 417	48 249	77 168
Call 7	12 999	11 645	1 354
Call 8	98 732	75 943	22 789
Call 9	56 440	34 928	21 512
Call 10	6 100	3 431	2 669
Call 11	173 410	83 181	90 229
Total FP7 (IMI1)	**965 726**	**719 644**	**246 082**

At the end of 2017, 75 % of the commitment appropriations had been paid out. EUR 179 million were paid as advances (pre-financing) and EUR 540.6 million were paid for cost claims submitted by the projects. 27 projects continue their activities. The outstanding operational payments will be made by the end of 2021 when the last IMI1 (FP7) projects conclude their activities as initially planned.

[7] Includes pre-financing.

The graph below shows the percentage of what has been paid and what remain to be paid out of committed funds for IMI1 (FP7).



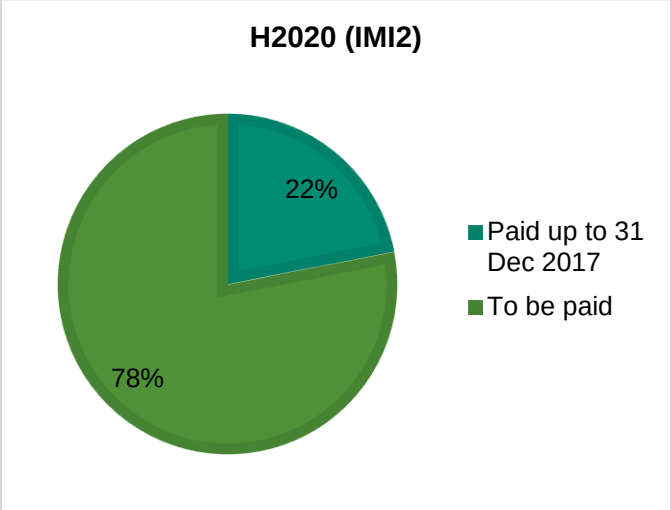
The table below outlines the breakdown per Call of EU committed funds for IMI2 (H2020).

			EUR '000
H2020 (IMI2)	**Committed**	**Paid (up to 31/12/2017)**	**To be paid**
Call 1	17 630	5 628	12 002
Call 2	114 090	69 630	44 460
Call 3	58 160[8]	28 105	30 055
Call 4	1 130	1 017	113
Call 5	47 477	16 377	31 100
Call 6	46 696	16 862	29 834
Call 7	46 795	17 073	29 722
Call 8	70 000	5 072	64 928
Call 9	57 606	19 886	37 719
Call 10 *	173 890	-	173 890
Call 11	5 000	-	5 000
Call 12	64 077	-	64 077
Call 13	116 460	-	116 460
Total H2020 (IMI2)	**819 010**	**179 650**	**639 361**

** The IMI2 - Call 10 level 1 commitment was de-committed at the end of 2017 and the amount will be carried over in 2018 because the Grant Agreements will be concluded and committed in 2018. Therefore the difference between total to be paid for H2020 and commitments outstanding for H2020 refers to the IMI2 - Call 10 amount.*

[8] Includes a contribution from the Bill and Melinda Gates Foundation (BMGF), an IMI2 Associated Partner.

The graph below shows the percentage of what has been paid and what remains to be paid out of committed funds for IMI2 (H2020).



As stated in Article 3 of the IMI2 JU founding regulation[9], the total IMI2 JU budget (in commitments) is EUR 1.638 billion, of which EUR 1.425 billion to match EFPIA in-kind contributions and EUR 213 million to match IMI2 Associated Partners' contributions. At the end of 2017, half of the IMI2 JU budget in commitments had been committed (EUR 819 million out of EUR 1.638 million EUR).

[9] The Council Regulation (EU) No 557/2014 of 6 May 2014 establishing the Innovative Medicines Initiative 2 Joint Undertaking is available online at http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32014R0557.

1.7 EFPIA and IMI2 Associated Partner contributions

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[10].

On the one hand, in IMI projects, legal entities eligible for JU funding (beneficiaries receiving JU funding) receive financial support from IMI to fund their activities[11].

On the other hand, EFPIA companies and Associated Partners do not receive any funding from IMI, but contribute their own resources to the projects. These contributions consist of:

- in-kind contributions[12], i.e. costs incurred by EFPIA companies and Associated Partners in the implementation of IMI projects for researchers, research equipment, and materials;
- financial contributions directly to IMI, or at project level to beneficiaries receiving IMI funding.

EFPIA companies and Associated Partners 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 contributions to both programmes (IMI1 and IMI2).

For each programme, Council regulations clearly define the matching requirements.

- IMI1: EC funding up to EUR 966 million, to match the equivalent contributions from EFPIA.
- IMI2: EC funding up to EUR 1.425 billion, to match the equivalent 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

IMI1 commitments

EFPIA's commitment to the IMI1 programme totalled EUR 958.9 million as of 31 December 2017, representing an increase of EUR 5.8 million following amendments of existing projects. The EU commitment remained unchanged at EUR 965.7 million.

IMI1 In million EUR	Up to 31.12 2016	2017	TOTAL
Number of signed projects	59	N/A	59
EU commitment	965.7	N/A	965.7
EFPIA commitment	953.1	5.8	958.9

The EFPIA commitment was initially EUR 996.3 million, but this decreased in 2016 by EUR 43 million to EUR 953.1 million (due to the decision by the COMBACTE-NET project to terminate work on a compound for scientific – safety / efficacy reasons).

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

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

[12] In-kind contribution is defined as follows:
IMI1: Article 11(4)(a) of the IMI JU Statutes annexed to the Council Regulation No 73/2008 – 'non-monetary contributions (hereinafter referred to as contributions in kind) by the research based pharmaceutical companies that are members of EFPIA, with resources (such as personnel, equipment, consumables, etc.) at least equal to the financial contribution of the Community'.
IMI2: Article 13(3)(b) of the IMI2 JU Statutes annexed to Council Regulation (EU) No 557/2014 - 'in kind contributions by the Members other than the Union and the Associated Partners, or their constituent entities or their affiliated entities, consisting of the costs incurred by them in implementing indirect actions, and in relation to advisory groups, if foreseen in the annual work plan, less the contribution of the IMI2 Joint Undertaking and any other Union financial contribution to those costs'.

In 2017, the EFPIA commitment increased by EUR 5.8 million to EUR 958.9 million, as a result of amendments of several IMI1 projects.

IMI1 EU and EFPIA contributions - comparison by year

As of 31 December 2017, EUR 529.9 million EFPIA contribution had been formally validated (checked by IMI staff and / or audited by external auditors) – see section below on Control. The table below gives an overview of validated IMI1 contributions for every year since the start of the programme.

At the end of 2017, 27 projects were still ongoing. The outstanding contributions will be made by the end of 2021 when the last IMI1 (FP7) projects conclude their activities as initially planned.

IMI1 In million EUR	2010	2011	2012	2013	2014	2015	2016	2017	TOTAL
EU validated cost claims (*)	0.5	15.2	33.5	59.4	80.5	80.4	141.9	129.2	540.6
EFPIA validated contributions			52.0	58.0	132.2	65.4	80.9	141.3	529.9

(*) excluding pre-financing

There is currently a small imbalance (EUR 10.7 million or 1.9 %) between EU and EFPIA funding which results from the fact that in some projects, tasks are not parallel, but sequential. In 2017, the IMI Programme Office continued to closely monitor the overall commitments of industry participants.

IMI1 EU and EFPIA contributions - comparison by Call

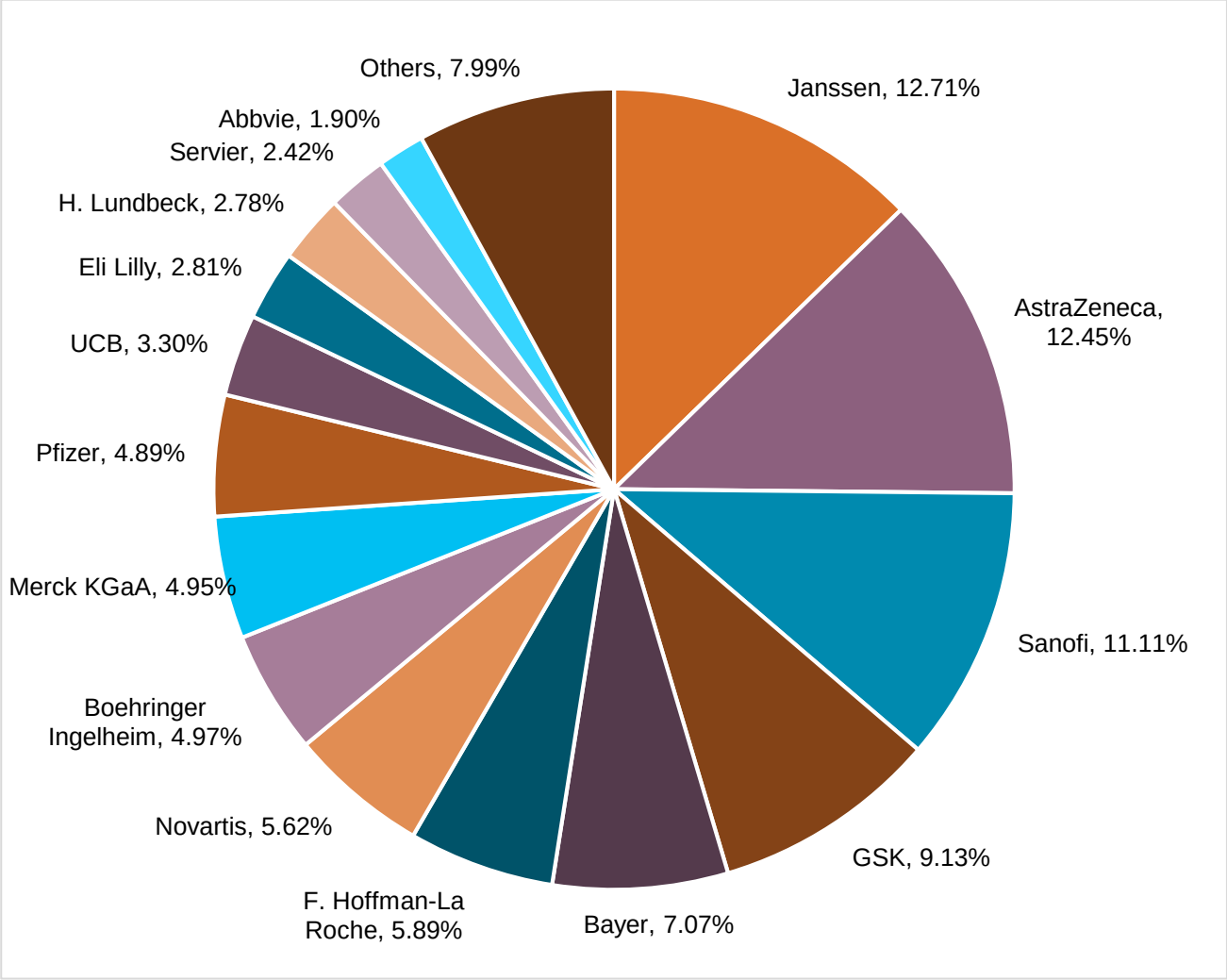
The table below provides a breakdown by Call of both EU (cost claims only) and validated EFPIA contributions for the whole IMI1 programme:

IMI1		EU (EUR million)			EFPIA (EUR million)		
Call	Projects	Committed	Payments[13]	%	Committed	Validated	%
1-2008	15	116.1	112.7	97.1	149.9	139.7	93.2
2-2008	8	85.8	83.9	97.8	74.0	66.9	90.4
3-2010	7	112.8	82.8	73.4	73.8	54.2	73.5
4-2011	7	97.9	71.0	72.6	110.2	82.8	75.1
5-2012	1	80.0	59.0	73.7	91.3	84.9	92.9
6-2012	2	125.4	33.6	26.8	98.2	19.2	19.6
7-2012	2	13.0	7.2	55.2	11.9	6.3	52.9
8-2013	4	98.7	37.6	38.1	48.0	22.4	46.6
9-2013	4	56.4	17.1	30.4	89.1	17.5	19.6
10-2013	1	6.1	1.5	24.2	6.1	1.0	16.3
11-2013	8	173.4	34.2	19.7	206.2	35.1	17.0
Total	**59**	**965.7**	**540.6**	**56.0**	**958.9**	**529.9**	**55.3**

[13] Excludes pre-financing.

IMI1 EFPIA contributions - by company

The pie chart below sets out the EFPIA companies' contributions to IMI1 projects since the start of the programme.



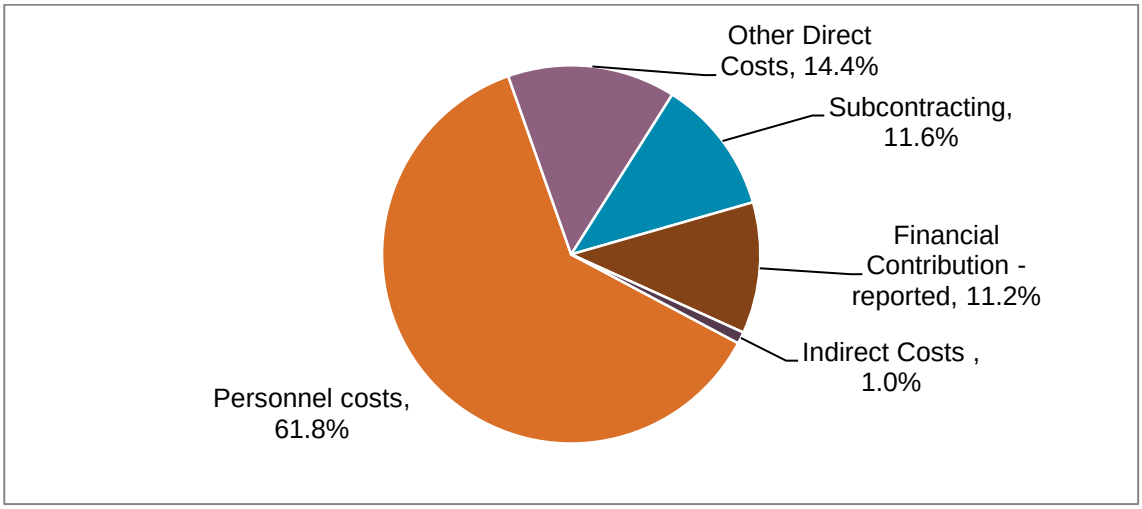
Companies listed under 'Others' are: Abbott, AiCuris, Almirall, Amgen, Astellas Pharma Europe, Basilea, Biogen Idec, Bristol Myers Squibb, Chiesi Farmaceutici, Eisai, Farmaindustria, Grünenthal, INFARMA, Ipsen, Laboratorios del Dr Esteve, Menarini, Merck Sharp & Dohme, Novo Nordisk, Orion Corporation,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

IMI1 EFPIA contributions - by cost category

The EFPIA contributions at project level 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.

The share of each cost category is shown in the chart below.



IMI2 programme

IMI2 commitments

As of 31 December 2017, 40 IMI2 projects (of which 37 were still running at the end of 2017) had been launched for a total amount of EUR 391.0 million in EU funding and EUR 381 million commitments from EFPIA companies (EUR 366.6 million) and Associated Partners (EUR 14.4 million).

The following table provides an overview of EU, EFPIA and Associated Partner contributions to IMI2 projects:

IMI2 (In million EUR)	Up to 31.12 2016	2017	TOTAL
Number of signed projects	25	15	40
EU funding commitment	275.9	115.1	391.0
EFPIA commitment	249.1	117.5	366.6
Associated Partner commitments	14.4		14.4
Total EFPIA and Associated Partner commitments	263.5	117.5	381.0

Both EFPIA and Associated Partner commitments include in-kind contributions, as well as financial contributions directly to the IMI2 JU operational costs[14], or at project level to beneficiaries receiving IMI funding.

The increase of commitment in 2017 of EUR 115.1 million (EU funding) and EUR 117.5 million (EFPIA and Associated Partner commitment), results from the conclusions of 15 new projects for IMI2 - Call 7 (7 projects); IMI2 – Call 8 (the Ebola open Call, 2 projects); and IMI2 - Call 9 (6 projects).

Of the EUR 381 million committed by EFPIA and Associated Partners as of 31 December 2017, 23 % comes from outside the EU and H2020 associated countries. This means that IMI continues to comply with the IMI2 regulation, which states that in-kind contributions incurred in third countries must be justified and may not exceed 30 % of the eligible costs incurred at programme level of the IMI2 programme.

IMI2 EU, EFPIA and Associated Partner contributions - comparison by year

As of 31 January 2017, EFPIA companies and Associated Partners had effectively contributed up to EUR 86.5 million to the IMI2 programme (amount certified by external auditors and validated by IMI). For comparison, accepted cost claims for EU funding from beneficiaries as of the end of 2017 stood at EUR 39.3 million.

EUR million	2016	2017	TOTAL IMI2
1. EFPIA companies – validated & certified contributions	47.2	34.1	81.3
2. Associated Partners —validated & certified contributions[15]	0	1.2	1.2
3. EFPIA & Associated Partner financial contributions paid directly to IMI operational costs[16]	3.0	1.0	4.0
Total EFPIA and Associated Partner contributions (in kind and financial)	**50.2**	**36.3**	**86.5**

Both EFPIA and Associated Partner contributions (rows 1 and 2) are made up of in-kind contributions as well as financial contributions at project level to beneficiaries receiving IMI funding. Financial contributions to IMI operational costs (row 3), which are paid directly to IMI2 JU, are reported separately.

IMI2 contribution (all figures in EUR million)	EFPIA companies	Associated Partners	Total contributions
Reported in 2016 for 2015, certified and validated by IMI	47.2	0	47.2
Reported in 2017 for year 2016, certified and validated by IMI	34.1	1.2	35.3
Reported early 2018 for 2017, not yet certified (estimates)	48.8	1.5	50.3
EFPIA & Associated Partner financial contributions to IMI operational costs	1.2	2.8	4.0
Total	**131.3**	**5.5**	**136.8**

[14] Article 13.4.b of the IMI2 Council regulation (financial contribution of Bill and Melinda Gates Foundation to IMI for the PERISCOPE project, and the contribution of EFPIA companies to IMI for the HARMONY and DRIVE projects).

[15] Article 13.3.b of the IMI2 Council regulation.

[16] Article 13.4.b of the IMI2 Council regulation (financial contribution of BMGF to IMI for the PERISCOPE project, plus the contribution of four EFPIA companies to IMI for the DRIVE project).

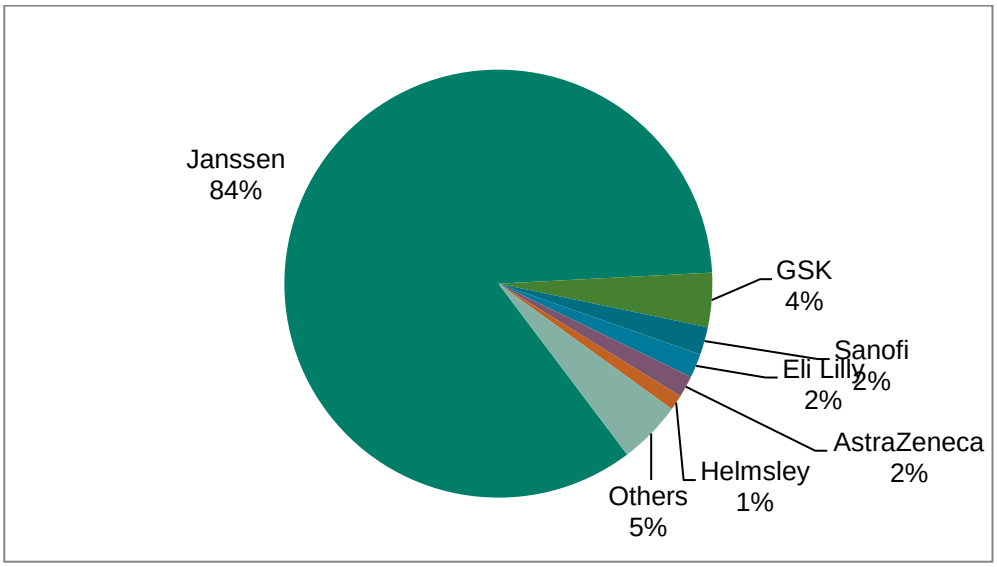
IMI2 EU, EFPIA and Associated Partner committed contributions - comparison by Call

Call	Projects	EU	EFPIA	Associated Partners
1	1	17.6	12.8	5.6
2	8	114.1	103.1	
3	5	49.1	44.7	7.0
4	1	1.1	2.2	
5	6	47.5	45.8	1.8
6	4	46.5	45.5	
7	7	46.8	48.5	
8	2	14.7	10.9	
9	6	53.6	53.1	
Total	**40**	**391.0**	**366.6**	**14.4**

The table above of committed contributions includes in-kind contributions; financial contributions at the level of the action to beneficiaries receiving JU funding; and commitments for financial contributions to the IMI operational costs. As there are no upfront commitments for SGGs, there are no SGG commitments in the table.

IMI2 validated EFPIA and Associated Partner contributions by organisation up to the end of 2017

As the organisational breakdown below shows, 84 % of the total validated IMI2 contribution (or EUR 82.5 million) is provided by one European company, Janssen (Belgium and The Netherlands). This is mainly due to the fact that Janssen is the main contributor to four Ebola projects, which were the first IMI2 projects to start following the 2014 Ebola virus epidemic in Sierra Leone. The remaining 16 % comes from other EFPIA companies and Associated Partners (The Leona M. and Harry B. Helmsley Charitable Trust and JDRF- the Juvenile Diabetes Research Funding and Advocacy). The remaining IMI2 projects are still in their start-up phase and it is expected that the breakdown by companies will be more balanced as the number of IMI2 projects increases; this is already evident in the graph lower down showing the reported contributions for the calendar year 2017, where Janssen's share is 45 %.

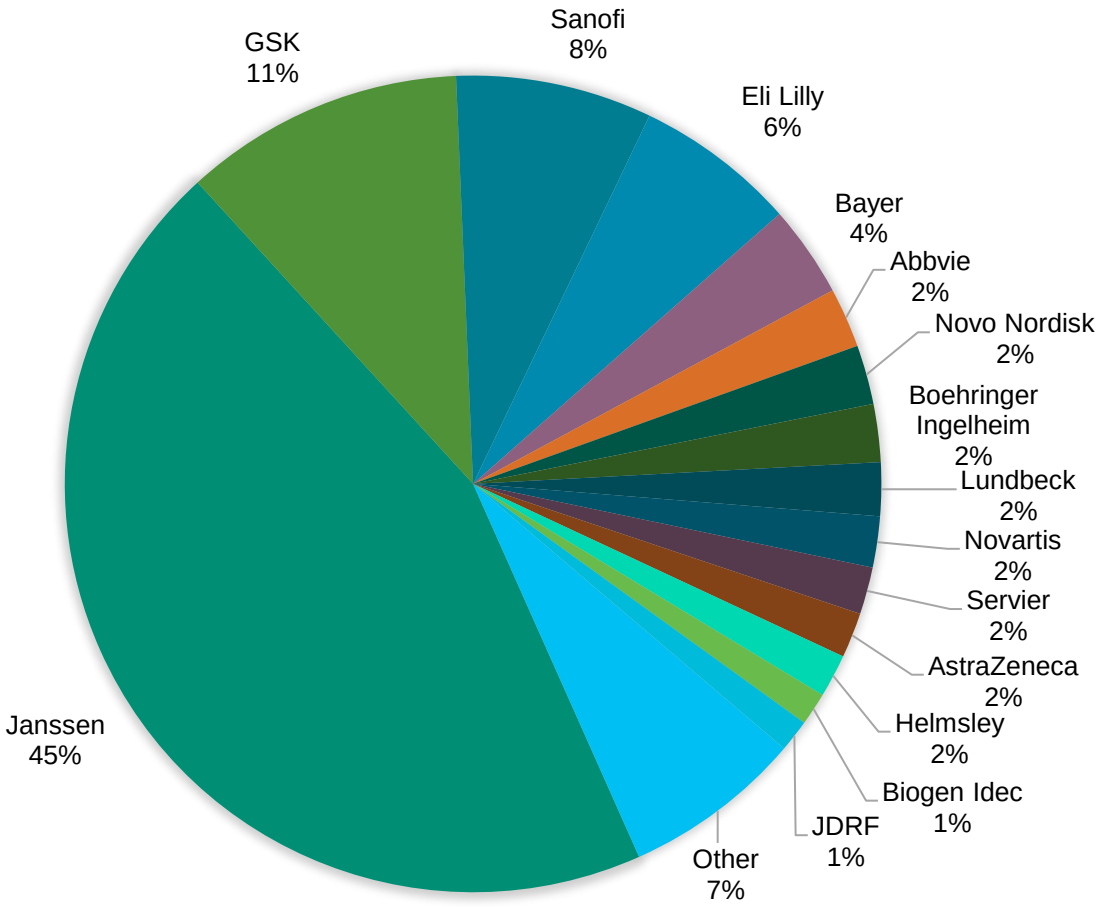


Organisations included under 'Other' are Abbvie, Bayer, Biogen Idec, Boehringer Ingelheim, Bristol Myers Squibb, EFPIA Office, Grünenthal, JDRF, Lundbeck, Merial, Novartis, Novo Nordisk, Pfizer, Servier, Takeda, and UCB.

The chart above includes both in-kind contributions and financial contributions at the level of the action to beneficiaries receiving IMI funding. It does not include financial contributions to IMI operational costs, which are paid directly to IMI and reported separately.

IMI2 reported EFPIA and Associated Partner contributions by organisation up to the end of 2017

The chart below includes both in-kind and financial contributions at the level of the action up to the end of 2017. EFPIA companies and Associated Partners have to report their estimated in-kind contributions to IMI by 31 January for the previous calendar year. The chart below shows the reported in-kind contributions, by organisation, for the year 2017.



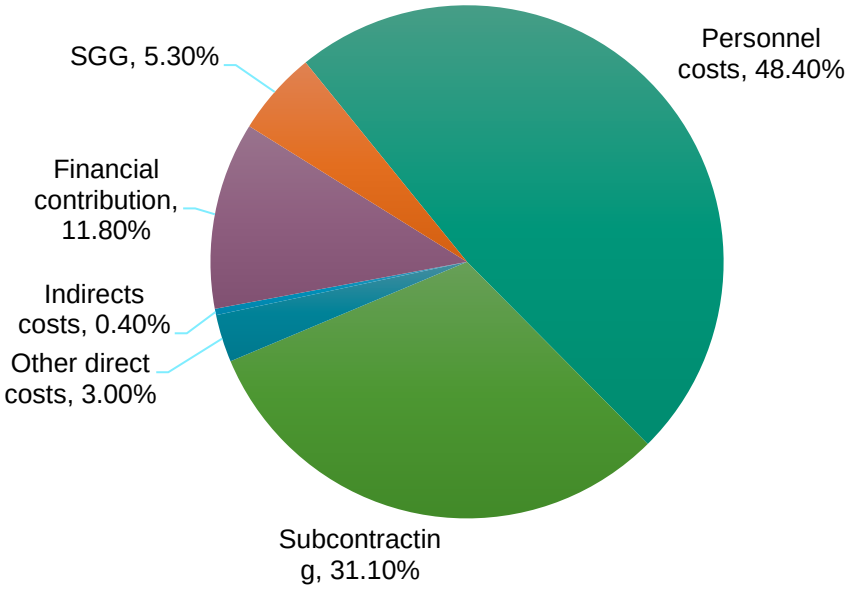
Companies included under 'other' are: Celgene, Takeda, MSD, GE Healthcare, UCB Biopharma, Zoetis, ESTEVE, Novavax, Grünenthal, Roche, Merck KGaA, EFPIA, Intervet, Menarini, Amgen, and Ipsen.

IMI2 EFPIA and Associated Partner reported contributions by cost category

EFPIA companies' and Associated Partners' contributions can be broken down into the following cost categories:

- Personnel costs: staff employed by EFPIA companies directly working on IMI projects.
- Subcontracting: clinical trials, subcontracting to clinical research organisations, subcontracting to data management companies, lab services, communication, project management support, etc.
- Other direct costs: consumables, equipment depreciation, samples, compounds.
- Financial contribution (FC): a transfer of funds from an EFPIA company to beneficiaries receiving IMI funding 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.
- Strategic Governance Group (SGG): Contribution to the SGG.

The breakdown of the reported EFPIA contribution to IMI2 projects as of the end of 2017, by cost category is shown in the graph below. The high percentage of subcontracting costs in IMI2 projects (31.10 %) compared to IMI1 projects (16.2 %) is due to the particularities of the Ebola projects, where significant tasks are subcontracted.



Ex-post controls of the in-kind contribution under IMI1 (FP7)

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 controls, using a risk-based approach as per IMI's audit strategy, is to independently verify that the in-kind contributions accepted by IMI 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 companies to declare in-kind contributions for all the IMI1 projects in which they participate, 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 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 16 EFPIA companies, covering a total of EUR 492.8 million of accepted contributions to IMI1 projects or 93 % of all EFPIA 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 31/12/2017 (EUR million)
Total finalised audits	492.8
Total all EFPIA companies	529.8
Audit coverage	**93 %**

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 3 667 326, corresponding to 3.65 % 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
529 861 189	492 811 103	93 %	- 1 782 780	1 884 546	3 667 326	3.65 %

A further four audits were launched at the end of 2017, to be finalised in 2018.

Controls of EFPIA and Associated Partner 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 EFPIA and Associated Partner contributions during project implementation. Under FP7, these 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 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. EFPIA and Associated Partner contributions are only validated for inclusion in IMI's accounts after these checks and adjustments[17]. IMI may carry out an additional audit itself, before validating the EFPIA and Associated Partner contributions. 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.

[17] 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

IMI's communications work in 2017 contributed to the IMI communications strategy, which has five main goals:

- promote IMI and raise awareness levels and perception of IMI among all target groups focusing on results and impact;
- attract the best researchers from relevant target groups to apply for funding under IMI2 Calls for proposals;
- increase the engagement of patients in IMI's activities;
- increase the engagement of SMEs in IMI's activities;
- gain support for IMI among key groups of policymakers and opinion leaders.

General outreach

The new IMI website

The first IMI website was launched in autumn 2010. Although the information on it was kept up to date, both IMI's needs and website designs have evolved since then. To respond to this, the IMI Programme Office worked during 2017 to overhaul its corporate website. The new website was launched in October 2017. Following suggestions from our main stakeholders and IMI's 2017 communication objectives, the revamped website was designed according to four main drivers:

- it is better tailored to IMI's different stakeholders;
- it gives a stronger voice to our projects;
- It provides greater visibility to IMI's advisory bodies;
- it is more visual.

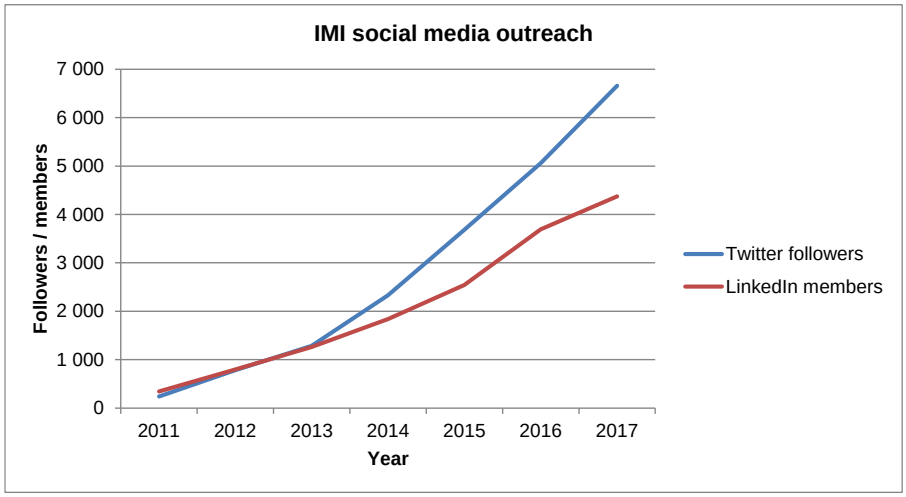
These four drivers have been translated into the following elements:

- an enhanced homepage with a contemporary layout and improved structure and navigation;
- an expanded 'Get involved' section, with tailored information for different stakeholder groups (SMEs, patients, academia, Associated Partners, etc.);
- three new subsections dedicated to our projects' outputs, including success stories, an interactive map, and a catalogue of accessible tools generated by our projects;
- new content for the SRG and SC webpages, jointly developed with IMI's advisory bodies.

The average number of visitors to the website per month in 2017 was 12 217, up from 11 546 in 2016. The fact that Belgium leads the number of sessions, followed by the UK and Germany, indicates that the website is not only visited by potential participants, but also by policymakers, industry and patient associations, media and consultancies, all based in Brussels.

Social media

IMI concluded 2017 with 6 659 followers on Twitter and 4 375 members in the IMI LinkedIn Group, continuing the steady growth since 2011, as shown in the graphic below



During the year, IMI, in collaboration with the European Commission, EFPIA, and IMI projects, engaged in a number of social media campaigns:

- June – July: Promoted the new video on IMI through the #CarryTheTorch hashtag;
- August: Tweeted success stories daily as part of the DG Research & Innovation health month, using the hashtags #ResearchImpactEU and #EUHealthResearch;
- October: Revived the hashtag #CarryTheTorch to promote the video as well as the new brochure and factsheet on the impacts of IMI project results;
- October: Together with other Joint Undertakings, used the hashtag #JUs4innovation to mark the joint JU event in the European Parliament.

Press

During 2017, IMI was mentioned in 5 077 articles in 50 countries. The tonality of the media coverage was predominantly neutral (91.5%), with 8.2% of articles registering a positive tone and only 0.3% a negative tone. A selection of the most significant articles can be found in Annex 11. Articles written by IMI included:

- European Files: A piece by Pierre Meulien on 'IMI - putting patients at the centre' was published in March edition. The December edition was dedicated to PPPs and the health section featured a number of articles by IMI;
- Parliament Magazine: An article by Pierre Meulien appeared in the health issue of Parliament Magazine in October. The issue was distributed at the Gastein forum.

IMI projects have also gained greater prominence in the European Commission's channels, notably Horizon Magazine and the RTD Infocentre.

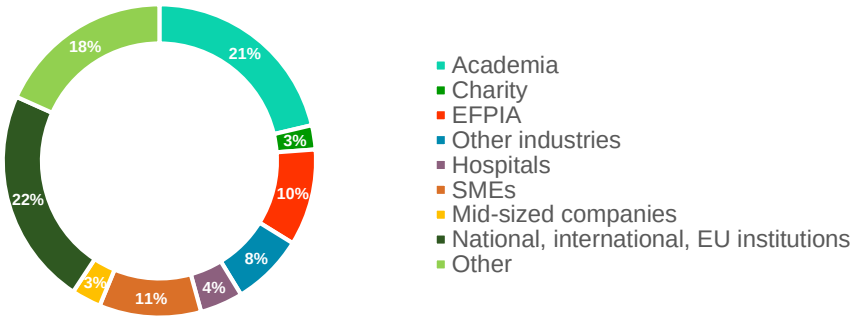
Publications

Publications produced by IMI in 2017 are:

- IMI Highlights 2017
- a detailed factsheet on IMI project results 'Carry the Torch'
- a booklet on IMI's antimicrobial resistance programme 'New Drugs for Bad Bugs'
- a factsheet summarising IMI's Ebola+ programme
- two infographics for the new website: one on IMI's funding model and one on the generation process of IMI's call topics
- 11 newsletters.

Stakeholder Forum

On 18 and 19 October IMI held its annual Stakeholder Forum in Brussels. The event was attended by 327 participants plus 60 live webstreaming connections. As the graph below shows, participants came from a range of sectors:



On the first day, the focus was on open innovation through the prism of a number of flagship IMI projects as well as the 'Think Big' process that sets out the core areas that will feature in IMI Calls for proposals in the coming years. During the second day, two parallel sessions were organised – one on the microbiome and one on patient engagement.

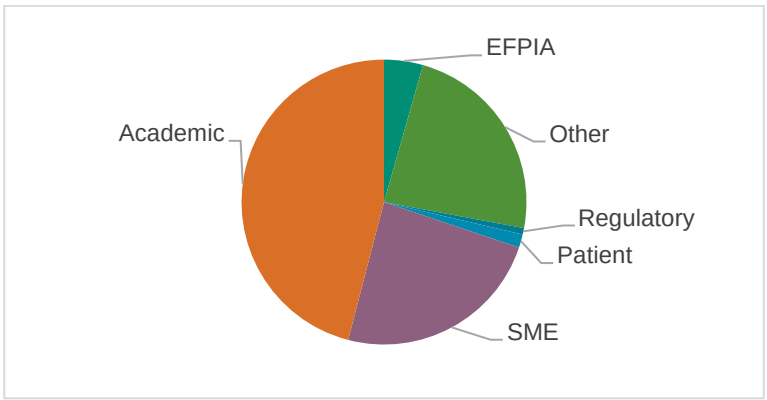
The patient engagement track formed part of IMI's efforts to build on its patient engagement strategy. The session, which was co-developed with the European Patient Forum, set out discussions on how to achieve real and meaningful patient engagement, how to measure and demonstrate its value, and how to secure willingness to collaborate. The goal of the event was to further the discussion on what are the most meaningful models of patient collaboration in order for patients' voices to be heard.

The microbiome track brought together the pharmaceutical, food / feed and diagnostics industries for an open and dynamic discussion with medtechs, regulators, researchers and other players on the needs for and benefits of collaborative research in the microbiome field.

Feedback on the event was positive; of those who responded to the evaluation survey, 90 % said that they agreed or strongly agreed that the event had improved their understanding of IMI.

Call outreach activities

IMI launched three Calls for proposals in 2017 (IMI2 – Calls 11, 12 and 13). These were actively promoted through all IMI channels, namely the website, social media, press, mailshots, flyers, and multipliers (notably the SRG and National Contact Points). IMI also held a total of 23 webinars for potential applicants, covering the Call topics, as well as IMI's rules and procedures and (for IMI2 – Call 13) opportunities for SMEs. In total, the webinars attracted 2 246 registrations. An analysis of the 1 319 registrations for the IMI2 – Call 13 webinars revealed the following breakdown by participant type:



Target audiences

Researchers

Biovision, France, 5 April: IMI and Lyonbiopole co-organised a workshop at Biovision, focused on 'Metagenomics: the technology leap on microbiota study and its impact on One Heath applications'. IMI's involvement was amplified by Pierre Meulien's participation at a debate on SME funding organised by the European Commission, and at a roundtable on regional case studies on health outcomes, run by Science Business. In addition, IMI shared an exhibition stand with the European Commission.

6th Pharmaceutical Science World Congress (PSWC), Sweden, 23 May: IMI organised a symposium at PSWC, showcasing five flagship projects that are championing open innovation. The event, entitled 'Putting open innovation into practice – case studies from Europe', gathered approximately 60 people for a highly interactive debate with some of IMI's key stakeholders.

BIO International Convention, US, 19-22 June: The highlight for IMI was a session in the education programme entitled: 'Detect, Predict, Prevent: Using Digital Technologies to Tackle Brain Disorders'. The session attracted over 100 participants and looked to answer such pressing questions as: How can we ensure the quality of the data generated? How can we best capture those breakthroughs that have the potential to improve patients' lives? The session highlighted the work of IMI's RADAR-CNS project. IMI was also present at the European Commission's booth at the BIO Exhibition.

EAPM (European Alliance for Personalised Medicine) Congress, UK, 29 November: IMI's session at this annual congress brought together representatives of three flagship IMI projects driving public-private collaboration for personalised medicine: U-BIOPRED, CANCER-ID, EU-AIMS.

European Parliament

The IMI Executive Director had meetings with relevant MEPs throughout the year in the framework of the European Parliament reports on the H2020 interim evaluation, the 2015 discharge and antimicrobial resistance.

Under the title *Innovation in Action*, IMI plus six other Joint Undertakings jointly organised a week-long event in the European Parliament in Strasbourg in October 2017 with the goal of raising awareness of the value of the JU model among policymakers. The week featured three key events hosted by Miroslav Poche MEP: an exhibition, the opening reception (where Commissioner Carlos Moedas gave a speech), and a working breakfast with MEPs and project representatives.

IMI staff were also invited to speak at a number of events in the European Parliament:

- EP Interest Group meeting on 'Fostering medical research excellence in Europe' (May).
- European Parliament Alzheimer Europe Lunch debate focuses on current and future treatment for Alzheimer's disease and other dementias (June).
- European Parliament Science and Technology Options Assessment (STOA) panel meeting (November).

SMEs

The communication team enhanced IMI's support for SMEs in a number of ways, including the dedicated SME section in the new IMI website (which includes testimonies from SME project participants), and by organising a webinar for SMEs for IMI2 – Call 13. In addition, the IMI office promoted SME participation by attending and speaking at a range of events where SMEs are present.

Most notably, from 6 to 8 November IMI partnered with the European Commission in Berlin for BIO-Europe in the organisation of a conference session entitled 'EU funding for health research SMEs: The European Innovation Council and beyond', and was present at a joint European Commission / IMI stand.

Patients

At the Drug Information Association (DIA) EuroMeeting (March 2017), IMI and DIA held a very well attended roundtable dedicated to patient centricity animated with the presentation of case studies, lessons learned and examples of best practices. The debate triggered a rich discussion on how to ensure patient perspectives are truly captured and implemented.

One of the two tracks of the Stakeholder Forum was also dedicated to patient engagement (see above for more information).

Regions

IMI's Executive Director contributed to the discussion on EU regions and R&I for personalised medicine during a workshop organised by the European Commission on 4-5 May with regional representatives responsible for drafting the RIS3 (research and innovation strategies for smart specialisation).

IMI participated in the ERRIN's Health Working Group meeting (European Regions Research and Innovation Network) on 23 February with a talk on IMI's funding mechanisms. In addition, IMI participated in several H2020 European health brokerage events.

Project communication and dissemination

IMI organised close-out meetings for 11 projects during 2017. For each project, the IMI communications team wrote a summary of achievements and an interview with the project coordinator(s). In some cases, an additional success story has also been published. The material is available at the following links:

- RAPP-ID: summary of project achievements | interview with project coordinators
- Pharma-Cog: summary of project achievements | interview with project coordinators
- Mofina: summary of project achievements | success story article| interview with project coordinator
- PharmaTrain: summary of project achievements | interview with project coordinators
- Eu2P: summary of project achievements | interview with project coordinators
- EMTRAIN: summary of project achievements | interview with project coordinators
- SafeSciMET: summary of project achievements | interview with project coordinators
- MIP-DILI: summary of project achievements, interview with project coordinators
- OncoTrack: summary of project achievements | success story article | interview with project coordinators
- PREDECT: summary of project achievements | success story article | interview with project coordinators
- EUPATI: summary of project achievements | interview with project coordinators

These project successes were also promoted on IMI's social media accounts (Twitter, LinkedIn) and through the IMI newsletter.

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[18] 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[19] 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[20] 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[21]. 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[22], 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[23] of Regulation (EU, Euratom) No 966/2012[24] on the financial rules applicable to the general budget of the Union and Commission Delegated Regulation (EU) No 110/2014[25], IMI2 JU has adopted specific financial rules.

Changes in 2017

No change to the legal and financial framework occurred in 2017.

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

[19] 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 & Innovation (2014-2020) & repealing Decision No 1982/2006/EC (OJ L 347, 20.12.2013, p. 104).

[20] 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).

[21] 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.

[22] 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.

[23] 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.

[24] 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).

[25] 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).

2.3 Budgetary and financial management

2.3.1. 2017 budget approved

The total IMI budget for 2017 was EUR 322 396 498 in commitment appropriations (CA) and EUR 206 372 367 in payment appropriations (PA). The budget execution of the commitment appropriations and the payment appropriations reached a level of 97.07 % and 71.96 % respectively.

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 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 IMI Governing Board approved the 2017 budget on 23 December 2016. The Governing Board approved the first budget amendment on 11 July 2017 in order to include the carry over amounts from the previous year as well as to reduce the operational payment appropriations by EUR 56 million. The staff establishment plan for 2017 remained unchanged.

The Governing Board approved the second budget amendment on 28 November 2017 in order to further reduce the operational payment appropriations by EUR 25.8 million, in line with updated projects' spending. The staff establishment plan for 2017 remained unchanged.

Budget 2017 in EUR

Budget 2017 in EUR										
	Approved 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	182 953 171	201 697 134	134 467 173	22 699 079		(24 000 000)			317 420 344	200 396 213
EFPIA contribution	4 914 500	4 914 500							4 914 500	4 914 500
***Other Members contribution**		1 000 000							-	1 000 000
***Associated Partners contribution**		1 831 000				(1 831 000)			-	-
Others							61 654	61 654	61 654	61 654
Total revenue	**187 867 671**	**209 442 634**	**134 467 173**	**22 699 079**	**-**	**(25 831 000)**			**322 396 498**	**206 372 367**
Expenditure										
Title 1	5 702 000	5 702 000		124 575			82	82	5 702 082	5 826 657
Title 2	4 127 000	4 127 000		1 292 135			35 903	35 903	4 162 903	5 455 038
Title 3	178 038 671	199 613 634	134 467 173	21 282 369		(25 831 000)	25 669	25 669	312 531 513	195 090 672
Total expenditure	**187 867 671**	**209 442 634**	**134 467 173**	**22 699 079**	**-**	**(25 831 000)**	**61 654**	**61 654**	**322 396 498**	**206 372 367**

* This refers to cash contributions from individual EFPIA companies and Associated Partners to the IMI operational budget.

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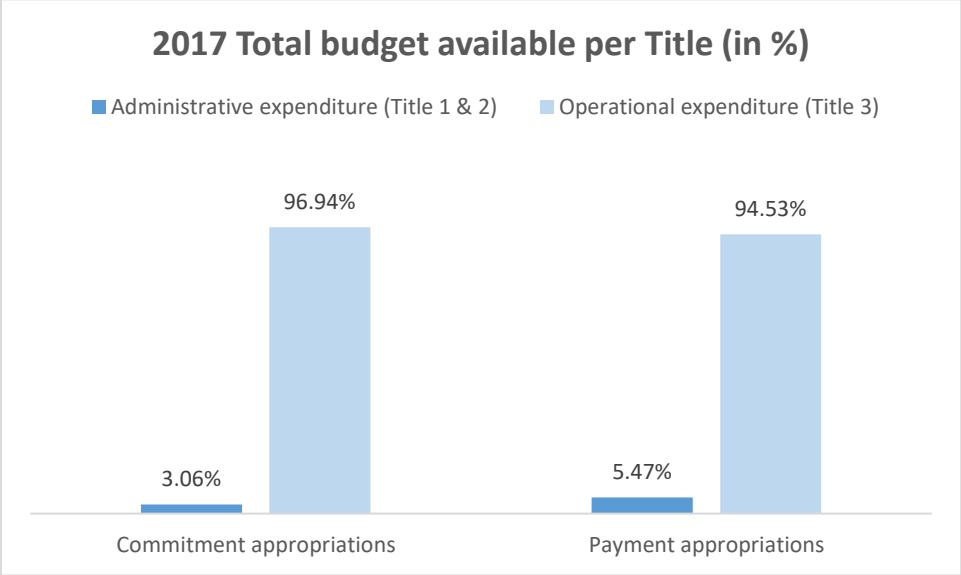
The assigned revenue shows the amounts recovered during the year from suppliers and projects. The graph below shows the total 2017 budget available per Title in %.



2.3.1 Budget transfers

No budget transfers between Titles were made during 2017. Budget transfers between chapters were authorised in 2017, which led to the following changes:

Chapter		Budget approved EUR	Budget transfer EUR	Budget after transfers EUR
11	Staff in active employment	5 242 000	(91 240)	5 150 760
14	Socio-medical structure	230 000	91 240	321 240
20	Investments in immovable property rental of buildings	679 000	90 154	769 154
21	Information Technology purchases	592 000	178 908	770 908
22	Movable property	153 000	(93 062)	59 938
23	Current administrative expenditure	123 000	(21 000)	102 000
24	Postage and telecommunications	68 000	10 000	78 000
26	Expenditure in connection with operational activities	300 000	14 000	314 000
27	External communication information and publicity	625 000	(132 000)	493 000
28	Studies	729 000	(260 000)	469 000
29	Expert contracts and meetings	700 000	213 000	913 000

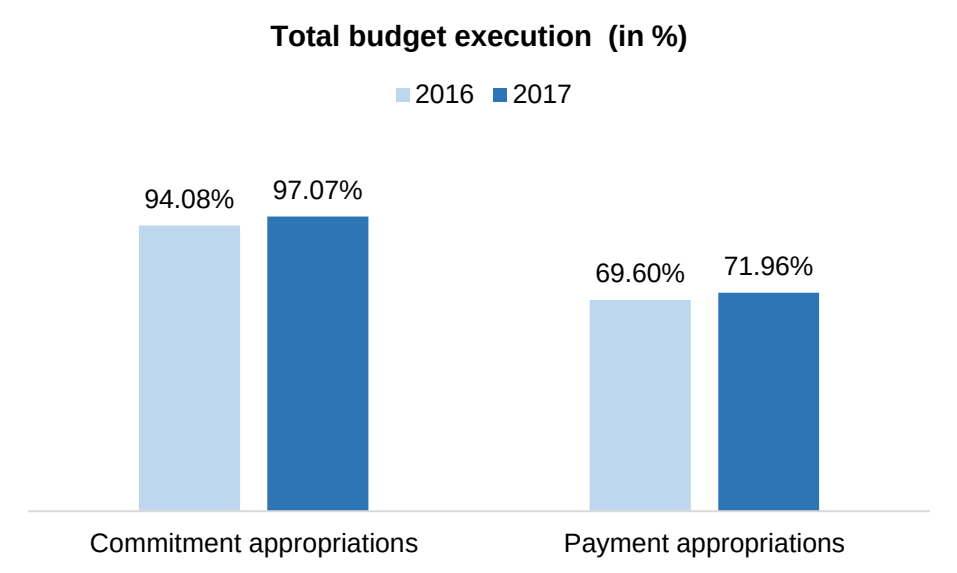
Overall, the budget transfers made in 2017 had no impact on the approved budget.

2.3.2 2017 budget execution

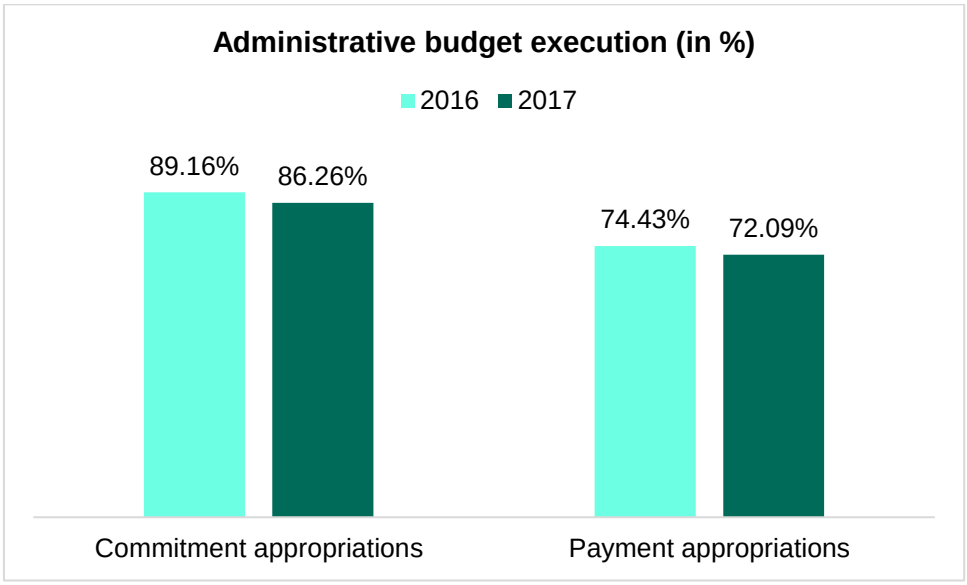
The table below shows the execution of the 2017 budget per Title in absolute amounts.

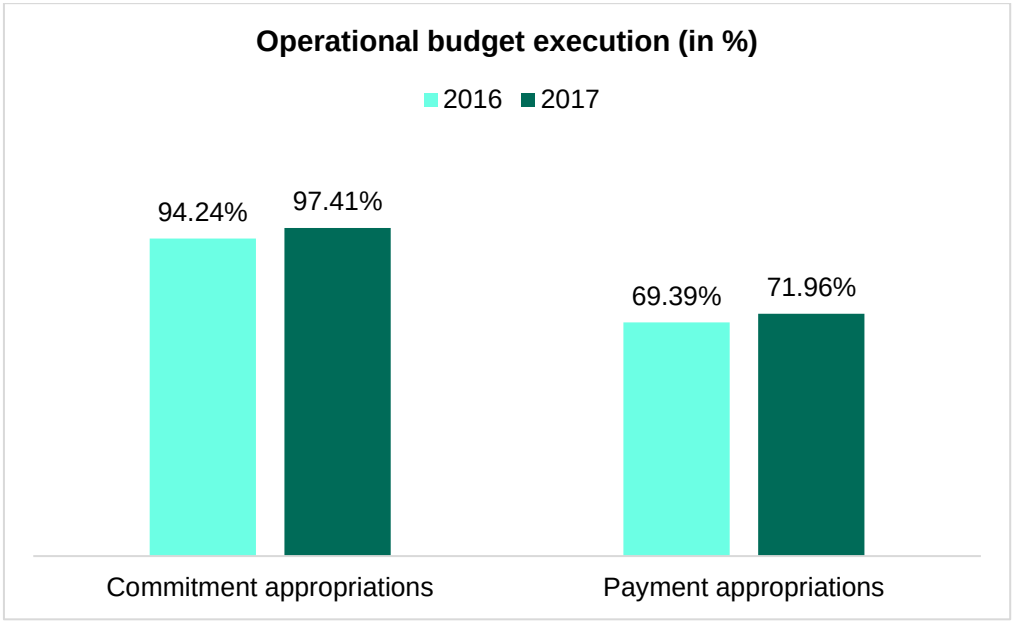
Title	2017 final budget execution per title in EUR					
	Commitment appropriations	Execution	%	Payment appropriations	Execution	%
Title 1	5 702 082	4 945 213	86.73	5 826 657	4 940 716	84.80
Title 2	4 162 903	3 564 619	85.63	5 455 038	3 192 260	58.52
Subtotal administrative expenditure	*9 864 985*	*8 509 832*	*86.26*	*11 281 695*	*8 132 976*	*72.09*
Title 3	312 531 513	304 431 513	97.41	195 090 672	140 381 318	71.96
Total (Title1, 2 and 3)	**322 396 498**	**312 941 345**	**97.07**	**206 372 367**	**148 514 294**	**71.96**

The graph below shows the 2017 total budget execution compared with 2016.



The graphs below show the 2017 budget execution for administrative costs (staff and infrastructure) and operational activities (project-related) compared with 2016.





As regards operational expenditure, details are set out in section 1.6.

Regarding the administrative costs, the budget execution of the commitment and payment appropriations reached a level of 86.26 % and 72.09 % respectively. IMI continued to execute its budget, applying principles of sound financial management, which resulted in savings in the communication, meetings and other administrative budget lines.

Despite recruitments carried out in 2017, the number of staff employed at the end of 2017 was lower than the maximum authorised, resulting in lower execution than planned.

It is important to note that the EC part of unused appropriations for administrative costs will be made available for operational activities in the 2018 budget – see section 2.3.5 for details.

In 2017, the TTP for administrative costs was significantly reduced and improvements are continuing. The following table shows the number and amount of all administrative transactions (including experts).

No of all administrative transactions made in 2017			
	No	**Amount (EUR)**	**% payments**
Total no payments	1167	3 692 141.12	100
No payments on time (within 30 days)	1037	3 252 325.56	88.9%
No late payments	130	439 815.47	11.1%

The following table shows the number and amount of all payments made to experts only. The percentage of payments made on time is improving thanks to the use of the H2020 tools, such as COMPASS, EMPP (expert management participant portal) and EMI (Expert Management Internal).

	No payments	%
Total experts' payments	301	
Total on time payments	276	92 %
Total late payments	25	8 %
Total amount paid (EUR)	902 129	

The table below shows the summary of commitments outstanding at the end of 2017.

	EUR
Commitments carried from previous year	723 532 856
De-commitments (-)	(174 956 518)
Payments made during 2017 related to commitments carried forward (-)	(119 176 065)
Commitments made during 2017	312 941 345
Payments made during 2017 related to commitments made during 2017 (-)	(29 338 229)
Total commitments outstanding at the end of 2017	**713 003 389**

2.3.3 Overview of the carry over appropriations to 2018

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, subject to Governing Board approval. IMI will re-enter into the 2018 budget the unused commitment and payment appropriations from 2017.

Administrative expenditure: Payment appropriations of EUR 1 449 527, corresponding to the amount of commitments carried forward from the 2017 to the 2018 budget.

Operational expenditure: Unused commitment and payment appropriations to be carried over to 2018 budget of EUR 183 390 055* corresponding to commitment appropriations, and EUR 56 158 881* corresponding to payment appropriations.

	Commitment appropriation (EUR)	Payment appropriation (EUR)
Unused appropriations (operational and administrative)	* 183 390 055	* 56 158 881

* estimated; subject to Governing Board approval

2.4 Procurement and contracts

The majority of the IMI's contractual commitments in 2017 were concluded on the basis of existing multi-annual framework contracts (FWCs). In terms of volume, the FWCs used most were in the field of IT, communications and audit services. Several of the framework contracts in question are inter-institutional, thus minimising the administrative burden and ensuring economies of scale.

The table below shows tender procedures in 2017 outside existing FWCs with a value exceeding EUR 15 000.

Subject	Procedure	Contractor	Value (in EUR)	Signature date
Media monitoring services	Negotiated	Comparex Belgium BVBA	16 350	17/01/2017
Media subscription services	Negotiated	Ebsco Information Services	21 752	24/01/2017
Meeting facilities	Negotiated	Crowne Plaza Brussels	43 202	24/04/2017
Media subscription services	Negotiated	Politico SPRL	18 436	18/08/2017

All procedures were carried out in compliance with the IMI2 JU Financial Rules to ensure fair competition amongst economic operators and the most sound and efficient use of IMI funds.

2.5 IT and logistics

IT activities in 2017 mainly focused on working on the transition to Horizon 2020 IT tools, the migration of the JUs' common IT infrastructure to 'infrastructure as a service' (IaaS), and enhancements of in-house developed applications and user support.

Transition to H2020 IT tools

During 2017, the EC IT teams supporting the H2020 applications successfully implemented the majority of requirements reflecting IMI2-specific business processes (identified previously in a gap analysis exercise).

Launching new IMI2 Calls for proposals is now a streamlined process under H2020 IT tools. Subsequently, all three IMI2 Calls for proposals that IMI launched in the course of 2017 are managed entirely in the tools, and five evaluation sessions have been concluded via the specific tools.

Furthermore, six projects from IMI2 - Call 9 (submitted and evaluated in SOFIA) were prepared and signed in SyGMA.

IMI has fully transferred IMI2 project data into the H2020 IT environment (SEP specifically). As of the beginning of 2018, all IMI2 project reporting and consequently monitoring and payment will be carried out via the H2020 tools.

The update of CORDA (COmmon Research DAta warehouse - central repository of data from research and innovation programmes) with IMI2-specific developments was initiated towards year end and is planned for completion in Q1 2018.

To enhance the IMI reporting system and to provide reliable data for analyses to different IMI stakeholders, management and staff, the IT team started a new IMI data warehouse (DW) project – a single repository, combining IMI1 (SOFIA) and IMI2 (CORDA) data. The DW will be used in three main areas: QlikView application, the IMI website and SOFIA (IMI2 data for the purpose of 'annual reporting of costs by EFPIA companies and Associated Partners' is still for the time being reported in SOFIA).

Migration of common JUs' IT infrastructure to 'infrastructure as a service' (IaaS)

The common JUs' IT infrastructure was migrated to IaaS in the framework of the project to replace outdated core ICT equipment. In moving to an IaaS model, there is increased system availability, consolidated disaster recovery and business continuity plans, better mobile and vpn solutions, easy scalability and improved cost control with less capital investment.

Most of the users were moved to Windows 10 and MS Office 2016 together with the import of locally stored e-mail archives (pst files) to an exchange server online archive (available from any device).

Enhancements of in-house applications

The following major new enhancement and change requests regarding the further development and maintenance of applications developed in-house were implemented:

- SOFIA (Submission of Information Application, which will continue to be used for the management of IMI1 projects):
  - total redesign of the whole application user interface, to improve usability and readability;
  - faster performance and response time;
  - new password handling process and policy;

- several changes to the EFPIA reporting process for IMI2 projects, including checklists of the financial and scientific assessment of IMI2 in kind and new reports;
- submission of periodic report adjustments after project end for IMI1;
- improvements in the XML export of IMI2 data for integration with CORDA.

- Cloud applications:
  - upgrade of content management system (CMS) and development technologies - Liferay upgrade from v 6.1 to v 6.2, JDK to 1.7, Primeface from 3.0 to 5.3, SVN Repository;
  - new generic version of the BIT and CDR applications to be used from all JUs;
  - new symposium submission platform;
  - improvements and new features in all existing applications: Vacancy, ISA (transfer of flexi-time to the new year), eMA (upload documents), DORA and SRG.

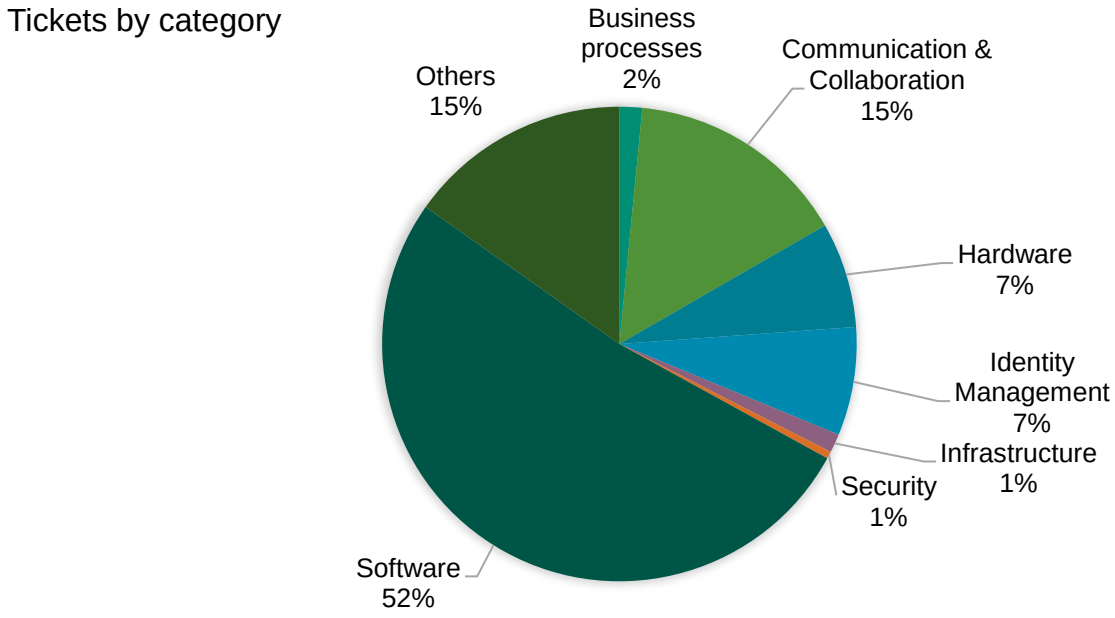
Recommendations from the cyber-capability assessment exercise of hosted infrastructure and in-house applications were implemented.

Furthermore, IT supported the development, hosting and CMS upgrade of a new website, which was officially in launched in October 2017.

Helpdesk support

In 2017, a total of 1 421 requests for support were sent to the IMI IT Helpdesk – the single point of contact and incident management system.

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



2.6 Human resources

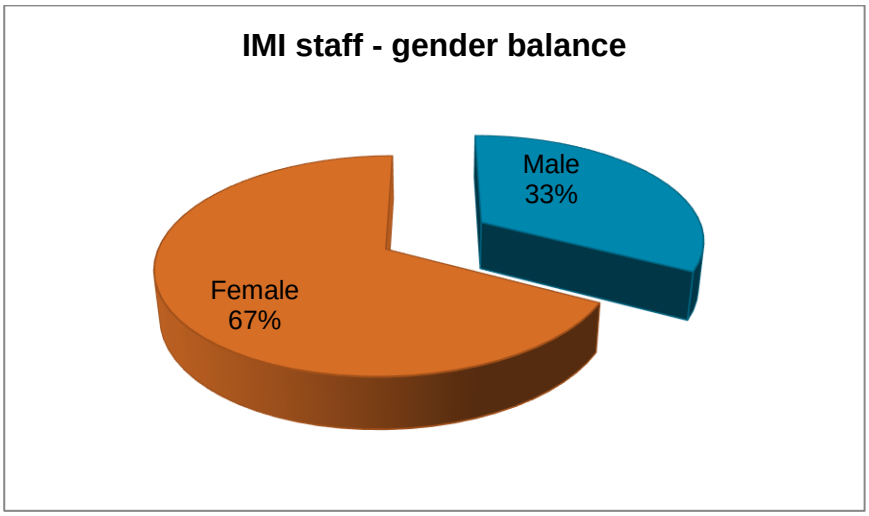
Staff and recruitment

The staff establishment plan allows for 39 temporary agents, 15 contract agents and 2 seconded national experts, in total 56 staff members. By 31/12/2017 there were 49 positions occupied (36 out of 39 temporary agents (92.30%), 13 out of 15 contract agents (86.66%) and 0 out of 2 seconded national experts) and one new staff member has been appointed as Financial Assistant FG III with a starting date of 16/01/2018.

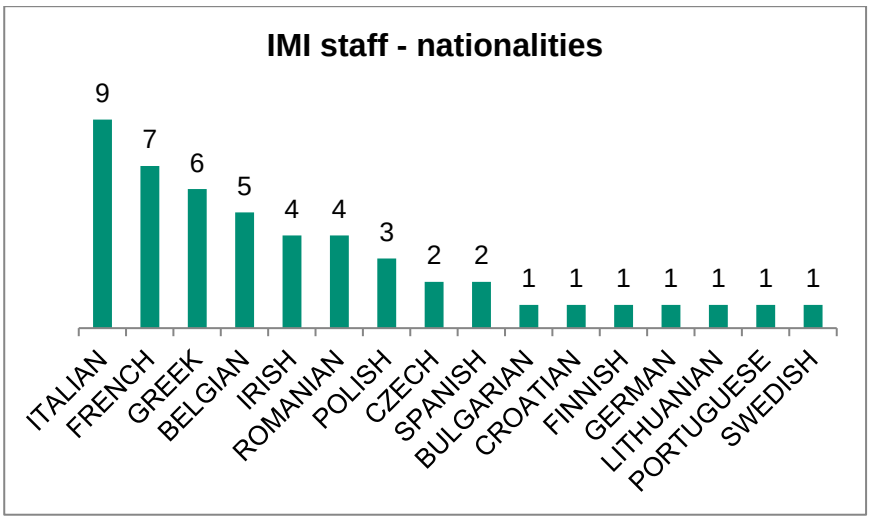
A total of 11 vacant positions were filled in 2017: 8 to support project management, and 3 to support other activities of the Programme Office.

Three staff members resigned in 2017. Two were replaced in 2017 and the third has been assigned to the operational team (Scientific Officer) and will be filled on 1 February 2018.

The two graphs below show the gender and geographical balance within IMI on 31/12/2017.



16 EU nationalities were represented in IMI by on 31/12/2017.



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 framework: Staff followed general training on various aspects of the Horizon 2020 framework. Specific attention was given to the H2020 IT tools in the context of IMI's migration to SEP, SyGMA and Compass.
- Financial framework: All actors in the IMI finance workflows were trained and kept up-to-date with new developments and best practices in ABAC.
- IT: Training was delivered to staff on various aspects including Microsoft Office (Word, Excel, PowerPoint) as well as IMI-specific cloud applications.
- Other training courses were carried out for ethics and integrity; personal development (soft skills) and languages.

The European Commission's 'EU Learn' system helped IMI staff in the selection of their training needs, on both hard and soft skills.

Reclassification

The reclassification exercise is a valuable tool to increase staff motivation. The first reclassification exercise took place successfully in 2017. Four staff members (2 temporary agents and 2 contract agents) were reclassified to the immediate higher grade.

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 Human Resources and Security Directorate General (DG HR) guidelines.

The following implementing rules were adopted by the IMI Governing Board in 2017:

- IMI2-GB-DEC-2017-14 Innovative Medicines Initiative 2 Joint Undertaking Decision of 25 July 2017 on Working Time;
- IMI2-GB-DEC-2017-15 Innovative Medicines Initiative 2 Joint Undertaking Decision of 25 July 2017 on general implementing provisions regarding Article 87(3) of the Conditions of Employment of Other Servants of the European Union;
- IMI2-GB-DEC-2017-16 Innovative Medicines Initiative 2 Joint Undertaking Decision of 25 July 2017 on laying down general implementing provisions regarding Article 54 of the Conditions of Employment of Other Servants of the European Union;
- IMI2-GB-DEC-2017-19 On the non-application of the Commission Decision of 28 August 2017 on the maximum duration for the recourse to non-permanent staff in the Commission services.

2.7 Data protection

In 2017, 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.

DPO network meetings are an important forum for the exchange of information and best practices. Much of the activities undertaken in this forum focussed on the entry into force and ramifications of the EU General Data Protection Regulation.

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 Research Participant Portal.

3 Governance

3.1 Governing Board

The Governing Board is the main decision-making body of IMI. 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 2017 the Governing Board held five meetings. The list of decisions taken by the Governing Board in 2017 can be found on IMI website.

The role of Chair of the Governing Board in 2017 was assumed as follows:

Dates	Chairperson
1 January – 30 April 2017	Marc de Garidel (EFPIA)
1 May – 6 June 2017	Carlo Incerti (EFPIA)
7 June – 6 July 2017	Jean-Christophe Tellier (EFPIA)
7 July – 31 December 2017	Jack Metthey (European Commission)

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

Dr Pierre Meulien was Executive Director of IMI throughout 2017.

3.3 States Representatives Group

The IMI States Representatives Group (SRG) is composed of one official delegate from each EU Member State and each country associated to the EU's research programmes. It supports IMI as an advisory body and acts as an interface between IMI and the relevant stakeholders within their respective countries. It may also provide opinions to the Governing Board, especially on IMI's programme orientation, progress and achievements.

Information on SRG membership, including CVs and links to national websites, can be found on the SRG page of the IMI website. In 2017, IMI reviewed the SRG page to better describe the role of this advisory body, the role of its Chair and Vice-Chair, and how the SRG collaborates with the IMI Scientific Committee.

The position of Chair is held by Marta Gómez Quintanilla (Spain) and the position of Vice-Chair by Gunnar Sandberg (Sweden). The respective mandate was exceptionally renewed for a period of one year until 4 February 2018. The process for electing a new Chair and Vice-Chair was launched during the year in order to ensure continuity in activities.

In 2017, the SRG met in March and June in Brussels (Belgium) and in September in Dublin (Ireland) back-to-back with the HUPO2017 Conference. At the meetings, detailed updates on IMI activities, with a specific focus on the involvement of patients and SMEs, were provided. A range of SRG members provided an overview of national and regional clusters in order to better investigate synergies between IMI activities and national and regional initiatives and activities. During 2017, the SRG was consulted on the Call topics and documents and on the Annual Work Plan (including two amendments), and was involved in the nomination process of new SC members and experts for scientific workshops organised by IMI.

In 2017, for the first time a joint meeting of the Scientific Committee and the SRG was organised (see below).

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 of the Call topics. The new Committee that was appointed upon suggestions made by the SRG met for the first time in February 2017 and Beatriz da Silva Lima and Isabelle Beatrice Bekeredjian-Ding were elected as Chair and Vice-Chair respectively. In 2017, some changes occurred in the composition of the Scientific Committee with the appointment of its 11th member, Zoltan Kalo, Professor of Health Economics at Eötvös Loránd University in Budapest, Hungary, and two new members to replace members who resigned (Prof Kjetil Tasken, Director, Centre for Molecular Medicine Norway replaced Professor Maria Blasco, Director, Spanish National Cancer Research Centre (CNIO) and head of Telomeres and Telomerase Group, Madrid, Spain; and Dr Corinne de Vries (ad hoc member), Head of Science and Innovation Support, European Medicines Agency replaced Professor Hans-Georg Eichler (ad hoc member), Senior Medical Officer, EMA).

The members have expertise in a range of medical fields, including bioinformatics, cancer, microbiology, molecular biology, neurology, pharmacology, proteomics and public health. The biographies of all current members are published on the Scientific Committee page of the IMI website.

Four Scientific Committee meetings took place in 2017 and three conference calls were organised in between to progress on actions.

The Committee has identified a number of matters for further consideration during its mandate with the view to provide advice to IMI (e.g. patient engagement, SMEs involvement, the long-term sustainability of key resources generated by IMI projects).

As part of their role, the members provided in 2017 advice on the proposed IMI scientific priorities for 2018 that are part of the AWP, as well as on the proposed topics that were included in IMI2 - Calls 11, 12 and 13, which were launched in 2017. Members representing the Scientific Committee in the different Strategic Governing Groups reported to the Committee on the work of the group. In addition, at least one member participated in the 16 IMI project reviews carried out in 2017 (see section 1.4.2) and whenever possible in the close-out meetings on IMI projects that have ended. Finally, representatives of the Committee participated in consultation workshops organised by IMI such as the workshops on microbiome and on diagnostics for reducing antimicrobial resistance (AMR).

In 2017, for the first time a joint meeting of the Scientific Committee and States Representatives Group (SC/SRG) was organised. The objective was to strengthen interactions and take full advantage of these two advisory bodies. The meeting provided an opportunity for a greater understanding of the roles and responsibilities of the respective bodies as well as sharing views on topics of mutual interest, like the need to engage with a wide range of stakeholders/sectors, with better geographical coverage, including for SMEs; broad support for increased role of patients in IMI activities and IMI's proposed approaches; and support for the IMI SME strategy. Considering the positive feedback, both advisory bodies agreed to meet once annually and to share agendas and minutes of their respective meetings.

3.5 Stakeholder Forum

The Stakeholder Forum was held in Brussels, Belgium on 18-19 October. More information on the event can be found in the Communication and Events section and the event web page.

3.6 Strategic Governing Groups (SGGs)

The Strategic Governing Groups (SGGs) were created in 2014 on the basis of Article 7.3.p of the legislation establishing the IMI2 JU programme. They are composed of representatives of companies active or interested in the thematic area covered by SGGs, as well as representatives from the European Commission, the IMI Programme Office and the IMI Scientific Committee. Their main activities are focused on:

- facilitating an efficient translation of the IMI2 JU Strategic Research Agenda;
- developing a coordinated approach for selected diseases leading into annual strategic priorities;
- providing recommendations for high quality and concrete call topic texts, taking into account ideas from industry, Associated Partners and third parties.

The SGG charter, as well as lists of members, can be found on the SGG page of the IMI website.

Cross-SGG coordination

Two dedicated cross-SGG meetings were held in May and October.

In 2017 the SGGs' efficiency mechanisms were significantly reinforced and improved. The SGG IT platform was completely redesigned and modernised, and is now operational. This tool allows users to easily find in one place the same place rules, templates, topic timelines, dates of meetings, etc. The guidelines on IMI and SGG processes were also prepared and posted on the platform. One of the significant developments is sharing publishable minutes from the SGG meetings across SGGs and with the IMI advisory bodies, especially the SRG.

SGG Neurodegeneration

The SGG Neurodegeneration met four times in plenary session during the year, twice at face to face meetings and twice via teleconference. The SGG Neurodegeneration provided input to the IMI Governing Board regarding the scientific priorities for 2018, and developed two topics that were launched in IMI2 – Call 12 and two topics that were launched in IMI2- Call 13. The Parkinson's disease research and support charity Parkinson's UK joined the SGG as an IMI2 Associated Partner and contributed to the two topics of IMI2 - Call 13.

SGG Translational Safety

The SGG Translational Safety met three times in 2017. Input to the IMI Governing Board regarding the scientific priorities for 2018 was provided. The SGG developed two topics that were launched in IMI2 – Call 13.

SGG Oncology

The SGG Oncology met three times in 2017. Discussions focused on the SGG scientific strategy to prioritise and implement new topics to be launched in future IMI Calls. One topic entitled 'Human tumour microenvironment immunoprofiling' was launched in 2017 under IMI2 - Call 13. Another topic which is part of the Big Data for Better Outcomes programme was developed and should be part of a 2018 Call.

SGG Immunology

The SGG Immunology held three meetings in 2017. Input to the IMI Governing Board regarding the scientific priorities for 2018 was provided. The SGG developed one topic that was launched in IMI2 – Call 12 and one that was launched in IMI2 – Call 13. A 'think big' initiative on immunology and microbiome was launched in 2017 and generated two topics that will be part of IMI2 – Call 14.

SGG Data and Knowledge Management

During 2017, the Data and Knowledge Management (DKM) SGG was re-structured and therefore did not meet. In 2018, many of the tasks of the DKM SGG will be taken on by the new Digital Health and Patient Centric Evidence Generation SGG.

Diabetes / metabolic disorders

The Diabetes and Metabolic Disorders SGG met three times in plenary session during the year. The SGG provided input to the IMI Governing Board regarding the scientific priorities for 2018, and developed one topic that was launched in IMI2 – Call 13.

Infections control

The SGG Infection Control had two face-to-face meetings in 2017 and two meetings by teleconference. At the meetings, new topics and ideas proposed by either industry or third parties for potential future IMI projects were discussed and priorities for 2018 were defined. In addition, updates on ongoing IMI projects are regularly presented at SGG meetings.

3.7 Associated Partners

Under the IMI2 programme, any legal entity (except for EFPIA companies) interested in contributing to the IMI2 objectives 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). So far, Associated Partner contributions to 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.

To better support the engagement and participation of Associated Partners, in 2017 IMI produced an information guide and created a page dedicated to Associated Partners as part of the new IMI website. In 2017, the number of Associated Partners almost doubled, rising from 8 to 15. As of the end the year, the following organisations had become IMI Associated Partners:

- Accelerate Diagnostics will contribute under the IMI2 - Call 13, topic 3 – The value of diagnostics to combat antimicrobial resistance by optimising antibiotic use;
- Autism Speaks will contribute to the IMI2 – Call 10 project on autism; they are also involved in the EU-AIMS project;
- Autistica will contribute to the IMI2 - Call 10 project on autism;
- BD Switzerland Sarl will contribute under the IMI2 - Call 13, topic 3 – The value of diagnostics to combat antimicrobial resistance by optimising antibiotic use;
- Bill and Melinda Gates Foundation contributes to the PERISCOPE project on pertussis (whooping cough) vaccines;
- Bio-rad Laboratories will contribute under the IMI2 - Call 13, topic 3 – The value of diagnostics to combat antimicrobial resistance by optimising antibiotic use;
- International Diabetes Federation contributes to the IMI2 – Call 10 project on diabetes;
- JDRF contributes to the diabetes projects INNODIA and BEAT-DKD;
- Leona M. and Harry B. Helmsley Charitable Trust contributes to the diabetes project INNODIA;
- Medicines for Malaria Venture (MMV) will contribute under the IMI2 Call - 13 topic 7 – European Screening Centre: unique library for attractive biology (ESCulab);
- Parkinson UK will contribute under the IMI2 - Call 13, topic 4 – Mitochondrial dysfunction in neurodegeneration and IMI2 - Call 13, topic 5 – Support and coordination action for the projects in the neurodegeneration area of the Innovative Medicines Initiative;
- Simons Foundation Autism Research Initiative (SFARI) will contribute to the IMI2 – Call 10 project on autism;
- Software AG will contribute under IMI2 - Call 12, topic 1 – Development and validation of technology enabled, quantitative and sensitive measures of functional decline in people with early stage Alzheimer's disease (RADAR-AD);
- Unitio (through its T1D Exchange programme) will contribute to the IMI2 – Call 10 topic on diabetes;
- Wellcome Trust will contribute under the IMI2 - Call 13. topic 3 – The value of diagnostics to combat antimicrobial resistance by optimising antibiotic use.

4 Internal Control Framework

4.1 Financial procedures

In accordance with the EU financial regulation, IMI has in place specific financial rules and operating procedures[26].These documents outline the financial processes to be applied and describe the responsibilities of the financial actors as well as the internal controls applied to assure adequate management of the risks relating to the legality and regularity of the underlying transactions; safeguard IMI's assets; check the accuracy and reliability of recorded accounting data; and promote effectiveness and efficiency in financial operations.

It should be noted that, for the management of the actions funded, IMI applies two different framework programmes - IMI1/FP7 and IMI2/H2020 - with different obligations and *modus operandi.* In 2017, in particular, IMI has continued to focus on the implementation of H2020 rules and the EC tools[27] which assure common workflows and interpretation of requirements.

4.2 Ex ante controls on operational expenditure

IMI's annual budget is implemented through the administrative expenditure (related to staff and day-to-day activities – Titles 1 and 2 of the budget) and the operational expenditure (related to the management of the research programme and payments of beneficiaries of IMI funding - Title 3 of the budget).

The two tables below present the balance between the actions implemented under the FP7 and H2020 programmes in terms of project portfolio and operational expenditure at the cut-off date of 31/12/2017.

IMI1 and IMI2 projects portfolio				Pre-financing payments	Interim & final payments[28]	Total paid
IMI1 (FP7)	**59**[29] of which	Running as at 01/01/2017	**38**	0	71 890 752	**71 890 752**
		Concluded[30] during 2017	**11**			
		Running as at 31/12/2017	**27**			
IMI2 (H2020)	**40** of which	Running at 01/01/2017	**25**	43 542 355	24 818 211	**68 360 566**
		Signed in 2017	**15**			
		Concluded[31] during 2017	**3**			
Total IMI1 & IMI2 projects	**99**	**Total running projects**	**64**	43 542 355	96 708 963	**140 251 318**

[26] Including the Manual of Procedures for Financial Operations and several specific Standard Operating Procedures (e.g. 'Assessment and approval of periodic and final reports', 'Preparation, submission and approval of Certified Financial Statements', etc.) adopted to assist operations and assure compliance.

[27] In particular, the Commission created the Common Support Centre which provides common services in legal support, ex-post audit, IT systems and operations, business processes, programme information and data.

[28] These amounts represent only direct payments to beneficiaries. Clearing of pre-financing is not considered in this table as it is accounted as part of the volume of operational transactions (see below).

[29] The total number of IMI1 projects concluded as at 31/12/2017 is therefore 32.

[30] IMI1 projects which have ended their activities and presented, or are being to present the final report.

[31] IMI2 projects which have ended their activities and presented, or are being to present the final report.

Comparative table of operational expenditure 2010 - 2017 (EUR million)									
	2010	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**Total**
IMI1 (FP7)	35.242	68.979	103.809	121.468	120.051	88.562	109.847	**71.891**	**719.849**
IMI2 (H2020)	/	/	/	/	/	45.953	65.336	**68.360**	**179.649**
Total	35.242	68.979	103.809	121.468	120.051	134.515	175.183	**140.251**	**899.498**

Outcome of ex-ante controls on operational expenditure

To assure the effective and efficient implementation of the operational expenditure, IMI has set out an internal control framework embedded across its organisational structure which relies on a combination of ex-ante and ex-post controls (summarised in the tables below).

	Ex-ante controls	Ex-post controls
Timing	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 are rectified before the transaction is approved.	Errors detected are corrected. Where the error give rise to an ineligible expenditure, a recovery order is issued or offsetting is made with future payments.
Level of assurance	Primary means of ensuring sound financial management and legality and regularity of transactions, based on desk review of available documentation.	Secondary means of ensuring sound financial management and legality and regularity of transactions, but more robust as normally carried out on-the-spot.

The following sections provide an overview of the functioning and outcomes of the ex-ante controls performed on the overall management cycle implementing IMI operational expenditure.

I - Call management and Selection and evaluation phase (SEP)

The IMI awards grants to selected proposals in a competitive evaluation procedure following the publication of Calls for proposals. For each year, IMI Calls are established in the work plan adopted by the IMI Governing Board. Annual work plans as well as announcements of individual Calls are published on IMI website and Participant Portal. The goal of controls performed at this stage 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. IMI also makes sure that the experts do not have any conflict of interest.

Indicator	Results 2017	Target 2017	Results 2016
% of annual coverage of call topics identified in AWP 2017	**100% (23 out of 23)**	100%	93%
Number of redress procedures on the result of the evaluation and selection procedure	**0**	0	0

II - Grant Agreement preparation phase (GAP)

Grant Agreement preparation starts after the evaluation, upon approval of the results by the IMI Governing Board, with the GAP invitation letter — no later than 5 months after the Call deadline (time-to-inform / TTI indicator). In this phase, the Grant Agreement (GA) is prepared and signed. The IMI Programme Office checks the budget and administrative data submitted, validates each participant, and reviews the full proposal. 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 to enable the start of projects' activities.

Indicators	Target	Results - 2016	Results - 2017
Total average Time to Inform (TTI)	153 days	76 days	**81 days**
Total average Time to Grant (TTG)[32]	243 days	232 days	**270 days**
Total average Time to Pay (TTP) for pre-financing	30 days	12 days	**11 days**

TTP for pre-financing improved considerably in 2017. On average it took 11 days to process pre-financing payments for newly-signed Grant Agreements and enable the projects to kick start their activities. This improvement can be explained by the use of H2020 IT tool SyGMA, which brought in efficiency, and also by the proactive approach of the Programme Office to speed up payments and implementation of Grant Agreements signed.

TTI slightly increased in 2017, however, it remains a good achievement, and is considerably below the target set by the H2020 rules. This may be explained by technical aspects related to bottlenecks in migrations to the H2020 IT tool. Some adjustments had to be made by IT developers because of IMI specificities, which caused some delays.

As for TTG, the target time was exceeded mainly due to some challenges that arise in the Grant preparation phase. The main reason for delays is the time needed for public and private partners who have not worked together before to enter into a consortium agreement. The complexity of managing an IMI2 project should not be underestimated. Extensive internal negotiations are necessary in order for the consortia to find suitable arrangements and agreements. Furthermore, IMI2 projects often mobilise actors that have not participated in previous framework programmes and this factor brings in additional complexity to the negotiations especially when non-European entities are involved.

In particular, 50 % of IMI2 grants in 2017 required more than the 243 days allowed due to the complexity of concluding a consortium agreement. Among the root causes for delays within consortia, a few examples can be mentioned:

[32] According to the H2020 vade mecum 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). See also Annex 6.

- lengthy discussions related to intellectual property (IP) rights or access rights to project results;
- changes in the leadership roles within consortia often due to the original coordinator being identified as financially weak, meaning another coordinator needs to be found;
- withdrawal of a participating partner or a contributing beneficiary requiring reallocation of tasks and resources;
- change of legal status of a participating entity.

III - 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 by beneficiaries as well as by (EFPIA) pharmaceutical companies (the so-called in-kind contribution) and Associated Partners.

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

- the project is progressing as planned, and demonstrates the necessary level of achievement;
- resources are being used according to the indicative plan in the description of work/action (DoW/DoA, e.g. FTEs associated to each of the work packages, subcontracts, 'other direct costs', etc.). In particular, costs are compared to the work done: if the costs (including person months per work package) are reasonable based on the work reported and if there are significant deviations from the work as planned in the description of work (on the basis of the SO assessment report).

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 (according to a risk control matrix which covers the majority of operational cases). On that basis, the IMI Programme Office can adapt the controls to verify if the use of resources reported by beneficiaries (for personnel, consumables, equipment, subcontracting, etc.) is justified in relation to each specific task, deliverable and milestone. Depending on the type and rating (high, medium or low) of the risk identified, the scientific and financial officers can therefore take the most appropriate measures. Once the report is accepted by the Scientific Officers ('certified correct' visa), the accepted costs are reimbursed to beneficiaries (interim payment) following the standard financial circuit outlined.

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 experts and their recommendations are closely followed up by the project managers. As described above, all the interim reviews performed in 2017 made positive conclusions[35].

Although through the ex-ante control IMI achieves the reasonable assurance that the costs claimed are accurate and in compliance with the applicable legal and contractual provisions, an additional level of assurance on costs paid is provided by the ex-post audits carried out at the beneficiaries' premises, after the costs have been incurred and declared (see Section 4.3).

The following paragraphs report and assess the elements identified by management that support the assurance on the achievement of the internal control objectives regarding the grant management process.

[33] Specific internal operating procedures are applied to IMI1 projects and for the acceptance of the in-kind contribution provided by industrial partners while for IMI2 funded actions IMI operates through the H2020 IT tools (SyGMA and COMPASS) and applies the vade mecum on grant management set out by the European Commission adjusted to IMI's legal environment.

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

[35] More information can be found in Section 1.5.2 above.

a) Volume of operational transactions

The total number of operational transactions (82) performed in 2017 demonstrates the significant resource input needed to handle the workload of the IMI Programme Office. Each transaction results from the control workflow described above. The verification process is complex due to the nature of the projects implemented by IMI, as well as the amounts at stake and the high number of participants per project (average 22). Another element to take into consideration while assessing control workload is the percentage of final payments (14) handled during the year. The 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.

The table below provides a cumulative overview of the number of pre-financing payments, interim, and final transactions made by IMI or compensated against pre-financing payments[36] made from 2012 to 2017. It also shows that in 2017, the total volume of financial transactions related to IMI projects has increased by 7 % and is expected to increase in the coming years as new projects are gradually added to the portfolio as Calls will continue to be launched up till 2020 and project implementation runs until 2024.

Cumulative number of operational transactions

	2012	2013	2014	2015	2016	2017
Pre-financing payments	12	14	18	16	16	**16**
Interim and final payments[37]	26	33	32	30	59	**66**
Total	38	47	50	46	75	**82**

The following table demonstrates the current pipeline of reports due and received by ongoing projects. The deviations that can be noticed between the number of reports due and reports received can be explained by the extension which is sometimes allowed for the closure of the project and in other cases may be due to the delay accumulated by the project coordinators who deliver the report after the agreed deadline.

At the same time, the number of payments made cannot correspond to reports received during the year because the reports received towards the end of the year are usually processed the following year.

Project reports received and cost claims paid

Cumulative planning of project reports due and received	2016	2017
Project reports (including cost claims) received	70	**53**
Cost claims received with the project report but not validated within the year	15	**7**
Cost claims paid or cleared against pre-financing	59	**65[38]**

[36] In some cases, payments for the interim or final periods are fully or partially compensated ('clearing') against the 'pre-financing' paid as an advance by IMI. In technical terms, the clearing is the recognition of costs incurred against the pre-financing paid to projects. See also the following section.

[37] Including the clearings of pre-financing.

[38] Of which 45 received in 2017 and 20 received in previous years and paid in 2017.

b) Value of operational transactions

The breakdown of the costs accepted and paid in 2017 by IMI based on the operational transactions described above is presented in the table below. In total, the 82 financial transactions managed amount to EUR 199 097 701 of which EUR 140 251 318.63 effectively paid to beneficiaries as pre-financing or interim/final payments while EUR 58 846 383 are the result of full and partial clearings operated against pre-financing.

		No of transactions		Value of payments	Value of clearings[39]	Value of all transactions
	Pre-financing payments	0		0		0
IMI1 (FP7)	Interim payments	**26**				
	Final payments	**14**	**53**	71 890 752	57 347 914	129 238 667
	Clearing	**13**				
IMI2 (H2020)	Pre-financing payments	**16**		43 542 355		43 542 355
	Interim payments	**13**	**29**	24 818 211	1 498 469	26 316 680
	Clearing	**0**				
TOTAL			**82**	**140 251 318**	**58 846 383**	**199 097 701**
		Budget execution %		**72 %**		

In 2017 the number of operational payments increased by 10 %, the number of total transactions by 9 %, and the total value of transactions by 2 % compared to 2016.

Despite the effort made during the year and notwithstanding the number and the amount of the transactions managed in 2017, the corresponding annual budget execution rate reached 72 %. As explained above in Section 1.6 'Operational budget execution', this was mainly due[40] to the reduction or postponement of clinical trials within some large and complex projects of the antimicrobial resistance and Ebola programmes.

However, budget execution was carefully monitored during 2017 by the Programme Office. The trend and reasons have been regularly presented and discussed at each meeting of the Governing Board. Actions taken aimed at liaising with all project coordinators in order to:

- re-assess the project needs and the work plan;
- thoroughly review the need for payments appropriations in 2018 as the basis for a revised forecast;
- enhance interactions between science and finance operations;
- closer monitoring of high-risk projects.

[39] Which include both full and partial clearing.

[40] In addition, other key operational elements contribute to lowering budget execution. These include difficulties to stick to set timelines for the launch of new Calls, delays in preparation of Grant Agreements or cost-neutral project extensions.

c) Costs rejected following ex-ante controls

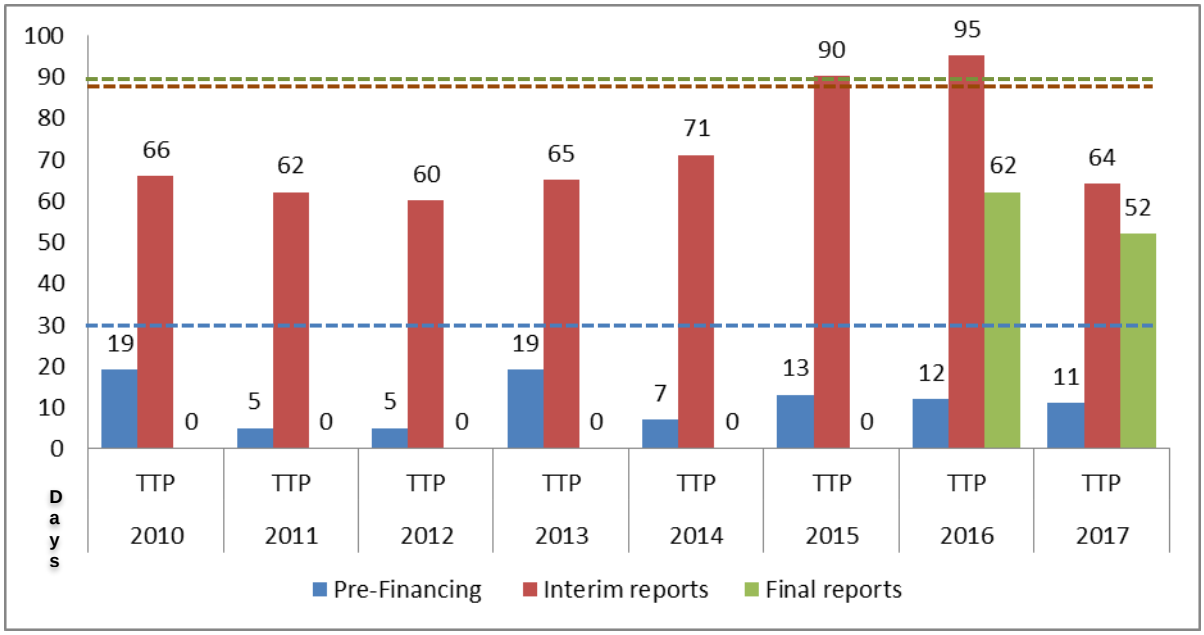
In order to monitor and measure the efficiency of the ex-ante controls, a key indicator is the percentage of declared costs considered ineligible (i.e. rejected) by the assessment of IMI services. In 2017 the financial impact of the systematic ex-ante controls performed on the cost claims before proceeding to the payment increased to 1.26 % of reported costs compared to 0.77 % of 2016. This may be explained by the revision of the workflows and overall by the increased number of resources working on financial files[41].

Total of reported costs	IMI1	140 627 179	167 216 891
	IMI2	26 589 712	
Of which covered by CFS[42]			96 882 336
Accepted costs			165 104 068[43]
Of which covered by CFS			96 250 041
Rejection			2 112 823
Rejection (in %)			1.26 %

d) Time to Pay (TTP)

Statistics for 2017 show a significant improvement in TTP for pre-financing payments as well as interim and final payments. IMI took measures to improve the payment situation by enhancing cooperation with consortia, reviewing internal procedures, and hiring more staff for the operational finance team. The IMI office managed to bring down the average time to pay interim payments from 95 to 64 days (33 % improvement). The duration for final payments further improved from 62 to 52 days (16 % improvement).

The table below represents the average time to process payments against the deadlines set by the Financial Regulation.



[41] However, the financial impact of ex-ante controls might be higher – at least for IMI1 files - as some cost claims and related information are corrected by beneficiaries after comments from IMI staff by means of informal request/exchange.

[42] For IMI2 / H2020, a certificate on financial statements (CFS) must be submitted only in the Final period and not anymore for interim periods.

[43] Of which the amount paid in 2017 was EUR 155 555 347.

Control efficiency and cost-effectiveness

This section presents an analysis of the costs and benefits of controls. However, the benefits of the grant management control system are to be considered as a whole, as they cannot only be expressed in monetary terms. Parts of these controls relate to the analysis of scientific deliverables and provide assurance that the projects are running as intended. The benefits are therefore both quantitative and qualitative since a purely quantitative cost-benefit evaluation would not reflect this reality.

a) Cost-effectiveness of ex-ante controls on operational expenditure

In terms of resource allocation, 13 FTEs (scientific, financial and other support officers) are involved in the ex-ante control of the grant preparation, grant management and payment cycle. This represents about 45 % of the FTEs allocated to the management of the operational programme and around 26.5 % of the staff currently employed.

Sector	Staff in the sector	FTE allocated to ex-ante control
Science	10	4
Operational Finance	7	5.5
Support activities (legal, AST, IT, internal control and audit)	12	3.5
Total	29	**13**

While IMI administrative costs in 2017 represent 5.48 % of the total IMI expenditure, the costs for ex-ante controls can be estimated at EUR 1 764 000 / year (of which EUR 201 000 for controls related to Grant preparation phase; EUR 1 313 000 for FTEs' standard salaries[44]; and EUR 250 000 on average for costs of externalised reviews and controls).

The estimated cost for ex-ante controls would then represent 1.18 % of the IMI operational expenditure as described in the first table below, and may be quantified in a cost of EUR 22 615 per Grant Agreement, which corresponds to 0.01 % of the total operational expenditure.

IMI budget 2017 (Payments in EUR)		% in total budget	Total estimated costs of ex-ante control	Cost of ex-ante control as % of annual expenditure
Administrative expenditure	8 132 976	5.48 %	1 764 000	21.6 %
Operational expenditure	140 381 318	94.52 %		1.25%
Total	**148 514 294**	**100 %**	***I***	**1.18 %**

Benefits of ex-ante controls (in EUR)	2 112 823
Total cost of ex-ante controls (in EUR)	1 764 000
Average cost (in EUR) of ex-ante control for one running Grant Agreement (Total costs / no. projects running in 2017, including projects that concluded their activities in 2017)	22 615

[44] 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 (full cost approach) implies a consideration of all costs related to the control of the overall programme life cycle, from submission, evaluation and selection to ex-post audit, including the benefit from the in-kind contribution provided by industry.

Sector	Estimated FTE allocated to controls	FTEs costs	Other costs related to controls	Total
		(Costs are indicated in EUR)		
Call management, selection and evaluation phase	2	268 000	16 000*	
Grant award	1.5	201 000	/	
Grant management	14.5	1 464 500	250 000*	
Ex-post control	2	204 000	326 132	
Total	**20**	**2 137 500**	**592 132**	**2 729 632**
Cost-effectiveness ratio	**Cost of controls / Total expenditure 2017 (Administrative and operational)**			**1.83 %**
	Cost of controls / Operational expenditure 2017			**1.94 %**
	Cost of controls / Total validated cost 2017 (Beneficiaries cost claims and EFPIA contribution)			**1 %**

* Estimates

In conclusion, the established control framework strikes the right balance between the efforts to simplify and minimise the administrative burden on beneficiaries, and the necessity to provide assurance as regards the sound financial management of the operational budget and the timely provision of financial means to beneficiaries allowing them to conduct their research in line with the Grant Agreement's provisions.

The different indicators presented above provide a robust indication of the cost-effectiveness of the control system put in place by IMI to ensure a sound financial management of the grant implementation throughout the lifetime of the projects, as well as the monitoring of their scientific progress.

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). It should be noted that out of the cost claims paid out in 2017, the majority were still under FP7 Grant Agreements (EUR 129 238 667 paid) compared to (EUR 26 316 680 paid) under H2020 Grant Agreements.

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** 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** 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 may present specific risks. This kind of audit provides IMI with flexibility, ensuring particular risks are adequately addressed.

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. 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. 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 regular audit fieldwork, 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)

The table below shows the coverage in completed audits compared to the total number of IMI1 projects, in terms of the number of beneficiaries and projects as well as the accepted costs.

	Total population	Audited	Audit coverage
Beneficiaries	681	212	31.1 %
Projects	59	50	84.7 %
Costs accepted by IMI (EUR, cumulative)	451 299 850.33[45]	78 343 856.93	17.36%

The following table gives an overview of the status of individual audit assignments as of 31 December 2017.

	Total Audits	Audits finalised[46]	Audits ongoing
Representative	218	201	17
Risk-Based	16	11	5
Total	234	212	22

In 2017, 23 audits were finalised in total. Two samples of representative audits were drawn in 2017, one in April and another in October.

Representative and residual error rates as of 31 December 2017

At this point, the **cumulative Representative Error Rate** (RepER) resulting from 2017 representative audits finalised is 2.38 % in terms of IMI contribution. The **cumulative Residual Error Rate** (ResER: error remaining in the population after corrections and recoveries) is 1.29 % in terms of IMI contribution. The residual error rate is thus below the 2 % materiality threshold established in Annex 10 of this report.

[45] Figure as of the cut-off date of 26 April 2017, corresponding to the last audit sample from which finalised audits were included in the current AAR.

[46] 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.

Implementation of audit results

When an audit report concludes that any amount has been unduly paid to a beneficiary, IMI launches the necessary corrective actions. Where the project is ongoing, the amount is offset against subsequent claims. Where the project is already closed, IMI issues a recovery order to reclaim the amount.

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 2017.

Number of cases of unduly paid amounts identified in audits	Number of cases implemented	Percentage of cases implemented	Amount implemented (EUR)
164	161	98 %	1,549,262

Extension of audit findings

When an audit uncovers findings of a systematic nature, IMI extrapolates them to all other cost claims of the same beneficiary ('extension of audit findings'). The unduly paid amounts thus identified are recovered or offset against subsequent cost claims of the beneficiary.

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

Implementation of extension of systematic findings	Beneficiaries
Audits finalised	212
Pre-information letters / letters of conclusion sent	208
Of which affected by systematic errors[47]	43
Extrapolation feedback received from beneficiary	38
Of which implemented	34

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

As regards the IMI2 programme, IMI's ex-post controls of grants are aligned with the harmonised strategy adopted for the entire H2020 programme[48]. 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. IMI works closely with CAS for the formulation of the H2020 ex-post audit approach in the relevant working groups as well as its implementation in practice, providing inputs during the audit cycle.

As part of the H2020 programme with a harmonised legal framework, IMI's cost claims are included in the programme level sampling, notably the H2020 common representative sample (CRS). Accordingly, IMI reports on the error rates drawn from these programme level controls. Going forward, additional assurance will be drawn from the extension of findings across the programme.

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

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

However, as the IMI2 Regulation[49] also establishes a requirement for an individual discharge procedure for IMI, this report also contains error rates and other indicators specifically related to the cost claim populations of the IMI2 programme.

Ex-post controls of the H2020 programme globally in 2017

Given the stage of the programme lifecycle, a limited number of cost claims totalling EUR 4.1 billion of requested funding had been received by the services under H2020 by the end of 2017. The first Horizon 2020 audits were launched in the middle of 2016 and further audits were launched in 2017. The first CRS, a common risk sample and an additional sample have been selected. In total, by December 2017, 625 participations had been selected for audit, covering all the services signing grants in Horizon 2020.

In total, the audit of 392 participations has been finalised (385 from the 2017 selection of 625 participations and 7 from the 2018 selection). This includes 110 out of 141 selected in the first CRS. The error rate on 31/12/2017 is:

Overall detected error rate based on 392 participations: 1.54 %

The detected error rate, based on 110 out of 141 participations selected in the first CRS, is 1.6 %. However, if we take into account the draft audit reports, then the expected representative error rate for the full sample will be around 2.9 %

Residual Error Rate for the research family: 1.44 %, expected to rise to around 1.9% when taking into account the draft audit reports.

Ex-post controls specific to IMI's population in 2017

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 specifically for IMI's assurance purposes in 2016. Of these, three were selected for a representative sample, while one was selected based on specific risks raised following ex-ante checks. These four audits were finalised in 2017. One further audit from CAS's risk-based selection of 2017 was finalised by 31 December 2017.

The total IMI contribution in the finalised audits is EUR 3 282 290. This represents 12.5 % of the total cost claims paid out, EUR 26 316 680.50, as of 31 December 2017.

As more cost claims have come through, a larger number of audits have been selected in 2017. 15 audits on IMI's cost claims are ongoing as of 31 December 2017.

Representative and residual error rates specific to IMI's population as of 31 December 2017

At this point, the error rates on IMI2 populations are as follows:

Cumulative representative error rate (RepER) resulting from the 3 representative audits finalised is 1.42 % in terms of IMI contribution.

Cumulative Residual Error Rate (ResER: error remaining in the population after corrections and recoveries) is 0.81 % in terms of IMI contribution.

[49] COUNCIL REGULATION (EU) No 557/2014 of 6 May 2014 establishing the Innovative Medicines Initiative 2 Joint Undertaking; Article 12

Comments on the control results

All the error rates set out above can only be a preliminary estimation and must be treated with care. The H2020 programme level CRS is not yet complete, and so is not yet fully representative of the expenditure that it covered. In addition, the first CRS was taken at an early stage of the programme in order to provide an early indication of the error rate and, also, whether the simplifications introduced in Horizon 2020 had been effective. The nature of expenditure in the first years of the programme may not be totally representative of the expenditure across the whole period of expenditure. The programme is in any case multi-annual, so the error rates, and especially the residual error rates, must be considered over time.

Similarly, only a limited number of audits have been carried out so far on IMI's specific population and these were selected very early in the programme. Furthermore, the population, i.e. the number of cost claims paid, remains limited as we are still in the early stages of programme execution. It is therefore difficult to draw firm conclusions.

However, the first audit results, as detailed above, suggest that the residual error rate will remain below the 2 % materiality level. Additional evidence to support this conclusion will arrive in 2018. However, to date there are no indications that the residual error rates identified in FP7 – below 2 % - will rise in Horizon 2020.

Implementation of audit results and extension of audit findings

Following the finalisation of each audit by CAS, 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 for the finalised audits under the IMI2 programme, on a cumulative basis, as of the cut-off reporting date of 31 December 2017.

Number of cases of unduly paid amounts identified in audits	Number of cases implemented	Percentage of cases implemented	Amount implemented (EUR)
2	2	100 %	354 914

As regards the extension of audit findings, none of the finalised audits in 2017 gave rise to an extrapolation process.

4.4 Audit of the European Court of Auditors including IMI external auditors

On 13 November 2017, the European Court of Auditors (ECA) published its report on IMI's annual accounts for the financial year 2016. 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 revenue and payments underlying the annual accounts.

Without calling into question its 'clean opinion', the ECA also provided some comments on the following:

- *Implementation of the 2016 budget* – the auditors noted that the low implementation rate for payment appropriations (EUR 263.4 million, 69.6 %) was mainly due to a reduction in spending on the Ebola+ programme and to delays in concluding Grant Agreements for calls under Horizon 2020.
- *Management of H2020 Grants* – the auditors noted that at the end of 2016, the transition of IMI2 control systems into the European Commission's common Horizon 2020 grant management and monitoring tools was partially completed.
- *Ex-ante checks and monitoring of cost claims* - some delays in making payments to beneficiaries with potential weaknesses in the monitoring procedures for project reports and related cost claims that were already reported in the AAR 2016.

IMI acted on ECA's comments and took immediate measures to mitigate the risks. Specifically:

- As further specified in section 2.5 of this report, by the end of 2017 significant progress was achieved in IT migration. IMI started using the H2020 IT tools for proposal submission, evaluation and grant preparation in December 2016 (with the launch of IMI2 - Call 10). Subsequently, all three IMI2 Calls for proposals that IMI launched in the course of 2017 are managed entirely in the tools. Five evaluation sessions have been concluded via the specific tools. As of the beginning of 2018, all IMI2 project reporting and consequently monitoring and payment will be carried out via the Horizon 2020 tools.
- As further described in section 4.1, IMI took measures to improve the time-to-pay record by enhancing cooperation with consortia, reviewing internal procedures, and hiring more staff for the operational finance team. As a result, the average time-to-pay is down to 61 days while the target is 90 days.

In accordance with the IMI2 Financial Rules, IMI's 2017 annual accounts are audited by the external audit company (Ernst&Young), who are contracted under an EC DG Budget framework contract for a period of two financial years. The preparatory work started in November 2017. The Court of Auditors will draw its audit opinion on the accounts on the basis of the work of independent external auditors and report on it in November 2018.

4.5 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 revised audit mission charter was adopted by the IMI Governing Board on 19 October 2017.

The IAS issued the final audit report on 'H2020 Grant Process (from the identification of the Call topics to the signature of the Grant Agreement) in the IMI2 JU' on 28 February 2017.

The audit objective was 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 audit scope included the involvement of IMI governance and advisory bodies in the identification of Call topics, the process for launching calls, the submission, evaluation and selection of proposals, as well as the preparation and signature of Grant Agreements under the H2020 rules in IMI2.

The IAS observed a number of good practices and positive developments, specifically:

- the professionalism and expertise of IMI staff involved in the audited processes (topic finalisation, Call preparation and management, expert selection, the consensus, facilitation and chairing of panels, grant preparation, etc.);
- the comprehensiveness of the documentation maintained on the consultation process (with the Scientific Committee and States Representative Groups) for topic development;
- the efficiency in the grant preparation phase reflected in the achievement of the target set for the 'time to grant' key performance indicator;
- the existence of a fully functioning evaluation review committee handling applicants' complaints;
- the completeness and good quality of reporting provided to the Governing Board to facilitate its monitoring and supervisory activities over the budget figures (including IMI2 JU contributions and EFPIA/Associated Partners' in-kind contributions), Grant Agreements signed, Grant Agreements under preparation, short proposals selected, etc.;
- the level of support provided by IMI staff to the advisory bodies.

The IAS concluded that IMI's internal control system for the steps of the grant management process from the preparation of Calls for proposals through to the signature of the Grant Agreements was overall efficient and effective. Nevertheless, the auditors identified some weaknesses and issued four recommendations for improvements, one classified as 'very important', two as 'important' and one as 'desirable'.

The IAS recommendations focused on the following actions:

- Establishment of a topic definition procedure explaining the activities undertaken by the IMI advisory bodies and their interaction with EFPIA and other potential generators of topics.
- Preparation of SGGs' meeting minutes, as advisory bodies to the Governing Board.
- Amendment of IMI manual for submission, evaluation and grant award in order to provide full and transparent information on the role and activities undertaken by the EFPIA representatives during the evaluation process.
- Reinforcement of the requirement to comply with the Code of Conduct by ensuring that all evaluators sign their respective declaration prior to the kick-off of the remote evaluation.
- Finalisation of the migration to the H2020 IT tools with a view to:
  - increase the operational efficiency in proposal submission and evaluation as well as in the grant preparation and reporting process;
  - ensure that the actors involved in the submission and evaluation of proposals are formally appointed to specific roles.
- Analysis of the feedback received from Independent Observers, follow up of identified weaknesses and publication of the replies or analysis of the independent observer reports.

IMI prepared an action plan which was approved by the IAS on 21 April 2017. All four recommendations were translated into nine actions and implemented by the end of 2017. The implementation is confirmed by a letter from the IAS. This has helped to improve IMI's internal control system and mitigated residual risks to the Authorising Officer's reasonable assurance.

In the course of 2017, the IAS carried out a preliminary survey and fieldwork at the IMI premises for the audit on ‘Coordination with the Common Support Centre [CSC] and implementation of CSC tools and services in IMI2 JU’. The audit aimed to assess the adequacy of the design and the efficiency and effectiveness of the IMI governance, risk management and internal control processes for the coordination with the CSC and the implementation of the CSC tools and services. The final report is due in 2018.

4.6 Risk management

Risk management at IMI is intended 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. To that end, IMI implements a robust enterprise risk management (ERM) process based on an annual risk assessment exercise (RAE)[50] which consists of all the actions connected to setting objectives, identifying risks, and the measurement, review, handling, reporting, follow-up, monitoring of and reaction to risks.

In 2017 as in previous years, the annual risk assessment was performed in parallel with the preparation of the AWP 2018. A report on risk management was adopted by the Executive Director on 8 December 2017. Risks were measured in terms of likelihood and impact based on semi-structured interviews, questionnaires and feedback from staff in each sector (as defined in the IMI organisational chart). As a result:

- An *Operating Risk Register* (ORR) was established and validated. The ORR is an operational tool to be implemented at each working level. It lists the actions to be taken to mitigate and manage risks and assigns responsibility to a specific team or individual.
- A *Strategic Risk Register* (SRR) brings together the most critical risks at corporate level. For each identified risk, recommended actions were identified on how to reduce either the probability of a risk materialising, or the severity of the exposure if the risk does occur.

Risks are then systematically monitored during the year in order to keep the risk management dynamic and to respond to evolving priorities. To improve the risk assessment and management process, the Executive Director established a working group comprised of staff members from the core areas to provide input to risk identification, risk assessment and mitigation.

Key results

The assessment and management of risks in 2017 confirms that some threats tend to persist within the JU. This is because these risks correlate with the mission and nature of IMI as a public-private partnership. They have therefore to be accepted as such and addressed to avoid or reduce their impact where needed (e.g. the risk of an imbalance between industry in-kind contribution and EU financial contribution).

For the management of risks identified in the AWP 2017, the Programme Office took a number of measures. These include improvements to the way topics are identified; simplification of administrative procedures; enhanced communication and external relations strategy; improvements to the approach used for project monitoring and reporting; as well as clearer definition and organisation of internal workflow objectives, responsibilities and tasks.

As for the risks identified in the assessment for the AWP 2018, the IMI Strategic Risk Register reports nine corporate strategic risks. Among them, four were considered as critical and reported in the Annual Work Plan 2018 with the planned mitigating actions.

Risk No. 1 - Mismatch between increasing business demands and resources available

The IMI Programme Office is streamlining and reengineering its business processes including the reallocation of internal resources to best meet business priorities. The full staff capacity will also be assured through the implementation of the staff establishment plan.

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

Risk No. 2 - Delays in defining annual scientific priorities and Call topic approval may affect annual budgetary planning and overall programme implementation

The Programme Office plans extensive preparatory consultations with the Members and is preparing a fixed plan of Call development stages shared with all stakeholders 12 months in advance. The SGGs should ensure coordination in certain strategic areas and make the development of new topics more transparent and effective. Moreover, IMI will enhance the collaboration between IMI Scientific Officers and Call topic writers and will organise targeted briefings and training courses for them.

Risk No. 3 - Imbalance between EU financial contribution and in-kind contribution provided by EFPIA

In line with the Grant Agreement, the Programme Office assures a systematic monitoring of financial management of projects through annual periodic reports and interim reviews. A regular assessment of the level of in-kind contributions (committed and reported) is made by the Governing Board at each meeting and reported in AARs.

In addition, EFPIA has developed a mitigation plan addressing a potential imbalance at the end of the IMI1 programme with operational and financial actions.

Risk No. 4 - Insufficient leverage of the contribution committed by non-pharma industry

Regarding this risk, IMI is enhancing its portfolio of partnerships and the development of beneficial alliances with appropriate organisations supporting the objectives of the IMI2 programme. This will ensure that the IMI brand is enhanced by the international strategy and relationship. Moreover, the Programme Office is: (i) promoting international cooperation in consultation with projects to explore opportunities on a case-by-case basis and to address actions by area; (ii) encouraging different ways of contributing to IMI projects as Associated Partners and Partners in Research on the IMI website; (iii) developing joint IMI-EFPIA events at regional and national levels, involving industry and policymakers.

In addition, Brexit negotiations will continue to be taken into consideration regarding the potential impact on the strategy and programme implementation of IMI. The full consequences of Brexit and the extent to which they will affect the future strategies of IMI stakeholders remain however unknown today.

4.7 Fraud prevention and detection

IMI has developed and implements its own antifraud strategy aligned with the common antifraud strategy of the Directorate-General for Research & Innovation (DG RTD)[51].

This strategy is implemented at JU level and in coordination with DG RTD and other research agencies through a multiannual action plan. The research family members meet several times a year, at the Fraud and Irregularity in Research (FAIR) Committee, to discuss common fraud matters, exchange information, make presentations and assessments of fraud topics (such as double funding, plagiarism, etc.), and follow the overall implementation of the action plan. Ad hoc working groups created among the members are also charged with implementation of specific actions of the plan (e.g. to develop clear guidance for simple checks that grant management officers are encouraged to perform at the various stages of the grant management cycle; to build up a number of case studies, etc.).

As part of the common antifraud strategy, IMI has appointed an antifraud correspondent to support internal activities and to coordinate relations with the European Commission, other agencies and OLAF[52].

The complementary antifraud strategy developed by IMI represents an additional measure to address the specificities of IMI programme and the complexity of a public-private partnership. The internal action plan offers a proactive approach to managing the risk of fraud, which is analysed at two levels: i) as part of the annual risk assessment exercise of JU activities; and ii) at programme management level where ex-ante controls are embedded in the grant preparation and management processes.

Regular information on fraud-related risks and on the procedures to be used in case of suspicion of fraud/irregularities is communicated to staff concerned who are encouraged to attend bespoke training on fraud prevention and detection in the research area. Additionally, attention is given to cross-sectional issues such as risk linked with conflict of interest, delegation of authority and segregation of duties.

As regards OLAF cases, in 2017 there were no instances of suspicion of irregularities in IMI projects. However the Programme Office received from OLAF two requests for information concerning two IMI beneficiaries that were subject to investigations in cases presented by the Commission or other agencies. In both cases, IMI provided the information requested. In one case, no measure was needed by IMI; in the other, IMI set up the recovery procedure. The table below summarises the number of OLAF cases relating to IMI beneficiaries over the year.

Number of pending OLAF cases on 01/01/2017	0
New cases reported to OLAF in 2017	0
Horizontal cases / requests for information handled by IMI in 2017 on the request of OLAF	2
Number of pending OLAF cases on 31/12/2017	0

[51] 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.

[52] Office européen de lutte antifraude (European antifraud office).

4.8 Assessment of the 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.

In 2017 this system was still based on the 16 internal control standards (ICS) adopted by the Governing Board[53] in line with equivalent standards laid down by the European Commission. However, in December 2017, the IMI Governing Board adopted[54] a revised internal control framework (ICF) aligned with the control framework adopted by the European Commission on 19 April 2017[55].

The ICF set up by the Executive Director based on the above standards takes 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 the management team (composed of the Head of Administration and Finance, the Head of Scientific Operations and the Head of Communications and Institutional Relations), the Audit Manager and the Internal Control Coordinator. IMI personnel at all levels ensure the implementation of the internal control framework.

Management's key internal control responsibilities include:

- promoting, coordinating and monitoring the implementation of the internal control framework including supervision of control activities;
- performing the annual self-assessment of the effectiveness of the internal control system, complemented by intermediate reports where needed;
- performing the annual risk assessment exercise and assuring the mitigation of risks threatening the achievement of the JU's objectives;
- reporting in the AAR on the JU's compliance with the internal control standards and on the effectiveness of the internal control system that the JU has in place.

This model is embedded across IMI's organisational structure and 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.

Management's assessment of the effectiveness of the internal control system

The 2017 annual self-assessment of the effective implementation of the Internal Control Standards was mainly based on the following elements.

- Interviews with the staff concerned, based on a pre-defined questionnaire focusing on 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 (Internal Audit Service) and external auditors (independent financial auditors and the European Court of Auditors) as well as a management overview on progress made on the implementation of the corresponding action plans.

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

[54] GB Decision of 20 December 2017 (IMI2-GB-DEC-2017-28).

[55] The new ICF moves away from a compliance-based to a principle-based system. It provides the necessary flexibility to adapt to specific characteristics and circumstances while ensuring a robust internal control with a consistent assessment throughout the IMI2 JU. This approach aims at helping the organisation to achieve its objectives and sustain operational and financial performance.

In order to assure that all aspects of IMI operations and control were covered by the assessment, the 16 standards have been analysed separately and then as a whole. Particular attention was given to the result of the actions implemented for the control standards prioritised in 2017 which focused on IMI's ethical and organisational values (ICS 2), definition of objectives and performance indicators (ICS 5), and management of information and communication (ICS 12).

Register of exceptions, analysis of internal control weakness or control failures recorded during the year

The IMI Programme Office has to report on all exceptions, internal control weaknesses and non-compliance events potentially leading to weaknesses through a dedicated procedure and using pre-defined templates. A central register is reviewed regularly by the ICC, the Internal Audit Service (IAS) and, in the course of the Declaration of Assurance (DAS) procedure, by the European Court of Auditors (ECA).

IMI management has analysed the root causes of the cases in order to further strengthen the internal control system, ensure compliance with rules and procedures, and further improve the efficiency and effectiveness of the operations. Related risks and financial impact have been assessed and monitored when material, corrective measures were introduced (e.g. training to staff, internal instructions, etc.). Other deviations considered of limited relevance after management assessment were controlled and documented in appropriate notes to the file. IMI will continue to raise awareness and inform staff on the most frequent issues.

Reliability of financial reporting and accounting

DG BUDGET has completed[56] an evaluation of the local financial systems set up in IMI for the implementation of the budget, as provided for in Article 22(1)(d) of the IMI2 JU Financial Rules.

The objective of this evaluation was to assess whether IMI's financial and accounting system met the validation criteria, the requirements of the Financial Rules, and the instructions of the accounting officer.

The evaluation did not identify any weaknesses in the design or implementation of the local systems in place in IMI which would affect compliance with the validation criteria laid down by the accounting officer of the Commission. Five recommendations were issued in order to further enhance internal procedures, to monitor timely registration of invoices, and monitor the quality of data in ABAC.

IMI has already prepared an action plan[57] addressing all the suggestions for improvements.

Assessment of the functioning of the internal control system

In conclusion, the results of the 2017 internal control assessment confirm that the IMI control system is compliant with all ICSs. The system is working to an acceptable level of effectiveness, and allows sufficient control of risks and achievement of control objectives. In this context, in 2017, the IMI internal control system was strengthened by fully implementing the action plans addressing the ECA and IAS audit recommendations.

Risks that might pose a threat to the achievement of IMI's mission and objectives were systematically assessed and managed through appropriate controlling and mitigating actions.

[56] Final report issued on 8 December 2017.

[57] IMI JU Action plan approved by the Accounting Officer on 5 February 2018.

5 Management assurance

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

5.1 Elements supporting assurance

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

IMI follows the 'three lines of defence' model for assurance and accountability. The Executive Director's assessment is based on the following sources supporting assurance, specifically:

- Governance, risk management and internal control framework:
  - reporting by the members of the management team[58]
  - reporting by the internal control coordinator and risk manager
  - results of ex post control (ex post audits on beneficiaries and verifications of industry partners' contributions)
  - Governing Board assessment.
- Findings and opinions from internal and external audits:
  - reports by the Internal Audit Service
  - recommendations by IMI audit manager
  - reports by independent financial auditors
  - reports by the Court of Auditors
  - conclusions by the Anti-fraud Office
  - reports by the accounting officer.
- Independent external reviews:
  - interim and final evaluation reports
  - project interim review reports
  - socio economic impact reports
  - bibliometric analysis.

The information reported covers both the operational budget related to the FP7 and H2020 programmes, as well as the administrative budget managed by IMI in 2017, 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 stage and reports on measures implemented to prevent, detect and correct fraud.

As demonstrated throughout this annual report, the results of the performance and control indicators positively support the statement of the declaration of assurance. Fraud prevention and detection mechanisms in place did not reveal anything that would impair the declaration of assurance. The audit results, the internal control self-assessment and the control indicators did not reveal any significant weaknesses that could have a material impact described 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. Although a few indicators (time to grant and time to sign), relating to the efficiency component of sound financial management, show slight deviations from the targets, these do not impair the declaration of assurance.

[58] Head of Administration and Finance, Head of Scientific Operations, Head of Communications and Institutional Relations

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[59]*.*

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 2018

……..

Pierre Meulien

[59]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 –Annual accounts

Annex 10 – Materiality criteria

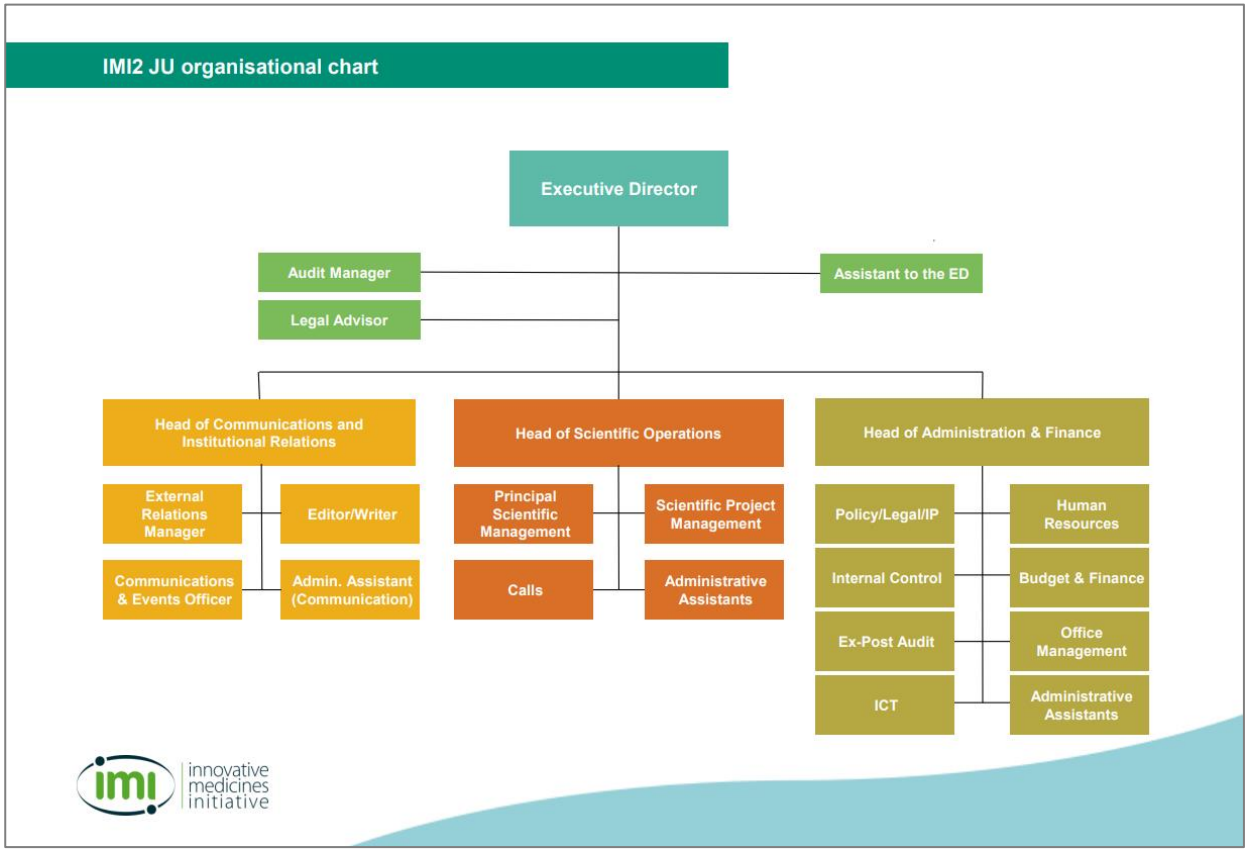
Annex 11 – Media highlights

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 2016			Year 2017											
	Establishment plan 2016			Evolution in posts						Organisational evolution			Establishment plan 2017		
				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		2	2											2	2
AD10															
AD9		3	3											3	3
AD8		7	7											7	7
AD7		6	6											6	6
AD6															
AD5		11	11											12	12
Total AD		32	32											33	33
AST11															
AST10															
AST9															
AST8		1	1											1	1
AST7															

Grade	Year 2016			Year 2017												
	Establishment plan 2016			Evolution in posts						Organisational evolution			Establishment plan 2017		
				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
AST6															
AST5															
AST4															
AST3		4	4											4	4
AST2															
AST1		1	1											1	1
Total AST		6	6											6	6
SC6															
SC5															
SC4															
SC3															
SC2															
SC1															
Total SC															
Overall total		38	38											39	39

Notes
Perm. = permanent staff
TA = temporary agent
LT = long-term contract
ST = short-term contract

Contract agents

Grade	2016	2017
CA FG IV	2	2
CA FG III	11	12
CA FG II	1	1
CA FG I	0	0
Total CA	**14**	**15**

SNE

	2016	2017
SNE	**0**	**2**

Notes:
CA = contract agent
FG = function group
SNE = seconded national experts

Annex 3 – Project outputs

IMI1 projects

New tools/resources for drug discovery & preclinical drug development

Project title	Description of result(s)
AETIONOMY Alzheimer's disease and Parkinson's disease	The project produced and released NeuroMMSig web server. Users submit multimodal, multiscale clinical data and the server returns pathophysiology mechanisms that map to the data.
BTCure rheumatoid arthritis	Identification of potential novel biomarkers for the development of new therapeutic agents for the prevention and cure of RA. Partners identified 5 candidates which could be further examined towards their biomarker potential which could serve as possible biomarkers for monitoring disease states or the response to specific; as well as specific metabolites identified through the use of predictive modelling, metabolic differences between Tg197, WT and Remicade treated animals.
BTCure rheumatoid arthritis	Demonstrated the first systematic examination of the pathogenic changes that occur in mouse synovial fibroblasts in progressive TNF-driven arthritogenesis and revealed significant correlations between mouse and respective human RA synovial fibroblasts data (Fleming/JSSN) (Ntougkos et al., 2017).
BTCure rheumatoid arthritis	Generated phenotypic data in the CAIA model upon Enbrel and Dexamethasone treatment, as well as a cytokine profile following *ex vivo* stimulation of arthritogenic splenocytes in the presence of 55 commercially anti-inflammatory drugs in the PIA transfer model (Redoxis).
BTCure rheumatoid arthritis	Identified two molecules (T23 and T8) that block the action of the protein tumour necrosis factor (TNF) and RANKL. Findings published in PLoS Computational Biology.
BTCure rheumatoid arthritis	First version to be tested in a complex real life environment with registry data, biobanks, biomarkers and genetic data. This has been going as planned and the project has now in fact ensured interoperability between different registries and databases and for example established links between biobanked samples, studies and ethical permissions.
COMPACT drug delivery	Two assays (split protein and biotin ligase reporter assays to study the delivery of nucleotides and peptides to the site of intracellular action) and one method (exosome labelling and uptake used for the monitoring cell uptake and intracellular trafficking) for the *in vitro* characterisation of drug delivery systems have been developed. These assays directly contribute to a better understanding of the intracellular fate of drug delivery systems (DDSs) newly developed by COMPACT, and indirectly contribute to the improvement of DDS for future use.
COMPACT drug delivery	A pulmonary 3D *in vitro* model for the study of anti-inflammatory treatments has been developed. Its suitability was demonstrated by a model drug. This model is used for the proof-of-concept of functional delivery and therapeutic effects of drugs.
COMPACT drug delivery	A method for the injection of nanoparticles into the skin using protein- and nanoparticle-containing dissolvable microneedles has been developed.
ELF drug discovery	The European Lead Factory's Joint European Compound Library now contains 500 095 compounds, taking it over the 500 000 goal set at the start of the project.

Project title	Description of result(s)
ELF drug discovery	The project has identified novel small molecules that have the potential to be transformed into a new medical treatment for depression and pain. The innovative target involved in these debilitating conditions was discovered by Dr Patrick McHugh of the University of Huddersfield. Pioneering ideas to improve antidepressant therapies are greatly required since existing antidepressants are moderately effective and the response rate in patients suffering from depression is approximately less than 50 %.
ELF drug discovery	Parkinson's UK has allocated GBP 1 million (approx. EUR 1.2 million) for the creation of a virtual joint venture biotech company with the University of Sheffield to further develop compounds that were identified through the European Lead Factory and that could prove useful in the hunt for a treatment for Parkinson's disease. The results of the HTS run by the ELF led to a spin-off to further develop the hits: Keapstone Therapeutics.
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	Identified novel biomarkers of β-cell function and ability to compensate for insulin resistance. The identified pathways include the branched chain amino acids and, unexpectedly, the diacylglycerol and protein-kinase-C-related pathway.
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	Identified pathways in the liver related to non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) and novel therapeutic possibilities are under study.
ENABLE antimicrobial resistance	During 2017, new antibiotic discovery programmes, three from SMEs and seven from academic teams, were submitted to ENABLE. Of these, two are being further evaluated. ENABLE's Portfolio Management Committee approved three of the ongoing programmes for lead status during 2017, a major success since this meets the project's goal. As per end of 2017, five active programmes are funded within ENABLE. Since 2014, 35 different European SMEs have submitted 43 out of a total 72 discovery programmes to ENABLE.
ENABLE antimicrobial resistance	Discovered new mechanism to target drug-resistant bacteria (published in PNAS).
eTOX knowledge management, drug safety	Publication NRDD 16 2017 811. *Legacy data sharing to improve drug safety assessment the eTOX project.* Scientists from IMI's safety project eTOX described their impressive legacy in a paper in Nature Reviews Drug Discovery. The heart of the project was an immense, shared database based on information provided by EFPIA companies from their own preclinical drug toxicity studies. By the end of the project, the database had information from over 8 000 toxicity studies on almost 2 000 compounds, of which around a fifth are approved drugs.
EU-AIMS autism	Successfully showed that their autism cellular models, based on either genetic risk of autism, sporadic autism, and environmentally provoked autism have the same cellular/molecular phenotype, indicating that they truly reflect the pathophysiology underlying the condition and not just the genetics of the condition.
EU-AIMS autism	The SME Noldus Information Technology continued its development of EthoVision XT as a tool for automating behavioural tests with rodent models of ASD. The new version (nr12) released to the research community features significant improvements and innovations relative to the previous versions.

Project title	Description of result(s)
iABC antimicrobial resistance	Developed a pre-clinical testing programme for an inhaled version of Polyphor's IMP POL7080 which has proven to be highly effective against *Pseudomonas aeruginosa*. Development and testing have begun with a view to proceeding to clinical trial in 2019.
K4DD drug discovery	An accessible suite of modelling & molecular dynamics tools & tutorials as well as mathematical models
K4DD drug discovery	First prototype assay 'kit' protocols for a membrane protein. Delivery of optimised reagent and kinetic assay protocol. Report on licensing/commercial relationship for sustainability off the-shelf kinetic assay kits.
K4DD drug discovery	Delivery of systems biology and *in vitro* PK/PD (pharmacokinetic / pharmacodynamics) models for cellular systems. Delivery of mechanism-based PK/PD models for *in vivo* animal models. Delivery of mechanism-based PK/PD models for the translation from *in vitro* cellular & *in vivo* animal models to humans.
K4DD drug discovery	Published a new mathematical model which predicts how long a drug effect will last. The model takes into account several important variables such as the concentration of the drug in the body and its rate of binding and unbinding with the biological target, and analyses them in order to predict the duration of the potential drug effect. This mathematical approximation, which was published in the journal Trends in Pharmacological Sciences, gives an idea earlier in the drug development process on whether a drug is worth pursuing or not.
K4DD drug discovery	A study of a cancer target protein revealed an unusual relation between binding site flexibility and drug-target lifetime. The results, published in Nature Communications, suggest a new strategy for drug discovery.
MIP DILI drug safety	Established a completely novel method for determination of drug-induced cholestasis, an important mechanism of liver drug induced toxicity, and showed that it has high specificity, as evident from validation with 19 different cholestatic drugs.
MIP DILI drug safety	Validated and published the MIP DILI Roadmap for the hazard identification and risk assessment of new chemical entities, including optimisation of existing, relatively low cost, models and knowledge on how to deploy these test systems for improved and optimal use by industry.
OrBiTo drug delivery	A new *in vitro* tool to integrate permeation into formulation evaluation based on an artificial membrane has been developed. This is an easy-to-implement tool that can be used for the reliable evaluation of absorption-enabling strategies of drugs. A manuscript describing the use of this system in formulation evaluation is currently being prepared.
PRECISESADS rheumatoid arthritis and lupus	One of the largest, well characterised multi-OMICs, multi-systemic auto-immune diseases studies and cohort (inclusion of 2 005 patients and 651 controls in a cross-sectional study). Multi-centre harmonisation of flow cytometers in the context of the project through 11 centres. Identification of new genetic markers for systemic autoimmune disease. IRF4, one newly identified as a common susceptibility locus for systemic sclerosis and rheumatoid arthritis in a cross-disease meta-analysis of genome-wide association studies (GWAS). To identify such markers required a meta-analysis with 8 830 patients with systemic sclerosis, 16 870 patients with rheumatoid arthritis and 43 393 healthy controls. A combined large-scale meta-analysis identifies COG6 as a novel shared risk locus for rheumatoid arthritis and systemic lupus erythematosus.

Project title	Description of result(s)
StemBANCC stem cells	Reprogramming and validation of additional 180 iPSC (induced pluripotent stem cell) lines that have been transferred to EBiSC for banking. The lines cover neurological diseases (Alzheimer's, autism, bipolar, migraine, neuropathy, schizophrenia, Parkinson's), as well as diabetes and healthy controls.
Translocation antimicrobial resistance	Translocation has uncovered the 3D structures and functional data of a Gram-negative bacterial outer membrane (OM) lipoprotein MlaA that works as 'molecular vacuum cleaner'. This discovery illuminates a fundamental and important process in Gram-negative bacteria, which is a starting point to determine whether the Mla system of Gram-negative pathogens could be a new drug target to decrease bacterial virulence and to make various antibiotics more effective.
ULTRA-DD drug development	Has identified potential new targets that could inspire the development of new treatments against autoimmune diseases such as lupus and myositis.
ULTRA-DD drug development	Published online open source datasets from experiments on autoimmune diseases such as lupus and myositis. Data is free to use by other researchers and may inform further discoveries that will add to our knowledge of autoimmune diseases and accelerate the development of medicines for patients with autoimmune disease, many of whom do not respond well to existing treatments. www.ultra-dd.org/tissue/cellassays
ZAPI infectious diseases	Several nanoparticle platforms have been developed and optimised as well as 4 different non-mammalian expression systems (baculovirus, *E. Coli*, Drosophila S2 and C1 fungal system) for the production and multivalent display of functional antigens for Rift Valley Fever Virus, Schmallenberg Virus and Middle East Respiratory Syndrome Coronavirus (MERS Co-V).
ZAPI infectious diseases	Establishment of small animal models (DPP4 knock-in mice / rabbit) and a target animal model (dromedary camel) to evaluate the *in vivo* protection against MERS-CoV, provided by vaccination with selected key immunogens.
ZAPI infectious diseases	Development of highly potent humanised MERS-CoV neutralising antibodies with higher *in vitro* neutralising activity than the most potent antibodies described in the literature. This achievement validates the ZAPI antibody discovery pipeline.

Biomarkers and tools developed to predict clinical outcomes (efficacy and safety)

Project title	Description of result(s)
BIOVACSAFE vaccines	Baseline transcriptomics profiles in whole blood samples that correlate with unwanted side effects from vaccines validated in two clinical trials. Can be applied to vaccine development after validation in larger trials as personalised medicine to identify people at risk of side effects, to optimise vaccine formulations, and better understand mechanisms of adverse reactions.
CANCER-ID cancer	Changes in the genes of cancer cells found in the blood could help to identify patients for whom a standard drug is most likely to be effective, according to a study by CANCER-ID. The findings, published in the journal Cancer Research, could ultimately result in tests that would allow doctors to distinguish between patients who should keep taking the drug and patients who would benefit from trying alternative treatments.
COMBACTE-NET antimicrobial resistance	The case of a young girl with a life-threatening infection has shed new light on how the body prevents common bacteria from causing serious disease. The research, funded in part through COMBACTE-NET, is published in the journal Cell

Project title	Description of result(s)
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	4 proteomic-based plasma markers for diagnosis. 4 proteomic-based plasma markers for prognosis. 2 novel combinatorial MRI (magnetic resonance imaging) marker algorithms for diagnosis. 2 novel combinatorial MRI marker algorithms for prognosis.
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	Measured branched-chain amino acids (BCAAs) metabolite, 3-hydroxyisobutyric acid (3-HIB) in plasma in around 10 000 extensively phenotyped individuals and showed that is a biomarker of increased risk of type 2 diabetes. https://doi.org/10.1016/j.ebiom.2017.12.008
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	Publication on the potential roles that omega-3 and omega-6 unsaturated fatty acids play in the progression of Alzheimer's disease: PLOS Medicine.
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	Investigation of the effect of medical history and lifestyle on Alzheimer's disease (AD) biomarkers in 1 394 subjects with mild cognitive impairment (MCI). This analysis suggests that risk factors predictive of AD in the general population may be of limited value in subjects with MCI.
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	Identified pleiotrophin 151-168 as a novel Alzheimer's disease biomarker using a novel, quantification-driven proteomic approach.
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	Using subjects' data retrieved from the EMIF tranSMART platform (https://emif.custodix.com/transmart/datasetExplorer), EMIF showed that the combination of low-cost imaging, cognitive, and neuropsychological variables provides slightly better results versus cerebro-spinal fluid biomarkers in terms of sensibility and type-1-error specificity. This represents an improvement in prediction of MCI to AD conversion compared to either data type alone.
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	A total of 286 711 cases of dementia aged 50+ and 28 661 163 controls were investigated for systolic/diastolic blood pressure (SBP/DBP), body mass index (BMI) and cholesterol levels recorded at different time periods prior to diagnosis. Results show exaggerated weight loss and decline in blood pressure prior to the onset of dementia. These need to be considered if dementia risk is estimated from clinical data.
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	Concluded the study on influence of insulin resistance (IR) on Alzheimer's disease (AD) using plasma and cerebrospinal fluid (CSF) biomarkers related to IR and AD in 58 cognitively healthy men (28 IR and 30 non-IR). Although CSF AD biomarkers did not differ between IR groups, 200 CSF and 487 plasma proteins differentially express between IR and non-IR subjects. Significantly enriched pathways, many of which previously implicated in AD, were identified.
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	Identified mannose as a novel biomarker of insulin resistance and non-alcoholic fatty liver disease (NAFLD). Additional studies showed that mannose also identifies individuals with future risk of developing type 2 diabetes and cardiovascular disease, and that genetic risk of type 2 diabetes is associated with elevated mannose levels long before disease onset. The mechanisms of action of mannose are under study.

Project title	Description of result(s)
EMIF, EPAD, AMYPAD Alzheimer's disease	Developed a strategic five-phase roadmap to foster the clinical validation of biomarkers in Alzheimer's disease, adapted from the approach for cancer biomarkers.
iABC antimicrobial resistance	A lung clearance index (LCI) sub study has begun in conjunction with the iBEST1 trial. New equipment was installed at key clinical trial sites with a supporting training programme including an e-learning tool developed for clinic staff. A central LCI reading service to provide operator certification and LCI data quality control for trial data is in operation at Queen's University Belfast.
iABC antimicrobial resistance	Developed a central laboratory microbiology manual for sputum microbiology and susceptibility testing which is operational in the Phase II iBEST1 study.
iABC antimicrobial resistance	Developed standard protocols for DNA extraction, PCR and NGS which will enable determination of changes in composition of the airway microbiome and resistome with treatment and which exploratory molecular endpoints are the best measure of treatment effect in clinical trials.
IMIDIA diabetes	Novel signature of type 2 diabetes identified.
IMIDIA diabetes	Uncovered clues that could help to identify people at risk of developing diabetes. Writing in the journal Molecular Metabolism, the researchers explain how they have identified a gene called Elovl2 that appears to play a key role in insulin secretion.
OncoTrack cancer	Identified two new biomarkers that can predict the effectiveness of two drugs commonly used to treat colorectal cancer, something which could lead to more personalised and effective treatments for patients with this disease. The study was published in Nature Communications.
PRECISESADS rheumatoid arthritis and lupus	Description of multiple metabolic alterations in plasma and urinary samples from Sjögren's syndrome patients. Several techniques (chemiluminescent immunoassay, indirect immunofluorescence, and turbidimetry) were developed to quantify a panel of 27 parameters of autoantibodies, complement fractions, and free light chains (FLC). Samples corresponding to 300 sera in phase I and 750 in phase II were received, tested and transmitted for the 27 analysed parameters at the end of 2017. Natural antibodies against phosphorylcholine and malondialdehyde (anti-PC and anti-MDA), have been done in 2 157 individuals including 198 from inception cohort.

Improved protocols for clinical trial design and processes

Project title	Description of result(s)
ABIRISK drug safety	Anti-drug antibodies (ADA) assays have been standardised and validated in order to early detect the immunogenicity of commonly used biopharmaceuticals (BPs), like interferon beta and natalizumab. Standardised and validated ADA testing could potentially decrease unnecessary use of inefficient drugs to the benefit of both the patient and the economy of the health care system.
COMBACTE-NET antimicrobial resistance	Publications of manuscripts by the Stat-Net team on improving the design and feasibility of clinical trials with antibacterial agents, in particular on advanced pharmacokinetics/pharmacodynamics modelling and novel randomised clinical trials strategies, endpoints for evaluation of new antibiotic therapies for severe infections.

Project title	Description of result(s)
EPAD Alzheimer's disease	Published recommendations for the ethical management of re-contact, informed consent and risk disclosure to research participants. These may be of value to other research collaborations in the process of developing readiness cohorts for prevention trials in Alzheimer's disease and other disease areas.
EU-AIMS autism	EU-AIMS demonstrated that the Development and Well-Being Assessment (DAWBA) for diagnosing ASD is a simpler, cost-effective and reliable tool to aid autism diagnosis in community settings. It requires little training, is easy to administer (online or by interview) and diagnosis is aided by an algorithm.
EU-AIMS autism	Published the design and methodologies used in their Longitudinal European Autism Project (LEAP) to identify and validate stratification biomarkers for autism spectrum disorders (protocol and standard operation procedures (SOPs) are accessible on https://www.eu-aims.eu/fileadmin/websites/eu-aims/media/EU-AIMS_LEAP/EU-AIMS-LEAP_SOP_StudyProtocol.zip).
FLUCOP vaccines	FLUCOP developed a new and robust assay to measure the antibody-dependent cellular cytotoxicity (ADCC) activity of influenza virus hemagglutinin (HA) antibodies induced after vaccination or infection. This assay offers advantages over existing methods, like ease to perform and possibilities to standardise.
FLUCOP vaccines	FLUCOP established a new method based on protein micro-array for the multiplex testing of antibodies to a large panel of contemporary and historic strains of influenza virus, which requires only minute amounts of serum. The method allows assessing the history of exposure to influenza viruses and pre-vaccination immune status, which is the most confounding factor of vaccine induced antibody responses.
GETREAL relative effectiveness	A series of eight papers on pragmatic trials published in the Journal of Clinical Epidemiology (Volume 88, August 2017) on design options with the practice of conducting pragmatic trials to help researchers to design pragmatic trials with an optimal chance of success in practice. Launch of 'PragMagic' tool, a decision support tool for pragmatic trial design (www.pragmagic.eu) giving insight into possible consequences of more pragmatic trial design choices and operational challenges to support trial design teams to maximise generalisability of trial findings to the routine care setting of interest while ensuring validity, stakeholder & ethical acceptability and operational feasibility of the trial.
GETREAL relative effectiveness	Release on the project website of the report *'Methodological guidance, recommendations and illustrative case studies for (network) meta-analysis and modelling to predict real-world effectiveness using individual participant and/or aggregate data*' that presents best practices and recommendations for the area of evidence synthesis, in particular (network) meta-analysis including aggregate and individual patient-level data from randomised and non-randomised studies, modelling to predict effectiveness from efficacy data, and software. In addition, release of the final version of the ADDIS software (https://addis.drugis.org) which is a tool for data management of a structured database of clinical trial results, evidence synthesis (combining and summarising the results of individual studies) and benefit-risk analysis (assessing trade-offs between favourable and unfavourable effects of treatments).
GETREAL relative effectiveness	Release of the online real-world evidence (RWE) Navigator resource (https://rwe-navigator.eu). The RWE Navigator is designed as an educational resource to help users from a broad range of research and healthcare to find out more about potential issues in demonstrating the relative effectiveness of new medicines. It also guides users to specific types of analyses or study designs that use RWE to support the development of medicines. Finally, it is a comprehensive directory of resources that support the use of RWE in medicines development. Release of the online Sure-Real simulation and interactive visualisation tool (http://www.imi-getreal.eu/Tools/Sure-Real) aiming to assess the impact of

Project title	Description of result(s)
	alternative evidence generation strategies in clinical drug development using real-world evidence. It is designed to be used as multi stakeholder tool, accessible to manufacturers, HTA agencies and academia, and to provide visual output for any involved in health technologies.
iABC antimicrobial resistance	First patient in iBEST-1 Phase II clinical trial of inhaled TIP in bronchiectasis patients recruited in February 2017. Recruitment progressing successfully with 90 % of sites active across 7 countries by end of 2017.
PreDiCT-TB tuberculosis	In 2017, an additional three tuberculosis models have been developed and transferred to the DDMoRe model repository leading to a total of eight TB models in the repository: http://repository.ddmore.foundation//search?query=tuberculosis

Biomarkers for the efficacy and safety of vaccine candidates

Project title	Description of result(s)
BIOVACSAFE vaccines	Standardised positron emission tomography to quantify muscle inflammation and lymph node activation after immunisation with vaccines as a biomarker of adverse reactogenicity and replacement for diary card studies. Status: initial research finding requiring further validation in larger trials. Benefits: more rapid prediction of reactogenicity, fewer trial participants exposed to potential harm.

New taxonomies of diseases and new stratifications of patient sub-populations

Project title	Description of result(s)
AETIONOMY Alzheimer's disease and Parkinson's disease	Created the next generation of Bayesian networks representing ADNI data (Alzheimer's Disease Neuroimaging Initiative http://adni.loni.usc.edu/). These networks allows the clustering of patients and definition of new sub-populations. This 'virtual cohort' of 100 000 ADNI-like virtual patients is currently analysed for their properties and the similarity to real ADNI patient data.
BTCure rheumatoid arthritis	Biomarkers for early RA. The onset of seropositive rheumatoid arthritis (RA) is preceded by the presence of specific autoantibodies in the absence of synovial inflammation. Only a subset of these at-risk individuals will develop clinical disease. In a prospective cohort study in 21 individuals at risk for RA based on the presence of autoantibodies, BTCure identified a novel marker is significantly associated with arthritis development within three years. In a validation cohort, the positive predictive value was 82 %, and the marker clearly added to the recently described clinical prediction rule ($p = 0.024$). This new marker can be used to identify individuals at high risk of rheumatoid arthritis, and thus builds a basis for clinical intervention in this very early stage, when the disease is thought to be more amenable to therapy.
PRECISESADS rheumatoid arthritis and lupus	Description of new shared genetic markers for systemic autoimmune disease. Opening new perspectives in evaluating and treating patients with lupus nephritis, focusing on intra-renal mechanisms of immune cell activation.

Development and use of cohorts, registries and clinical networks for clinical studies and trials

Project title	Description of result(s)
AETIONOMY Alzheimer's disease and Parkinson's disease	Recruited 403 people into the Parkinson's disease portion of its European clinical study. This concluded the recruitment in time and slightly exceeding the target number (400). Subjects are included into the study with clinical data and biological samples available for the validation of the taxonomy, further adding to the ~500 samples from PD patients and ~500 samples from Alzheimer's disease patients available from other parts of the project.
COMBACTE –CARE antimicrobial resistance	Patient recruitment phase of REJUVENATE study completed with the database lock planned for February 2018. This is a major milestone allowing for the final analysis of the study results to start in Q1 2018. Rejuvenate is a Phase 2a, pharmacokinetic (PK) and safety study of aztreonam-avibactam (ATM-AVI) in patients with complicated intra-abdominal infections. In total 40 patients have been enrolled. From a planned interim cohort review this year, this study has already confirmed the dose for ATM-AVI that will be evaluated in the Phase 3 study.
COMBACTE-CARE antimicrobial resistance	The global collaboration between the consortium, Pfizer and the Biomedical Advanced Research and Development Authority (BARDA) has started to initiate the Phase 3 ATM-AVI study with a contract research organisation (CRO) selected, the final protocol completed and site selection currently ongoing.
COMBACTE-CARE antimicrobial resistance	Around 70 % of the study population has now been enrolled in the EURECA study, a prospective observational study to assess the risk factors, clinical management and outcomes of patients with multidrug-resistant Gram-negative bacteria infections, and to inform the development programmes for new antibiotics. 1 321 patients (out of the 2 000 planned) have now been recruited in 47 of 50 planned sites, mainly in central and eastern Europe. With some subgroups of the study already completed (Carbapenem resistant *Acinetobacter baumanii* infections) and with others very close to completion (case controls and matched cohorts subgroups), the EURECA study faces the final stage of the study. Publication in the BMJ Open of the protocol of the EUropean prospective cohort study on Enterobacteriaceae showing REsistance to CArbapenems (EURECA).
COMBACTE-MAGNET antimicrobial resistance	Early December 2017, 355 adult intensive care unit (ICU) patients have been enrolled in the EVADE study, of which 65 have now been randomised in this Phase II, controlled safety and efficacy trial of MEDI3902, a bispecific monoclonal antibody against two *Pseudomonas aeruginosa* proteins, for the prevention of ventilator-associated pneumonia in adult ICU patients. There are 60 active sites in Austria, Belgium, Croatia, Czech Republic, France, Greece, Hungary, Israel, Portugal, Spain and Turkey.
COMBACTE-MAGNET antimicrobial resistance	Completion of the RESCUING study gathering observational data about the treatment of some 1 000 patients with complicated urinary tract infections. The database is now locked and analysis being performed. Data were collected retrospectively in 25 medical centres located in 8 countries where the prevalence of multidrug-resistant Gram-negative bacteria is seen to be high (Bulgaria, Greece, Hungary, Israel, Italy, Romania, Turkey and Spain).
COMBACTE-MAGNET antimicrobial resistance	Publication of a number of manuscripts by the EPI-NET team, in particular on the surveillance for control of antimicrobial resistance (Lancet Infectious diseases, 25 October 2017); the methodology of surveillance for antimicrobial resistance and healthcare-associated infections in Europe (SUSPIRE): a systematic review of publicly available information; a review of antimicrobial resistance surveillance programmes in livestock and their meat in Europe, with a focus on antimicrobial resistance patterns in humans (Clinical microbiology and infection).

Project title	Description of result(s)
COMBACTE-MAGNET antimicrobial resistance	Publication of the results of a systematic review showing that despite strong encouragement of patient and public involvement (PPI) at the international and national levels, evidence for the extent, quality and impact of PPI in antimicrobial drug development research has not yet appeared in the peer-reviewed literature.
COMBACTE-NET antimicrobial resistance	Further strengthening of the clinical trials network CLIN-NET, which included as of December 2017 some 893 clinical sites and 2 732 clinical investigators. A national coordinators meeting was organised and 5 country visits took place (Romania, Croatia, Serbia, Czech Republic and Slovakia). Further strengthening of the laboratories network LAB-NET, which included 656 laboratories as of December 2017. Since the start of the project, the consortium has approached and invited 627 laboratories for feasibility for one or more studies. Of those who completed a questionnaire, currently, 163 laboratories are participating in one or more studies.
COMBACTE-NET antimicrobial resistance	As of December 2017, over 400 adult surgical patients as subjects had been enrolled in the ASPIRE-SSI study cohort (out of 5 000 planned), a prospective, observational, multicentre cohort study that aims to better understanding of *Staphylococcus aureus* infections in Europe incurred in surgical site infections (SSIs). More than 10 sites across Europe are currently activated.
COMBACTE-NET antimicrobial resistance	As of December 2017, over 1 200 patients (out of the 2 000 planned) are now enrolled in ASPIRE-ICU, a prospective, observational, multicentre, epidemiologic cohort study that aims to advance understanding of *Staphylococcus aureus* and *Pseudomonas aeruginosa* ICU pneumonia, especially ventilator-associated pneumonia (VAP). 45% of subjects have now completed the study that is carried out in some 30 sites in 11 European countries.
COMBACTE-NET antimicrobial resistance	Over 600 patients who are at high risk of developing ventilator-associated pneumonia in an intensive-care unit have been enrolled into the SAATELLITE study, of which over 1/3 have been randomised and dosed. There are currently more than 30 sites active, spread over 9 countries (Belgium, Czech Republic, France, Germany, Greece, Hungary, Spain, Switzerland, and UK). SAATELLITE is a Phase II, randomised, double-blind, placebo-controlled trial to test the safety, the pharmacokinetic and pharmacodynamic characteristics, and the efficacy of MEDI4893. Collaboration has been initiated with the Antibacterial Resistance Leadership Group (ARLG) in the US to select additional sites in the US to participate in the study.
COMBACTE-NET antimicrobial resistance	Completion of the enrolment of patients in ANTICIPATE (1 019 patients) an observational study in in more than 30 European clinical centres in the Netherlands, Germany, Greece, Spain, Romania and France. Patients are being followed over a 3-month period to detect any occurrence of *Clostridium difficile* infections following antibiotic treatment and over 80 % have now completed the study. The aim is to identify the risk factors for these infections and establish for whom the prevention of this pathology will prove the most effective.
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	Cohort of 260 cognitively normal subjects with AD biomarkers baseline data, including 196 monozygotic twins.

Project title	Description of result(s)
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	Completed the clinical data harmonisation and upload in tranSMART of the subjects participating in the multimodality biomarker discovery study in the biomarker discovery cohort. 1 221 subjects with a mean age of 67.9 (standard deviation 8.3). Plasma samples were contributed for 1 189 (97 %), DNA samples for 975 (80 %), magnetic resonance scans for 851 (70 %) and cerebro-spinal fluid samples for 774 (63 %) subjects. This cohort will allow large-scale data analyses to discover new AD biomarkers.
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	Detailed Alzheimer's disease (AD) phenotyping performed in 260 cognitively normal subjects, including 196 monozygotic twins, as part of the PreclinAD cohort. First results on differences in amyloid beta (Aβ) aggregation between twins indicated that besides genetic factors, also non-genetic factors substantially influence Aβ aggregation.
EPAD Alzheimer's disease	The longitudinal cohort study (LCS) has 10 sites enrolling. 422 research participants have been screened, of which 387 are currently enrolled.
EPAD Alzheimer's disease	In total 27 parent cohorts (PCs) have been fingerprinted, representing 579 760 participants. An initial set of 9 PCs have been selected for inclusion in the EPAD register, of which several are already connected to the 'Participant Register for EPAD' (PREPAD) software tool, encompassing 17 000 potential research participants without dementia and over 50 years of age.
EU-AIMS autism	The EU-AIMS clinical network has further expanded to 106 sites, across 37 European countries.
EU-AIMS autism	Conducted in-depth clinical characterisation and multimodal biomarker assessment on 437 children and adults with autism spectrum disorder (ASD) and 300 controls between the ages of 6 and 30 years, with intelligence quotient (IQs) varying between 50 and 148 and from 6 research centres in 4 European countries. The Longitudinal European Autism Study (LEAP) represents the only autism study worldwide that has the necessary power to identify multi-modal stratification biomarkers for ASD worldwide.
iABC antimicrobial resistance	The EMBARC European Bronchiectasis Registry, coordinated by the University of Dundee, continued to grow with more than 11 000 patients now enrolled across 27 countries. It is set to make a major contribution to understanding bronchiectasis, its causes, the effect on patients and how future clinical trials will be designed and planned.
iABC antimicrobial resistance	The registry has received more than 30 requests from researchers to use the data, resulting in >10 conference abstract presentations and contributing to a number of publications. In addition, the registry has support successful grant applications totalling over EUR 2 million to date for additional bronchiectasis studies. It is anticipated that the data generated by the registry will contribute to a large number of peer reviewed publications and grant applications over the next 12-24 months.
PRECISESADS rheumatoid arthritis and lupus	Patient recruitment: A total of 2 871 participants were recruited, divided into the Inception cohort (215 newly diagnosed patients, with 3 follow up visits – 3rd and final visit almost completed), cross-sectional phase 1 study (302 participants), and cross-sectional phase 2 (2 354 participants). In relation to sample collection and biobanking, 102 077 sample tubes / aliquots from 3 148 donations have been received and registered by the biobank.
SPRINTT Geriatrics	Successful completion of the recruitment of participants in the SPRINTT trial that aims at investigating whether physical disability may be prevented in older subjects with physical frailty and sarcopaenia. 1 519 community-living people aged 70 years and older, mainly women (>70 %) across 11 European countries have been randomised to one of the two interventions that are being compared:

Project title	Description of result(s)
	- a multicomponent intervention (MCI), based on physical activity and nutrition counselling, with support of specific technological devices; - a healthy aging lifestyle education programme. Participants are now being followed for up to 36 months. This trial is the first of its kind and scale to identify a precise subset of frail elderly with unmet medical needs and implement a MCI aimed at preventing incident mobility disability and other major negative health-related events.
SPRINTT geriatrics	Publication of a special issue entitled 'The "Sarcopenia and Physical fRailty IN older people: multi-componenT Treatment strategies" (SPRINTT) project' in Aging Clinical and Experimental Research in February 2017 (https://link.springer.com/journal/40520/29/1/page/1) composed of 14 original papers plus 1 editorial, describing all the different aspects characterising the SPRINTT project from both academic and industrial points of view. The papers describe not only the operational definition of physical frailty and sarcopaenia and the trial methodology and interventions, but present also the industrial perspectives, the ICT possibilities, stakeholders' expectations and ethical and health economics aspects. This special issue is an important achievement to disseminate SPRINTT information to researchers and healthcare professionals worldwide.
StemBANCC stem cells	Creation of an exceptional cohort of 495 patients covering a wide range of diseases and phenotypes as well as matched controls. The cohort is used for the provision of bio-materials (skin biopsy to generate dermal fibroblast cell lines and hair samples for the derivation of keratinocytes) to generate iPSCs from patients with peripheral nervous system disorders, central nervous system disorders (neurodegeneration and neurodysfunction), type 2 diabetes and for toxicology testing.

Big data solutions to leverage knowledge / implementation of data standards

Project title	Description of result(s)
ADVANCE vaccines	Creation of an ontology – named VaccO – as a common representation of vaccine-related descriptions in different European electronic health record databases. Development of three applications of VaccO in the conduct of studies about vaccine benefit/risk assessment. Development of web applications to accelerate the conduct of multi-database vaccine studies.
ADVANCE vaccines	A white paper on procedures for data access, sharing, linkage and integration, including privacy and ethics was delivered and the output of a survey on meta-data on vaccine-related data sources is available in the EMIF catalogue.
BTCure rheumatoid arthritis	Development of TheRAbase (www.therabase.eu), a relational database for archiving and validating data generated from the commonly used murine and rat models (CAIA, CIA, PIA and Tg197), as well as human samples, with the potential to further expand with additional animal models.
BTCure rheumatoid arthritis	Successfully ensured interoperability between different registries and databases in a complex real life environment with registry data, biobanks, biomarkers and genetic data. Established links between biobanked samples, studies and ethical permissions.
BTCure rheumatoid arthritis	BTCure along with other organisations worked to harmonise data collection for clinical studies of RA resulting in the formation of a EULAR task force group for standardising a minimum data collection for RA observational research.
CANCER ID cancer	Feasibility is tested with partner Alacris based on the 120+ available patient data sets so far; more is planned for the future.

Project title	Description of result(s)
eTRIKS knowledge management	61 projects have been supported resulting in 187 studies that have been curated and loaded to the eTRIKS public server (cumulative, not just 2017). eTRIKS labs tools available for other projects: https://www.etriks.org/etriks_labs/
eTRIKS knowledge management	Data federation model – a model proposing a global approach to data sharing using a federated system has been published.
OrBiTo drug delivery	A database for literature and novel gastro-intestinal physiological data for different species of relevance has been created. This database can be used for biopharmaceutics understanding and prediction.
OrBiTo drug delivery	Historical *in vivo* pharmacokinetic and biopharmaceutics data have been gathered into a database, as source for refinement and validation of *in vivo* predictive methods. Measures are currently taken by the consortium to ensure the sustainability of the database beyond the project's end.

Education and training for new and existing R&D scientists and stakeholders

Project title	Description of result(s)
CANCER ID cancer	Currently, 40 young researchers are presenting at internal and external meetings and there have been multiple visits in other labs to exchange knowledge.
CHEM21 green chemistry	The project has contributed strongly to a massive open online course ('MOOC') on industrial biotechnology run by the University of Manchester. The course has six modules – three on the core principles of industrial biotechnology, and three on specific applications. All modules comprise a mixture of recorded presentations, videos, reading material and multiple choice tests.
COMBACTE-NET antimicrobial resistance	CLIN-Net training: 181 investigators participated in the online Good Clinical Practices course, of which 111 received a GCP certificate after passing the exam. In addition, 131 investigators participated in the face-to-face GCP course of which 115 received a GCP certificated after passing the exam. (4 face-to-face GCP course trainings held in Bulgaria, Montenegro, Romania and Portugal jointly with LAB-NET Good Laboratory Practices courses).
EBiSC stem cells	Creation of a freely available training tool composed of videos and test questionnaire. The tool provides the opportunity to learn more about EBiSC standard operating procedures (SOPs), to be used when working with EBiSC iPSC lines. At the end of each training video, the stakeholders can test their knowledge by filling in the multiple-choices tests.
EPAD Alzheimer's disease	Launched EPAD academy.
eTRIKS knowledge management	A series of 12 webinars were performed resulting in over 300 scientists trained in the eTRIKS suite of software tools for translational research. Many are available at: https://www.etriks.org/etriks_labs/.
eTRIKS knowledge management	eTRIKS engaged over 20 patients and patient advocates, during a two-day conference 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.
eTRIKS knowledge management	The BioTransR 2017 was a significant and successful conference on 'Building a multi-disciplinary community of translational researchers and bioinformaticians' that took place on 15–16 May in Barcelona and was attended by over 100 people.

Project title	Description of result(s)
EUPATI education and training	The 3rd EUPATI Expert Training Course for the academic year 2017-18 started in September 2017. 60 trainees will follow the expert-level training in medicines research and development, consisting of a mix of independent e-learning coursework and face-to-face training events over a 14-month period.
GETREAL relative effectiveness	1st first edition of the online GETREAL introductory course 'Real-World Evidence in Medicine Development' (from 2 October to 16 November 2017). 42 participants from all over the world and with various professional backgrounds (public organisations and pharmaceutical industry, former GETREAL partners or not) participated in the course consisting of web lectures, reading of various articles, several (group) assignments and webinars.
K4DD drug discovery	K4DD has funded more than 20 post-docs and PhD students in the last 5 years. The programme has provided fellows with the opportunity to gain a thorough understanding of the connection between drug discovery and drug development by offering them an extensive drug discovery course and several binding-kinetics-oriented symposia.
PreDiCT-TB tuberculosis	The project reported an innovative public engagement tool based on a computer game on tuberculosis disease simulations and models
QUIC-CONCEPT cancer	Two PhD students defended their theses based on QUIC-CONCEPT research projects.

Impact on regulatory framework

Project title	Description of result(s)
ADVANCE vaccines	In 2017, two important components of the ADVANCE best practice guidance to support vaccine benefit-risk monitoring in Europe were finalised and published in a white paper: a code of conduct for collaborative vaccine studies and guidance on governance for transparent, ethical and trustable public-private collaborations. The guidance includes recommendations of how stakeholders' concerns, such as scientific independence and public trust, can be addressed. These outputs should serve as reference for ongoing and future public private and collaborative approaches in the field of vaccines.
ADVANCE vaccines	Key milestone event hosted by the EMA in March 2017, to present and gain stakeholder input on the ADVANCE framework and governance principles for public-private collaborations and partnerships for vaccine benefit-risk monitoring in Europe.
DRIVE-AB antimicrobial resistance	Researched options to drive investment in antibiotics that include a combination of incentive mechanisms along with finance and governance options to support their implementation. These were presented to a wide range of stakeholders at final DRIVE-AB conference in September 2017.
EU-AIMS autism	Provided comments and inputs into the new EMA guideline 'Clinical development of medicinal products for the treatment of Autism Spectrum Disorder (ASD)' (released 9 November 2017). The guideline directly refers to their work in relationship with stratification biomarkers and diagnostic and prognostic tools.
GETREAL relative effectiveness	Issued recommendations on real world evidence in drug development, identifying seven key themes that require attention and actions by stakeholders and policy makers regarding the use of real-world data (RWD) and real-world evidence (RWE) in effectiveness research for new drugs.
iABC antimicrobial resistance	FDA accepted lung clearance index (LCI) and next-generation sequencing (NGS) as secondary/exploratory outcome measures in Phase II clinical trial for bronchiectasis.

Project title	Description of result(s)
OrBiTo drug delivery	The consortium has continued exchanges with European and US regulatory authorities about how new tools developed within the project could be applied in future regulations (i.e. reduction of the number of clinical bioequivalence studies). This led to the publication of scientific article in a in a peer-reviewed journal (doi: 10.1021/acs.molpharmaceut.6b00824).
PROactive chronic obstructive pulmonary disease (COPD)	Draft qualification opinion issued by EMA on two PRO tools, the D-PPAC and the clinical visit (C-PPAC) developed by the consortium to capture physical activity (PA) data in patients with COPD in clinical trial settings. Both tools are hybrid tools, combining information from questionnaire items with physical activity monitors' read-out data. The qualification aims to declare the two new PRO tools are suitable to capture PA in COPD patients as intended. With a recall period of 24 hours the D-PPAC allows to collect data on a daily basis. The D-PPAC qualifies for a context of use where a clear (primary) focus is on measuring PA. The C-PPAC has a recall period of 7 days, which is considered an adequate period to capture PA data reflecting weekly (repeated) routines of COPD patients' daily life. The suggested context of use for trial settings where patients' experience of PA is a supportive outcome and/or where patient burden of completing PROs can be expected to be high is endorsed in principle by EMA. http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2017/12/WC500240706.pdf
PROTECT pharmacovigilance	Publication in the journal Pharmacoepidemiology and Drug Safety of the analysis of the impact of PROTECT project on regulatory science and practice, in particular in terms of improved processes for signal detection, recommendations for pharmacoepidemiology studies, and greater understanding for benefit-risk assessment**.**
SPRINTT geriatrics	The consortium is building a network of European researchers on frailty and sarcopaenia, focusing on health economics and health policy topics and a first health economics workshop was held in Rome during the HTAi Annual Meeting (17-21June 2017) gathering HTA members, academics and industry partners. This is an important initial step to start exploring the heath economics issues associated with frailty.
WEB-RADR pharmacovigilance	Research on the necessity of monitoring social media for identification of adverse drug reactions has resulted in some draft recommendations from the EMA: https://webradr.files.wordpress.com/2017/08/web-radr-stakeholder-event_theme-1b-ppt.pdf.

Implementation of project results inside industry

Project title	Description of result(s)
ABIRISK drug safety	A terms and definition guidance which was developed by ABIRISK is applied in industry and referenced in haemophilia A (HA) guidance. ADA assays developed in the project are being used by industry partners. T cell assays and MHC-associated peptide proteomics are applied by industry partners more extensively and with more confidence (including in decision taking for drug design / selection).
CANCER ID cancer	Circulating tumour cells technology providers are harmonising preanalytical sample handling and molecular agents for detection. Use of partner technologies as backend technologies to deliver results. Implementation of results in clinical studies in pharmaceutical industry planned in the future.

Project title	Description of result(s)
CHEM21 green chemistry	At least two practical processes carried out in EFPIA sites.
CHEM21 green chemistry	Proof of principle for green metric improvement in several EFPIA member processes.
CHEM21 green chemistry	New manufacturing process – flucytosine.
EBiSC stem cells	Protocols established are being used in industry (e.g. tau aggregation induced in iPSC derived neurons). EBiSC repository is accessed by industry for purchasing iPSC lines for R&D activities.
FLUCOP vaccines	FLUCOP harmonised haemagglutinin inhibition assay and FLUCOP harmonised neuroaminidase ELLA assay are being used by industrial partners in parallel with their internal methodology (for comparison purposes in pilot studies).
MIP-DILI drug safety	The roadmap developed by the project and its recommended assays are already implemented by several of the industry partners of the project in their internal activities.
PROactive chronic obstructive pulmonary disease (COPD)	The PRO are already used.
Translocation antimicrobial resistance	Drug uptake assays are being used in industry and in collaboration with ENABLE, to understand penetration and, if possible, prioritise work across sub-series. Strains and data from siderophore uptake studies are being considered and/or used in industry.

Accessibility of resources/outputs beyond consortium

In order to help scientists outside of our projects in their research efforts, we have started building a catalogue of accessible tools generated by our projects. The list, which is not exhaustive, can be found in the 'projects and results' section of the IMI website.

Project title	Description of result(s)
ADVANCE vaccines	In 2017, two important components of the ADVANCE best practice guidance to support vaccine benefit-risk monitoring in Europe were finalised and published in a white paper: a code of conduct for collaborative vaccine studies and guidance on governance for transparent, ethical and trustable public-private collaborations. The guidance includes recommendations of how stakeholders' concerns, such as scientific independence and public trust, can be addressed. These outputs should serve as reference to ongoing and future public private and collaborative approaches in the field of vaccines.
ADVANCE vaccines	Key milestone event hosted by the EMA in March 2017, to present and gain stakeholder input on the ADVANCE framework and governance principles for public-private collaborations and partnerships for vaccine benefit-risk monitoring in Europe.
AETIONOMY Alzheimer's disease and Parkinson's disease	NeuroMMSig is publicly available at http://neurommsig.scai.fraunhofer.de/.

Project title	Description of result(s)
BTCure rheumatoid arthritis	Development of 'TheRAbase' (www.therabase.eu), a relational database, for archiving and validating data generated from the commonly used murine and rat models (CAIA, CIA, PIA and Tg197), as well as human samples, with the potential to further expand with additional animal models.
CANCER ID cancer	Results disseminated in 150 papers so far (as of Dec 2017), 50 in 2017, mostly in open access journals. Presentations and posters at numerous meetings (e.g. AACR, ACTC Rhodes).
CANCER ID cancer	A software tool (ACCEPT) for automated identification of circulating tumour cells (CTCs) has been developed and made available in the public domain. Ongoing validation of standards (most advanced for CTCs) and developed protocols in clinical samples to support clinical utility of standardised liquid biopsy technologies. Both are expected to contribute to help making liquid biopsy biomarkers pharmacodynamic markers.
DRIVE-AB antimicrobial resistance	Researched options to drive investment in antibiotics that include a combination of incentive mechanisms along with finance and governance options to support their implementation, presented to wide range of stakeholders at final DRIVE-AB conference in September 2017.
EBiSC stem cells	A global iPSC banking facility has been established to distribute iPSC lines. Validated procedures for collecting, expanding and characterising cell lines as well as procedures for shipping, tracking and recovery of cell lines have been established. The EBiSC biobank currently contains 688 different cell lines generated from a wide range of donors representing specific diseases (neurodegenerative diseases, eye and heart diseases, and lines from healthy control donors for age and sex matching) for disease modelling and other forms of preclinical research. New iPSC lines commissioning by using the validated, standard procedures is also possible for new disease representative and control lines.
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	EMIF catalogue now contains aggregate data from 344 datasets in Alzheimer's disease, vaccines, child health and other cohorts.
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	The EMIF-AD catalogue is a catalogue with metadata of clinical studies on aging and Alzheimer's disease; The catalogue includes currently information on 46 studies that have enrolled 47 000 subjects. The catalogue is accessible after registration (https://emif-catalogue.eu).
eTOX knowledge management, drug safety	Part of AstraZeneca's contribution to the IMI project eTOX was in the form of extensive data on the safety/toxicity profiles of (potential) medicines. Now, the company has decided to make the data provided to eTOX available to the wider scientific community through the company's Open Innovation portal.
eTRIKS knowledge management	eTRIKS data catalogue released to give free access to IMI project data to other researchers: https://datacatalog.elixir-luxembourg.org/. Currently holds data from 74 datasets.
EU-AIMS autism	The EthoVision XT vs 12 tool developed by SME Noldus Information Technology is released to the research community and commercially available from the company.
EUPATI education and training	Please refer to the IMI webpage Catalogue of project tools.

Project title	Description of result(s)
Get Real relative effectiveness	PragMagic tool (an innovative tool to aid in pragmatic clinical trial design) free access. Aggregate Data Drug Information System (ADDIS) is a data management and analytical tool for evidence based decision making in healthcare (a tool for conducting (network) meta-analyses and benefit-risk analyses). Free access. Sure-Real Software (Software licence contained in the end-user license agreement). Real-World Evidence in Medicine Development Course (free to enrol on the course). Real-World Evidence Navigator (free).
iABC antimicrobial resistance	FDA accepted lung clearance index (LCI) and next-generation sequencing (NGS) as secondary/exploratory outcome measures in Phase II clinical trial for bronchiectasis.
iPiE environmental issues	ECOdrug, a new database that connects drugs to their protein targets across different species. The ECOdrug database draws on data from multiple sources and has information on over 600 species, including other primates, rodents, birds, fish, microscopic animals, fungi, and plants. The user-friendly interface has two tabs – one for drug-related information and one for drug targets. A search of a drug name brings up a table showing the targets of the drug and how well they are conserved across different species. Similarly, a search by drug target uncovers links to all drugs that target that protein, and the interface shows an evolutionary tree showing the numbers of species in different groups that have an equivalent to the drug target.
PROactive chronic obstructive pulmonary disease (COPD)	Conceptual framework on physical activity (free).
PROTECT pharmacovigilance	Adverse drug reactions database (free). Benefit-risk assessment website (free). Drug consumption databases in Europe (free). PROTECT recommendations on good signal detection practices (free).
QUIC-CONCEPT cancer	Pre-clinical and clinical data in an imaging repository and data sharing policy is in place.
StemBANCC stem cells	To ensure that the StemBANCC cell lines become a sustainable resource to StemBANCC partners and the scientific community, StemBANCC lines were transferred on to the IMI initiative EBiSC for distribution.
U-BIOPRED asthma	Please refer to the IMI webpage Catalogue of project tools. A short guide to successful patient involvement in EU-funded research (free). Human Experimental Exacerbation Study - Rhinovirus (RV16) for use in human viral challenge studies An access request form can be obtained from BioSci Consulting: link (fee). Adult and paediatric cohorts of patients with asthma. Biobank of 50 000 samples (fee). Full set of 100+ standard operating procedures and protocol related-documents which can be shared with researchers upon signature of a standard memorandum of understanding (free).

Project title	Description of result(s)
WEB-RADR pharmacovigilance	As well as developing mobile apps for reporting drug side effects (adverse drug reactions, ADRs) in UK, NL, HR, the WEB-RADR consortium has also delivered an off-the-shelf app development package that allows other countries to easily develop ADR reporting apps themselves. To showcase this app development pack, the project prepared ADR reporting apps for Zambia and Burkina Faso in collaboration with the WHO.

IMI2 projects

New tools/resources for drug discovery & preclinical drug development

Project title	Description of result(s)
PHAGO Alzheimer's disease	Two of the PHAGO project partners have independently revealed the mechanism behind the shedding in the gene called 'triggering receptor expressed on myeloid cells 2' (TREM2) and the role of a rare AD-linked mutation in this receptor. This mutation increases the risk of developing Alzheimer's disease. These results will allow the consortium to develop tools such as antibodies and small molecules that block TREM2 cleavage, or non-cleavable TREM2, which will help to detangle the functions of the different forms of TREM2 in phagocytosis. Modulating the amount of the different forms of TREM2 and thereby phagocytic activity, might develop into a therapeutic strategy for AD.

Biomarkers and tools developed to predict clinical outcomes (efficacy and safety)

Project title	Description of result(s)
EbolaMoDRAD Ebola and related diseases	Developed a fast, local test for Ebola virus infection and started work on validation.
INNODIA diabetes	The discovery of a new neo-autoantigenic epitope generated by post-translational modification in T1D patients.
INNODIA diabetes	The discovery that miRNAs regulate the expression of pro-apoptotic BH-3-only proteins DP5 and PUMA in pancreatic beta cells.
INNODIA diabetes	Discovered a new miRNA as a biomarker in the circulation of NOD mice and patients.
INNODIA diabetes	Identification of interferon-alpha as a key regulator of early markers of beta-cell dysfunction/death in human diabetes, and the validation of 3 new blockers of interferon-alpha signalling, preventing ER stress and apoptosis in human islets, suggesting this inflammatory cytokine could be a target for novel clinical interventions to prevent diabetes.
INNODIA diabetes	A new biomarker for human beta cell imaging (DPP6) has been identified and validated for *in vivo* imaging.
INNODIA diabetes	Discovered that circulating CD8+ T cells are found at similar frequencies in T1D and healthy donors, suggesting a universal state of 'benign' beta-cell autoimmunity.
INNODIA diabetes	Developed a robust method for large-scale production of 3-dimensional islet-like aggregates from human pluripotent stem cells.
MOFINA Ebola and related diseases	Delivery of system capable of providing a rapid bedside test for Ebola.
PERISCOPE vaccines	A pre-clinical pertussis disease model has been established. Model transfer from USA to Europe (CEA, France) has taken place, where it can be used by EU and global vaccine researchers and developers.

Project title	Description of result(s)
ROADMAP big data, Alzheimer's disease	The ROADMAP consortium has prepared a report of systematic review of published and unpublished data identifying important and relevant outcomes in AD and criteria for disease progression. This has been complemented by a report on existing health economic models, resource use, costs and health-related quality of life across the full spectrum of Alzheimer's disease and dementia.

Improved protocols for clinical trial design and processes

Project title	Description of result(s)
EBOVAC1 Ebola and related diseases	Promising immunogenicity data at one year after vaccination from a Phase 1 clinical study in the UK published in JAMA, March 2017. All of the active vaccine recipients maintained Ebola virus–specific antibody responses at day 360. Vaccine-induced T-cell responses persisted in 60 % to 83 % of participants receiving Ad26.ZEBOV first followed by MVA-BN-Filo as a booster compared with 69 % to 100 % of those receiving the reverse regimen.
EBOVAC1 Ebola and related diseases	Obtained promising immunogenicity data at one year after vaccination from Phase 1 trial in Kenya, Uganda and Tanzania, presented at ASTMH and West African Sub-Regional Conference on Ebola. Ad26.ZEBOV/MVA-BN-Filo vaccine regimens were well tolerated and immunogenic among healthy African adults. Antibody responses were elicited early on and persisted to day 360.
EBOVAC1 Ebola and related diseases	Enrolment of different age groups in staged Phase IIb EBOVAC-Salone trial in Sierra Leone successfully ongoing, with adult enrolment completed and long-term follow-up ongoing, adolescent enrolment completed end of 2017 (192 adolescents aged 12-17 enrolled), and children enrolment ongoing (132 children aged 4-11 enrolled by end of 2017).
EBOVAC1 Ebola and related diseases	Randomisation of participants in the Sierra Leone arm of the PREVAC trial, a randomised, double-blind, placebo-controlled trial of three Ebola vaccine strategies, successfully ongoing.
EBOVAC1 Ebola and related diseases	Clinical trial site and annex building in Mambolo Town, Kambia District, in Northern Sierra Leone, were renovated and are up and running to support the PREVAC trial.
EBOVAC2 Ebola and related diseases	By end of 2017, >45 % of enrolment completed in Phase 2 trial with Janssen prime-boost Ebola vaccine regimen in Europe (UK and France; 290 participants enrolled), and > 85 % of enrolment completed in Phase 2 trial in Africa (Burkina Faso, Ivory Coast, Kenya, Uganda; 1 011 participants enrolled).
FILODIAG Ebola and related diseases	Completed field tests (Sierra Leone) of a system for providing rapid bedside testing for Ebola.
INNODIA diabetes	Established a clinical trial network, allowing the conduct of smart clinical trials using adaptive clinical trial designs. For this, a network of well characterised and accredited clinical centres throughout INNODIA has been established. A clinical trial coordination centre and an accreditation database were established. A self-assessment questionnaire was a first step for identification of the clinical trial performing capacity of the INNODIA members in a standardised way. Through this, a clinical profile of centres was made concerning clinical capacity (size of clinics, number of patients, adult and/or paediatric, clinical network capacity, access to an electronic patient record, meeting international standards of diabetes care …). It became apparent that although all clinical centres of partners in INNODIA are well established and have excellent clinical reputations, level of trial experience in T1D studies varies. During the last 12 months, the main aim was to prepare and execute audits of participating centres on site based on a structured

Project title	Description of result(s)
	review process outlined in the specific handbook. These visits are conducted in close association with work package (WP) 1 and finally performed at the same time when the centres are trained and initiated for the planned sample collection within WP1. This should make it possible to examine, immediately before the start of the study, the specific local conditions (structure and function of the service / infrastructure, clinical research (general), clinical research (outcomes / indicators), coordination of clinical trials / patient pathways) regarding the suitability of the centre to carry out the planned observational study. Importantly all visited centres could be accredited as eligible clinical research centre for the INNODIA trial initiated from WP1.
PERISCOPE vaccines	The protocols for a multi-centre clinical study to investigate the effects of an acellular pertussis booster vaccination in children, young adults and the elderly, on long-term immunity against *B. pertussis*, were approved by the consortium's steering committee and ethics advisory boards. The study has received ethical approval in Finland and the Netherlands, and was launched in the Netherlands.
PERISCOPE vaccines	The protocol for a clinical study aimed at developing a controlled human infection model for pertussis in volunteers was finalised and approved by the consortium's governance bodies and local ethical committees. This trial has been successfully launched at in Southampton (UK) and the first volunteers have been successfully challenged.
PREFER patient involvement in R&D	To identify the desires, expectations, concerns, and requirements of stakeholders about methodologies for patient-preference elicitation, and to identify existing processes, conditions, and contextual factors that influence the utility and role of patient-preference studies and the rationale behind such influence, the consortium has conducted16 exploratory interviews; a literature review consulting scientifically published and other publicly available documents; semi-structured interviews with 143 stakeholders (patients, informal caregivers, patient representatives, physicians, regulators, reimbursement agency representatives, health technology assessment representatives, industry representatives, academics) from Sweden, Romania, Italy, the UK, the Netherlands, Germany, France and the US; focus groups with stakeholders in four European countries. In addition to a scoping literature review, 71 semi-structured interviews and 2 sets of validation meetings were conducted to identify assessment criteria used at decision points throughout the medical product life cycle. These are important steps to provide input on the case studies to be conducted as well as on the translation of case study findings to recommendations for patient-preference elicitation.

Biomarkers for the efficacy and safety of vaccine candidates

Project title	Description of result(s)
PERISCOPE vaccines	Advances were made towards developing a toolbox of immunological and microbiological tests to be used to explore immune responses to pertussis vaccination and infection.
VSV-EBOVAC Ebola and related diseases	Six monocyte-associated cytokines/chemokines have been identified as correlating with viraemia and biological responses to VSV-ZEBOV, with D28 antibody responses and with the frequency and intensity of early reactogenicity and of arthritis in high-dose vaccinees. (Huttner A. et al. Sci Transl Med. 2017 Apr 12;9(385). doi: 10.1126/scitranslmed.aaj1701).

Development and use of cohorts, registries and clinical networks for clinical studies and trials

Project title	Description of result(s)
PERISCOPE vaccines	Launched first of nine clinical studies.
PRISM neurological disorders	The clinical study on the biological underpinnings of social withdrawal in Alzheimer's disease (AD) and schizophrenia (SZ) has enrolled the first 28 subjects out of 200. Participants will undergo a range of tests, including brain scans, blood tests and questionnaires and will use a smartphone app called BeHapp to measure people's sociability and social exploration in their daily lives.
RADAR-CNS neurological disorders	Commencement of epilepsy and depression studies using wearable sensors (fitbit charge 2), mobile apps, and clinician visits.
RESCEU respiratory disease	RESCEU became member of the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC), a global initiative aiming to ensure that clinical researchers have the open access protocols and data-sharing processes needed to facilitate a rapid response to emerging diseases that may turn into epidemics or pandemics.
RESCEU respiratory disease	Three cohort studies on vulnerable populations (infants, older adults, chronic obstructive pulmonary disease) and one case-control study on infants after respiratory syncytial virus (RSV) infection have started, with the aim of gathering data and addressing knowledge gaps on the impact of RSV infections.
RHAPSODY diabetes	Establishment of a research database for type 2 diabetes mellitus (T2D) with analysis and visualisation tools to allow cross cohort data interrogation at EU level; establishment of all regulatory/administrative requirements for data sharing.

Education and training for new and existing R&D scientists and stakeholders

Project title	Description of result(s)
EBODAC Ebola and related diseases	In February 2017, held highly recognised symposium in Dakar, Senegal, to reflect on the key learnings of communication, community engagement and enabling technologies when conducting Ebola clinical trials in an outbreak setting. The meeting contributed to consolidating the lessons learned from the field to build a more prepared community of experts for future outbreaks.
EBODAC Ebola and related diseases	Developed an online tool to share the learnings on community engagement from the symposium with a wider community www.ebovac.org/ebodac/training-resource/
EBODAC Ebola and related diseases	Used drama and produced various plays and a radio jingle targeted at different age groups to explain the Ebola vaccine trial they are conducting.
EbolaMoDRAD Ebola and related diseases	A three-day workshop on outbreak management was successfully held in April 2017. There were a wide variety of interesting talks from a large number of partners with the focus of the workshop a retrospective look at the Ebola response and its evolution over the course of the outbreak, with a particular focus on the European response. There was also a visit to the Public Health England (PHE) deployment training labs, where PHE trained staff deployed to Sierra Leone.
INNODIA diabetes	Established a Patient Advisory Committee (PAC). The PAC plays an important role in the writing of sampling protocols and preparing information materials. Prepared testimonials and nine videos and interactive tools on how to take part in the project as a patient or family member. Cartoons, flyers, an animation video

	and a booklet for children have been made by the PAC to inform children and their families on why it is important for them to participate in the work of INNODIA Tools have been elaborated in close collaboration with the INNODIA ethics committee.
VSV-EBOVAC Ebola and related diseases	7 post-docs, 4 PhDs, 3 students, 5 technicians were trained.

Impact on regulatory framework

Project title	Description of result(s)
ADAPT-SMART	Publication on the project website 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 questions are designed to initially trigger discussions at the company level (i.e. the medicine developer) and subsequently during discussions between the company and other stakeholders. Publication on the project website of a report 'Seamless Process and Decision Points of an Adaptive Pathway' that proposes a framework with pictographic representation of an adaptive pathway containing key moments, events and involved stakeholders, in each phase.

Accessibility of resources/outputs beyond consortium

In order to help scientists outside of our projects in their research efforts, we have started building a catalogue of accessible tools generated by our projects. The list, which is not exhaustive, can be found in the 'projects and results' section of the IMI website.

Project title	Description of result(s)
ADAPT-SMART MAPPs	Free access to the glossary providing working definitions for common terms relevant for the consortium and includes references. http://adaptsmart.eu/wp-content/uploads/2016/04/D2-02-ADAPT-SMART-Glossary-first-edition.pdf
EBOVAC1 Ebola and related diseases	Generated mathematical models on Ebola virus disease. The models fed into the WHO SAGE working group recommendations for Ebola vaccines.
MOFINA Ebola and related diseases	Delivered a system capable of providing a rapid bedside test for Ebola; the test is now commercially available.
RADAR-CNS neurological disorders	Released their Data Capture Platform to the public. Available free of charge on github repository.
VSV-EBOVAC Ebola and related diseases	Results obtained by the project are published as open access in papers published in peer review journals with the VSV-EBOVAC acknowledgment: Medaglini D. et al., Curr Opin Virol. 2017 Apr;23:88-94 One article was published in peer review journals with the VSV-EBOVAC acknowledgment: Huttner A. et al., Sci Transl Med. 2017 Apr 12;9(385). pii: eaaj1701

Annex 4 – Publications from projects

Hot papers from 2017

Aleku, GA; France, SP; Man, H; Mangas-Sanchez, J; Montgomery, SL; Sharma, M; Leipold, F; Hussain, S; Grogan, G; Turner, NJ (2017) A reductive aminase from Aspergillus oryzae. NATURE CHEMISTRY 9(10): 961-969

Bell, CC; Hendriks, DFG; Moro, SML; Ellis, E; Walsh, J; Renblom, A; Puigvert, LF; Dankers, ACA; Jacobs, F; Snoeys, J; Sison-Young, RL; Jenkins, RE; Nordling, A; Mkrtchian, S; Park, BK; Kitteringham, NR; Goldring, CEP; Lauschke, VM; Ingelman-Sundberg, M (2016) Characterization of primary human hepatocyte spheroids as a model system for drug-induced liver injury, liver function and disease. SCIENTIFIC REPORTS 6: 25187

Fitzpatrick, AWP; Falcon, B; He, S; Murzin, AG; Murshudov, G; Garringer, HJ; Crowther, RA; Ghetti, B; Goedert, M; Scheres, SHW (2017) Cryo-EM structures of tau filaments from Alzheimer's disease. NATURE 547(7662): 185+

Hocher, B; Adamski, J (2017) Metabolomics for clinical use and research in chronic kidney disease. NATURE REVIEWS NEPHROLOGY 13(5): 269-284

Siravegna, G; Marsoni, S; Siena, S; Bardelli, A (2017) Integrating liquid biopsies into the management of cancer. NATURE REVIEWS CLINICAL ONCOLOGY 14(9): 531-548

IMI highly-cited papers at the end of 2017

This list includes those papers in the world's top 1 % of most highly-cited papers. (A longer list of the papers included in the top 10 % of most highly-cited papers would take up too much room. This information will however be included in the detailed analysis of IMI publications by Clarivate Analytics which will be published on the IMI website.)

Ajeganova, S; van Steenbergen, HW; Verheul, MK; Forslind, K; Hafstrom, I; Toes, REM; Huizinga, TWJ; Svensson, B; Trouw, LA; van der Helm-van Mil, AHM (2017) The association between anti-carbamylated protein (anti-CarP) antibodies and radiographic progression in early rheumatoid arthritis: a study exploring replication and the added value to ACPA and rheumatoid factor. ANNALS OF THE RHEUMATIC DISEASES 76(1): 112-118

Alix-Panabieres, C; Mader, S; Pantel, K (2017) Epithelial-mesenchymal plasticity in circulating tumor cells. JOURNAL OF MOLECULAR MEDICINE-JMM 95(2): 133-142

Bardelli, A; Pantel, K (2017) Liquid Biopsies, What We Do Not Know (Yet). CANCER CELL 31(2): 172-179

Budin-Ljosne, I; Teare, HJA; Kaye, J; Beck, S; Bentzen, HB; Caenazzo, L; Collett, C; D'Abramo, F; Felzmann, H; Finlay, T; Javaid, MK; Jones, E; Katic, V; Simpson, A; Mascalzoni, D (2017) Dynamic Consent: a potential solution to some of the challenges of modern biomedical research. BMC Medical Ethics 18: 4

Calvani, R; Marini, F; Cesari, M; Buford, TW; Manini, TM; Pahor, M; Leeuwenburgh, C; Bernabei, R; Landi, F; Marzetti, E (2017) Systemic inflammation, body composition, and physical performance in old community-dwellers. JOURNAL OF CACHEXIA SARCOPENIA AND MUSCLE 8(1): 69-77

Catrina, AI; Svensson, CI; Malmstrom, V; Schett, G; Klareskog, L (2017) Mechanisms leading from systemic autoimmunity to joint-specific disease in rheumatoid arthritis. NATURE REVIEWS RHEUMATOLOGY 13(2): 79-86

Colloca, L; Ludman, T; Bouhassira, D; Baron, R; Dickenson, A; Yarnitsky, D; Freeman, R; Truini, A; Attal, N; Finnerup, NB; Eccleston, C; Kalso, E; Bennett, DL; Dworkin, R; Raja, SN (2017) Neuropathic pain. NATURE REVIEWS DISEASE PRIMERS 3: 17002

Demeyer, H; Louvaris, Z; Frei, A; Rabinovich, RA; de Jong, C; Gimeno-Santos, E; Loeckx, M; Buttery, SC; Rubio, N; Van der Molen, T; Hopkinson, NS; Vogiatzis, I; Puhan, MA; Garcia-Aymerich, J; Polkey, MI; Troosters, T (2017) Physical activity is increased by a 12-week semiautomated telecoaching programme in patients with COPD: a multicentre randomised controlled trial. THORAX 72(5): 415-423

Dujic, T; Zhou, K; Yee, SW; van Leeuwen, N; de Keyser, CE; Javorsky, M; Goswami, S; Zaharenko, L; Christensen, MMH; Out, M; Tavendale, R; Kubo, M; Hedderson, MM; van der Heijden, AA; Klimcakova, L; Pirags, V; Kooy, A; Brosen, K; Klovins, J; Semiz, S; Tkac, I; Stricker, BH; Palmer, CNA; 't Hart, LM; Giacomini, KM; Pearson, ER (2017) Variants in Pharmacokinetic Transporters and Glycemic Response to Metformin: A MetGen Meta-Analysis. CLINICAL PHARMACOLOGY & THERAPEUTICS 101(6): 763-772

Efthimiou, O; Mavridis, D; Debray, TPA; Samara, M; Belger, M; Siontis, GCM; Leucht, S; Salanti, G (2017) Combining randomized and nonrandomized evidence in network meta-analysis. STATISTICS IN MEDICINE 36(8): 1210-1226

Fitzpatrick, AWP; Falcon, B; He, S; Murzin, AG; Murshudov, G; Garringer, HJ; Crowther, RA; Ghetti, B; Goedert, M; Scheres, SHW (2017) Cryo-EM structures of tau filaments from Alzheimer's disease. NATURE 547(7662): 185-+

Frisoni, GB; Boccardi, M; Barkhof, F; Blennow, K; Cappa, S; Chiotis, K; Demonet, JF; Garibotto, V; Giannakopoulos, P; Gietl, A; Hansson, O; Herholz, K; Jack, CR; Nobili, F; Nordberg, A; Snyder, HM; Ten Kate, M; Varrone, A; Albanese, E; Becker, S; Bossuyt, P; Carrillo, MC; Cerami, C; Dubois, B; Gallo, V; Giacobini, E; Gold, G; Hurst, S; Lonneborg, A; Lovblad, KO; Mattsson, N; Molinuevo, JL; Monsch, AU; Mosimann, U; Padovani, A; Picco, A; Porteri, C; Ratib, O; Saint-Aubert, L; Scerri, C; Scheltens, P; Schott, JM; Sonni, I; Teipel, S; Vineis, P; Visser, PJ; Yasui, Y; Winblad, B (2017) Strategic roadmap for an early diagnosis of Alzheimer's disease based on biomarkers. LANCET NEUROLOGY 16(8): 661-676

Fujisawa, T; Filippakopoulos, P (2017) Functions of bromodomain-containing proteins and their roles in homeostasis and cancer. NATURE REVIEWS MOLECULAR CELL BIOLOGY 18(4): 246-262

Gaulton, A; Hersey, A; Nowotka, M; Bento, AP; Chambers, J; Mendez, D; Mutowo, P; Atkinson, F; Bellis, LJ; Cibrian-Uhalte, E; Davies, M; Dedman, N; Karlsson, A; Magarinos, MP; Overington, JP; Papadatos, G; Smit, I; Leach, AR (2017) The ChEMBL database in 2017. NUCLEIC ACIDS RESEARCH 45(D1): D945-D954

Gerber, PA; Rutter, GA (2017) The Role of Oxidative Stress and Hypoxia in Pancreatic Beta-Cell Dysfunction in Diabetes Mellitus. ANTIOXIDANTS & REDOX SIGNALING 26(10): 501-+

Glenwright, AJ; Pothula, KR; Bhamidimarri, SP; Chorev, DS; Basle, A; Firbank, SJ; Zheng, HJ; Robinson, CV; Winterhalter, M; Kleinekathofer, U; Bolam, DN; van den Berg, B (2017) Structural basis for nutrient acquisition by dominant members of the human gut microbiota. NATURE 541(7637): 407-+

Grieben, M; Pike, ACW; Shintre, CA; Venturi, E; El-Ajouz, S; Tessitore, A; Shrestha, L; Mukhopadhyay, S; Mahajan, P; Chalk, R; Burgess-Brown, NA; Sitsapesan, R; Huiskonen, JT; Carpenter, EP (2017) Structure of the polycystic kidney disease TRP channel Polycystin-2 (PC2). NATURE STRUCTURAL & MOLECULAR BIOLOGY 24(2): 114-+

Grieco, FA; Sebastiani, G; Juan-Mateu, J; Villate, O; Marroqui, L; Ladriere, L; Tugay, K; Regazzi, R; Bugliani, M; Marchetti, P; Dotta, F; Eizirik, DL (2017) MicroRNAs miR-23a-3p, miR-23b-3p, and miR-149-5p Regulate the Expression of Proapoptotic BH3-Only Proteins DP5 and PUMA in Human Pancreatic beta-Cells. DIABETES 66(1): 100-112

Guo, D; Heitman, LH; IJzerman, AP (2017) Kinetic Aspects of the Interaction between Ligand and G Protein-Coupled Receptor: The Case of the Adenosine Receptors. CHEMICAL REVIEWS 117(1): 38-66

He, YP; Selvaraju, S; Curtin, ML; Jakob, CG; Zhu, HZ; Comess, KM; Shaw, BL; The, J; Lima-Fernandes, E; Szewczyk, MM; Cheng, D; Klinge, KL; Li, HQ; Pliushchev, M; Algire, MA; Maag, D; Guo, J; Dietrich, J; Panchal, SC; Petros, AM; Sweis, RF; Torrent, M; Bigelow, LJ; Senisterra, G; Li, FL; Kennedy, S; Wu, Q; Osterling, DJ; Lindley, DJ; Gao, WQ; Galasinski, S; Barsyte-Lovejoy, D; Vedadi, M; Buchanan, FG; Arrowsmith, CH; Chiang, GG; Sun, CH; Pappano, WN (2017) The EED protein-protein interaction inhibitor A-395 inactivates the PRC2 complex. NATURE CHEMICAL BIOLOGY 13(4): 389-+

Hensvold, AH; Frisell, T; Magnusson, PKE; Holmdahl, R; Askling, J; Catrina, AI (2017) How well do ACPA discriminate and predict RA in the general population: a study based on 12 590 population-representative Swedish twins. ANNALS OF THE RHEUMATIC DISEASES 76(1): 119-125

Hocher, B; Adamski, J (2017) Metabolomics for clinical use and research in chronic kidney disease. NATURE REVIEWS NEPHROLOGY 13(5): 269-284

Kuo, CHS; Pavlidis, S; Loza, M; Baribaud, F; Rowe, A; Pandis, I; Hoda, U; Rossios, C; Souse, A; Wilson, SJ; Howarth, P; Dahlen, B; Dahlen, SE; Chanez, P; Shaw, D; Krug, N; Sandstrom, T; De Meulder, B; Lefaudeux, D; Fowler, S; Fleming, L; Corfield, J; Auffray, C; Sterk, PJ; Djukanovic, R; Guo, YK; Adcock, IM; Chung, KF (2017) A Transcriptome-driven Analysis of Epithelial Brushings and Bronchial Biopsies to Define Asthma Phenotypes in U-BIOPRED. AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE 195(4): 443-455

Lambin, P; Zindler, J; Vanneste, BL; Van De Voorde, L; Eekers, D; Compter, I; Panth, KM; Peerlings, J; Larue, RTHM; Deist, TM; Jochems, A; Lustberg, T; van Soest, J; de Jong, EEC; Even, AJG; Reymen, B; Rekers, N; van Gisbergen, M; Roelofs, E; Carvalho, S; Leijenaar, RTH; Zegers, CML; Jacobs, M; van Timmeren, J; Brouwers, P; Lal, JA; Dubois, L; Yaromina, A; Van Limbergen, EJ; Berbee, M; van Elmpt, W; Oberije, C; Ramaekers, B; Dekker, A; Boersma, LJ; Hoebers, F; Smits, KM; Berlanga, AJ; Walsh, S (2017) Decision support systems for personalized and participative radiation oncology. ADVANCED DRUG DELIVERY REVIEWS 109: 131-153

Lewczuk, P; Matzen, A; Blennow, K; Parnetti, L; Molinuevo, JL; Eusebi, P; Kornhuber, J; Morris, JC; Fagan, AM (2017) Cerebrospinal Fluid A beta(42/40) Corresponds Better than A beta(42) to Amyloid PET in Alzheimer's Disease. JOURNAL OF ALZHEIMERS DISEASE 55(2): 813-822

Lo, MT; Hinds, DA; Tung, JY; Franz, C; Fan, CC; Wang, YP; Smeland, OB; Schork, A; Holland, D; Kauppi, K; Sanyal, N; Escott-Price, V; Smith, DJ; O'Donovan, M; Stefansson, H; Bjornsdottir, G; Thorgeirsson, TE; Stefansson, K; McEvoy, LK; Dale, AM; Andreassen, OA; Chen, CH (2017) Genome-wide analyses for personality traits identify six genomic loci and show correlations with psychiatric disorders. NATURE GENETICS 49(1): 152-156

Lotta, LA; Gulati, P; Day, FR; Payne, F; Ongen, H; van de Bunt, M; Gaulton, KJ; Eicher, JD; Sharp, SJ; Luan, JA; Rolfe, ED; Stewart, ID; Wheeler, E; Willems, SM; Adams, C; Yaghootkar, H; Forouhi, NG; Khaw, KT; Johnson, AD; Semple, RK; Frayling, T; Perry, JRB; Dermitzakis, E; McCarthy, MI; Barroso, I; Wareham, NJ; Savage, DB; Langenberg, C; O'Rahilly, S; Scott, RA (2017) Integrative genomic analysis implicates limited peripheral adipose storage capacity in the pathogenesis of human insulin resistance. NATURE GENETICS 49(1): 17-26

Malmstrom, V; Catrina, AI; Klareskog, L (2017) The immunopathogenesis of seropositive rheumatoid arthritis: from triggering to targeting. NATURE REVIEWS IMMUNOLOGY 17(1): 60-75

McCarthy, MI (2017) Painting a new picture of personalised medicine for diabetes. DIABETOLOGIA 60(5): 793-799

Mikus, M; Drobin, K; Gry, M; Bachmann, J; Lindberg, J; Yimer, G; Aklillu, E; Makonnen, E; Aderaye, G; Roach, J; Fier, I; Kampf, C; Gopfert, J; Perazzo, H; Poynard, T; Stephens, C; Andrade, RJ; Lucena, MI; Arber, N; Uhlen, M; Watkins, PB; Schwenk, JM; Nilsson, P; Schuppe-Koistinen, I (2017) Elevated levels of circulating CDH5 and FABP1 in association with human drug-induced liver injury. LIVER INTERNATIONAL 37(1): 132-140

Mobasheri, A; Rayman, MP; Gualillo, O; Sellam, J; van der Kraan, P; Fearon, U (2017) The role of metabolism in the pathogenesis of osteoarthritis. NATURE REVIEWS RHEUMATOLOGY 13(5): 302-311

Naaijen, J; Bralten, J; Poelmans, G; Glennon, JC; Franke, B; Buitelaar, JK (2017) Glutamatergic and GABAergic gene sets in attention-deficit/hyperactivity disorder: association to overlapping traits in ADHD and autism. TRANSLATIONAL PSYCHIATRY 7: e999

O'Connor, JPB; Aboagye, EO; Adams, JE; Aerts, HJWL; Barrington, SF; Beer, AJ; Boellaard, R; Bohndiek, SE; Brady, M; Brown, G; Buckley, DL; Chenevert, TL; Clarke, LP; Collette, S; Cook, GJ; Desouza, NM; Dickson, JC; Dive, C; Evelhoch, JL; Faivre-Finn, C; Gallagher, FA; Gilbert, FJ; Gillies, RJ; Goh, V; Griffiths, JR; Groves, AM; Halligan, S; Harris, AL; Hawkes, DJ; Hoekstra, OS; Huang, EP; Hutton, BF; Jackson, EF; Jayson, GC; Jones, A; Koh, DM; Lacombe, D; Lambin, P; Lassau, N; Leach, MO; Lee, TY; Leen, EL; Lewis, JS; Liu, Y; Lythgoe, MF; Manoharan, P; Maxwell, RJ; Miles, KA; Morgan, B; Morris, S; Ng, T; Padhani, AR; Parker, GJM; Partridge, M; Pathak, AP; Peet, AC; Punwani, S; Reynolds, AR; Robinson, SP; Shankar, LK; Sharma, RA; Soloviev, D; Stroobants, S; Sullivan, DC; Taylor, SA; Tofts, PS; Tozer, GM; van Herk, M; Walker-Samuel, S; Wason, J; Williams, KJ; Workman, P; Yankeelov, TE; Brindle, KM; McShane, LM; Jackson, A; Waterton, JC (2017) Imaging biomarker roadmap for cancer studies. NATURE REVIEWS CLINICAL ONCOLOGY 14(3): 169-186

Pfeifle, R; Rothe, T; Ipseiz, N; Scherer, HU; Culemann, S; Harre, U; Ackermann, JA; Seefried, M; Kleyer, A; Uderhardt, S; Haugg, B; Huebert, AJ; Daum, P; Heidkamp, GF; Ge, CR; Bohm, S; Lux, A; Schuh, W; Magorivskal, I; Nandakumar, KS; Lonnblom, E; Becker, C; Dudziak, D; Wuhrer, M; Rombouts, Y; Koeleman, CA; Toes, R; Winkler, TH; Holmdahl, R; Herrmann, M; Bluml, S; Nimmerjahn, F; Schett, G; Kronke, G (2017) Regulation of autoantibody activity by the IL-23-T(H)17 axis determines the onset of autoimmune disease. NATURE IMMUNOLOGY 18(1): 104-113

Pinero, J; Bravo, A; Queralt-Rosinach, N; Gutierrez-Sacristan, A; Deu-Pons, J; Centeno, E; Garcia-Garcia, J; Sanz, F; Furlong, LI (2017) DisGeNET: a comprehensive platform integrating information on human disease-associated genes and variants. NUCLEIC ACIDS RESEARCH 45(D1): D833-D839

Proitsi, P; Kim, M; Whiley, L; Simmons, A; Sattlecker, M; Velayudhan, L; Lupton, MK; Soininen, H; Kloszewska, I; Mecocci, P; Tsolaki, M; Vellas, B; Lovestone, S; Powell, JF; Dobson, RJB; Legido-Quigley, C (2017) Association of blood lipids with Alzheimer's disease: A comprehensive lipidomics analysis. ALZHEIMERS & DEMENTIA 13(2): 140-151

Rodriguez-Carrio, J; Hahnlein, JS; Ramwadhdoebe, TH; Semmelink, JF; Choi, IY; van Lienden, KP; Maas, M; Gerlag, DM; Tak, PP; Geijtenbeek, TBH; van Baarsen, LGM (2017) Altered Innate Lymphoid Cell Subsets in Human Lymph Node Biopsy Specimens Obtained During the At-Risk and Earliest Phases of Rheumatoid Arthritis. ARTHRITIS & RHEUMATOLOGY 69(1): 70-76

Schutte, M; Risch, T; Abdavi-Azar, N; Boehnke, K; Schumacher, D; Keil, M; Yildirimman, R; Jandrasits, C; Borodina, T; Amstislavskiy, V; Worth, CL; Schweiger, C; Liebs, S; Lange, M; Warnatz, HJ; Butcher, LM;

Barrett, JE; Sultan, M; Wierling, C; Golob-Schwarzl, N; Lax, S; Uranitsch, S; Becker, M; Welte, Y; Regan, JL; Silvestrov, M; Kehler, I; Fusi, A; Kessler, T; Herwig, R; Landegren, U; Wienke, D; Nilsson, M; Velasco, JA; Garin-Chesa, P; Reinhard, C; Beck, S; Schafer, R; Regenbrecht, CRA; Henderson, D; Lange, B; Haybaeck, J; Keilholz, U; Hoffmann, J; Lehrach, H; Yaspo, ML (2017) Molecular dissection of colorectal cancer in pre-clinical models identifies biomarkers predicting sensitivity to EGFR inhibitors. NATURE COMMUNICATIONS 8: 14262

Shephard, E; Milosavljevic, B; Pasco, G; Jones, EJH; Gliga, T; Happe, F; Johnson, MH; Charman, T (2017) Mid-childhood outcomes of infant siblings at familial high-risk of autism spectrum disorder. AUTISM RESEARCH 10(3): 546-557

Siravegna, G; Marsoni, S; Siena, S; Bardelli, A (2017) Integrating liquid biopsies into the management of cancer. NATURE REVIEWS CLINICAL ONCOLOGY 14(9): 531-548

Sirven, N; Rapp, T (2017) The cost of frailty in France. EUROPEAN JOURNAL OF HEALTH ECONOMICS 18(2): 243-253

Sissoko, D; Duraffour, S; Kerber, R; Kolie, JS; Beavogui, AH; Camara, AM; Colin, G; Rieger, T; Oestereich, L; Palyi, B; Wurr, S; Guedj, J; Nguyen, THT; Eggo, RM; Watson, CH; Edmunds, WJ; Bore, JA; Koundouno, FR; Cabeza-Cabrerizo, M; Carter, LL; Kafetzopoulou, LE; Kuisma, E; Michel, J; Patrono, LV; Rickett, NY; Singethan, K; Rudolf, M; Lander, A; Pallasch, E; Bockholt, S; Rodriguez, E; Di Caro, A; Wolfel, R; Gabriel, M; Gurry, C; Formenty, P; Keita, S; Malvy, D; Carroll, MW; Anglaret, X; Gunther, S (2017) Persistence and clearance of Ebola virus RNA from seminal fluid of Ebola virus disease survivors: a longitudinal analysis and modelling study. LANCET GLOBAL HEALTH 5(1): E80-E88

ten Kate, M; Barkhof, F; Boccardi, M; Visser, PJ; Jack, CR; Lovblad, KO; Frisoni, GB; Scheltens, P (2017) Clinical validity of medial temporal atrophy as a biomarker for Alzheimer's disease in the context of a structured 5-phase development framework. NEUROBIOLOGY OF AGING 52: 167-182

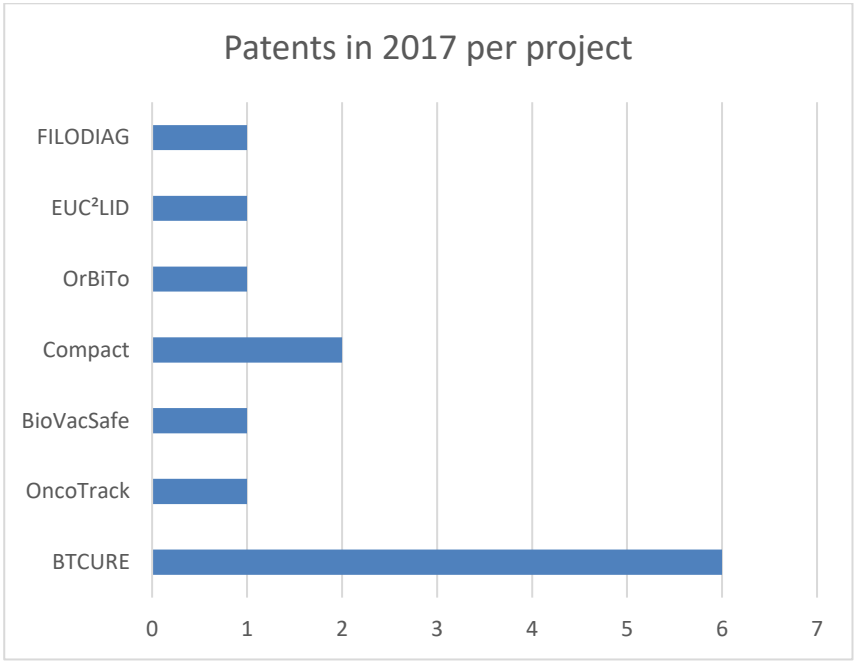
Trouw, LA; Rispens, T; Toes, REM (2017) Beyond citrullination: other post-translational protein modifications in rheumatoid arthritis. NATURE REVIEWS RHEUMATOLOGY 13(6): 331-339

Wilkes, M; Madej, MG; Kreuter, L; Rhinow, D; Heinz, V; De Sanctis, S; Ruppel, S; Richter, RM; Joos, F; Grieben, M; Pike, ACW; Huiskonen, JT; Carpenter, EP; Kuhlbrandt, W; Witzgall, R; Ziegler, C (2017) Molecular insights into lipid-assisted Ca2+ regulation of the TRP channel Polycystin-2. NATURE STRUCTURAL & MOLECULAR BIOLOGY 24(2): 123-+

Zuidgeest, MGP; Goetz, I; Groenwold, RHH; Irving, E; van Thiel, GJMW; Grobbee, DE (2017) Series: Pragmatic trials and real world evidence: Paper 1. Introduction. JOURNAL OF CLINICAL EPIDEMIOLOGY 88: 7-13

Annex 5 – Patents from projects

In 2017, IMI projects have submitted 13 patent applications. The total number of patent applications filed as a consequence of IMI support therefore rises from 33 at the end of 2016 to 46 by 31 December 2017. The 13 new patent applications were filed by 7 IMI projects, of which 6 IMI1 projects and 1 IMI2 project, as shown in the graph below.



Annex 6 – Scoreboard of H2020 common KPIs

Table I[60] - 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 2017
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

[60] 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 2017
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)]	43.48 %
	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 patent application was filed in 2017 from 1 IMI2 project.
	16	Number of prototypes testing activities and clinical trials[61]	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]	At least 4
	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]	16 (19.28 %)

[61] 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 2017
	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]	In 2017, one commercialisation was launched supported by the results of one IMI2 project
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: 36 (100 % on time) No. information letters for Full Proposals: 7(100 % on time) Average TTI: 81 days Statistics refer to letters sent out in 2017 (FPs for IMI2 – Calls 8 & 9; SPs for IMI2 – Call 10). Letters for IMI2 – Call 10 FPs and IMI2 – Call 11 will be sent out in 2018.
	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	Number and % of grants signed within target Average TTG in calendar days Maximum TTG in calendar days	TTG < 243 days (as % of GAs signed)	7 out of 15 (47 %) were signed within the target Average TTG: 270 days. Maximum TTG: 453 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 2017
			transparent grant preparation process			
	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	1 out of 15 (7 %) was signed within the target. Average TTS: 181 days Maximum TTS: 369 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: 11 days (for 16 pre-financing) Interim payment: 64 days (for 40 interim payments) Final payment: 52 days (for 14 final payments)
HR	**NA**	Vacancy rate (%)		% of post filled in, composition of the JU staff		Vacancy rate: 12.5 % (7.69 % TA, 13.33 % CA, 100 % SNE)
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	97.07 % CA to total budget 71.96 % PA to total budget

	Correspondence to general Annex 1	Key Performance Indicator	Definition/Responding to question	Type of data required	Target at the end of H2020	Results in 2017
	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 management principle	Number of delayed payments % of delayed payments (of the total)		1 167 payments of which 130 were late (11.1 %)

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[62] - 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 2017
2	Widening the participation	2.1 Total number of participations by EU-28 Member State	Nationality of H2020 applicants & beneficiaries (number of)	YES	Applications: 2 593 Participations from 1 184 unique Legal Entities (applicants) Beneficiaries: 737 Participations from 383 unique Legal Entities (participants) (IMI2 cumulative figures up until 31/12/2017)
		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	EUR 379 617 255.72

[62] 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.

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2017
NA		Total number of participations by Associated Countries	Nationality of H2020 applicants & beneficiaries (number of)	YES	Applications: 182 participations from 95 unique Legal Entities (participants) Beneficiaries: 55 Israel : 1 Norway: 4 Switzerland: 50
NA		Total amount of EU financial contribution by Associated Country (EUR millions)	Nationality of H2020 beneficiaries and corresponding EU financial contribution	YES	Beneficiaries: EUR 1 133 593.39 Israel: EUR 0 Norway: EUR 548 241.00 Switzerland: EUR 585 352.39 (IMI2 cumulative figures up until 31/12/2017)
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		Participants: 56 (15.6 %) of 358 beneficiaries receiving EU funding are SMEs EU contribution: EUR 33 824 247.75 (8.4 %) of EUR 402 183 483.11 goes to beneficiaries flagged as SMEs (IMI2 cumulative figures up until 31/12/2017)
6	Gender	6.1 Percentage of women participants in H2020 projects	Gender of participants in H2020 projects	YES	Not available
		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

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2017
		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: 24 out of 40 appointed nominees (60 %) SC: 5 out of 11 full members (45 %) Expert evaluators: 80 out of 175 experts (46 %) Interim review experts: 39 %
7	International cooperation	7.1 Share of third-country participants in Horizon 2020	Nationality of H2020 beneficiaries	YES	Third Countries: Participations: 35 out of 827 (4.2 %) United States: 25 Gabon: 3 Brazil: 1 Tanzania: 1 Sierra Leone: 1 Burkina Faso: 1 Benin: 1 Australia: 1 Unique Legal Entities (participants): 24 (5.5 %) out of 433 (IMI2 cumulative figures up until 31/12/2017)

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2017
		7.2 Percentage of EU financial contribution attributed to third country participants	Nationality of H2020 beneficiaries and corresponding EU financial contribution	YES	EU contribution to Third Countries: EUR 21 432 634.00 (5.3 %) of EUR 402 183 483.11 Sierra Leone: EUR 9 861 078.00 Burkina Faso: EUR 5 075 000.00 United States: EUR 3 785 619.00 Gabon: EUR 820 125.00 Benin: EUR 566 312.00 Tanzania: EUR 502 000.00 Brazil: EUR 306 250.00 Australia: EUR 300 000.00 Senegal: EUR 216 250.00 (IMI2 cumulative figures up until 31/12/2017)
9	Bridging from discovery to market [63]	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

[63] This indicator (9.2) is initially intended to monitor the Digital Agenda (its applicability could be only partial)

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2017
NA		Scale of impact of projects (High Technology Readiness Level)	Number of projects addressing TRL[64] 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		Participations: 380 out of 827 (45.9 %) Unique Legal Entities (participants): 190 (43.9 %) out of 433 (IMI2 cumulative figures up until 31/12/2017)
		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		EUR 74 997 077.41 (18.6 %) of EUR 402 183 483.11 (IMI2 cumulative figures up until 31/12/2017)
12	Funding for PPPs	12.1 EU financial contribution for PPP (Art 187)	EU contribution to PPP (Art 187)		EUR 391 million (total cash contribution EC in 2017)
		12.2 PPPs leverage: total amount of funds leveraged through Art. 187 initiatives, including additional activities, divided by the EU contribution	Total funding made by private actors involved in PPPs - 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)		EUR 381 million (EFPIA + Associated Partners)

[64] 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 2017
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		29 different countries[65] (120 experts)
		14.3 Proposal evaluators by organisations' type of activity	Type of activity of evaluators' organisations	YES	62 - academia and research institutes 12 – consultants 18 – private sector 5 – public sector 2 – international organisations 21 – other type of organisations

[65] Argentina (1), Australia (1), Austria (1), Belgium (7), Bulgaria (2), Canada (2), Croatia (4), Denmark (4), Finland (1), France (6), Germany (11), Greece (2), Hungary (2), Ireland (3), Israel (3), Italy (13), Latvia (1), Netherlands (7), Poland (2), Portugal (4), Romania (1), Slovakia (2), Slovenia (1), Spain (14), Sweden (6), Switzerland (1), United republic of Tanzania (1), United Kingdom (10), United States (7)

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2017
NA	Participation of RTOs and Universities	Participation of RTO[66]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	REC (Research Organisations): Participations: 164 out of 827 (19.8 %) Unique Legal Entities (participants): 117 (27.08 %) out of 433 EU contribution: EUR 101 074 308.00 (25.1 %) of EUR 402 183 483.11 HES (Higher or Secondary Education Establishments): Participations: 272 out of 827 (27.4 %) Unique Legal Entities (participants): 126 (29.1 %) out of 433 EU contribution: EUR 223 772 654.40 (55.6 %) of EUR 402 183 483.11 (IMI2 cumulative figures up until 31/12/2017)
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)[67]		0

[66] RTO: Research and Technology Organisation

[67] Data relates to pre-granting ethics review. This time span runs in parallel to granting process.

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2017
NA	Audit	Error rates	% of common representative error; % residual error		Representative error rate: 1.42 % Residual error rate: 0.81 %
NA		Implementation	Number of cases implemented; in total EUR million; ´of cases implemented/total cases		Cases implemented: 2 (100 %) Amount: EUR 354 914

Annex 8 – Scoreboard of KPIs specific to IMI

Table III[68] - KPIs specific to each single JU

#	Key Performance Indicator	Objective	2017 target	Results in 2017
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	8
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	42 % of projects completed at least 90 % of pre-set deliverables Average deliverable completion rate: 83 %
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	3 808 publications for EUR 899.2 million of funding 42 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 = 6.28 EU = 3.89 IMI is 61.4 % higher

[68] Table III presents the KPI specific for each JU, as transmitted by the Programme Offices or the operational services.

#	Key Performance Indicator	Objective	2017 target	Results in 2017
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 = 1.10 IMI is 84.5 % 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 Average of MRC (2.02), Wellcome Trust (2.12), CSIRO (1.60), C-Path (1.34) & FNIH (2.12) = 1.84 IMI is 10.3 % 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 = 24.99 % Average of MRC (25.45), Wellcome Trust (25.48), CSIRO (19.69), C-Path (11.61) & FNIH (28.70) = 22.19 IMI is 12.6 % 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	9
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 projects can only inform regulatory guidelines 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	15

#	Key Performance Indicator	Objective	2017 target	Results in 2017
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	13 patents in 2017 1.3 per EUR 10 million of costs accepted and reimbursed by IMI
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	17 % 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	2 574 (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 %	SME beneficiaries receiving EU funding IMI2: 56 out of 358 (15.6 %) IMI1: 154 out of 620 (24.8 %) (IMI1 and IMI2 cumulative figures up until 31/12/2017)
16	**IMI2 KPI 15:** Percentage of overall budget for projects that has been allocated to SMEs	Measure business development and sustainability	20 %	IMI2 EU contribution: EUR 33 824 247.75 (8.4 %) of EUR 402 183 483.11 IMI1 EU contribution: EUR 127 868 264.00 (13.2 %) of EUR 965 730 983.00 (IMI2 cumulative figures up until 31/12/2017)
17	**IMI2 KPI 16:** Percentage of projects involving patient organisations as consortium partners, members of advisory boards, ethical advisory boards	Measure patient participation	Annual target: 100 %	47.4 % 20.5 % of IMI projects active in 2017 have patients organisations represented in

#	Key Performance Indicator	Objective	2017 target	Results in 2017
	or on consultancy basis for topics of relevance			the consortium as full partners. 26.9 % of IMI projects have patient organisations represented in advisory boards or have consulted with patient groups on specific topics.
18	**IMI2 KPI 17**: Impact for patients	Measure patient participation	N/A	KPI under revision
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	12 217
21	**IMI2 KPI 20:** Performance of communication activities	Measure information, communication and dissemination	N/A	KPI under revision

Annex 9 – 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 annual accounts 2017.

Balance sheet

EUR '000

	Note	31.12.2017	31.12.2016
NON-CURRENT ASSETS			
Property, plant and equipment	*2.1*	*100*	*123*
Pre-financing	*2.2*	*173 471*	*182 426*
		173 570	**182 549**
CURRENT ASSETS			
Pre-financing	*2.2*	*59 451*	*62 204*
Exchange receivables and non-exchange recoverables	*2.3*	*76 317*	*95 389*
		135 768	**157 592**
TOTAL ASSETS		**309 339**	**340 141**
CURRENT LIABILITIES			
Payables and other liabilities	*2.4*	*(174 167)*	*(203 695)*
Accrued charges	*2.5*	*(134 836)*	*(103 887)*
		(309 003)	**(307 582)**
TOTAL LIABILITIES		**(309 003)**	**(307 582)**
NET ASSETS			
Contribution from Members	*2.6*	*1 626 324*	*1 323 107*
Accumulated deficit		*(1 290 548)*	*(1 060 729)*
Economic result of the year		*(335 440)*	*(229 819)*
NET ASSETS		**336**	**32 559**

Statement of financial performance

EUR '000

	Note	2017	2016
REVENUE			
Revenue from non-exchange transactions			
Recovery of expenses		*55*	*34*
Other		*–*	*0*
		55	**34**
Revenue from exchange transactions			
Financial revenue		*(6)*	*10*
Other exchange revenue		*33*	*25*
		27	**35**
Total revenue		**82**	**70**
EXPENSES			
Operating costs	*3.1*	*(327 103)*	*(221 209)*
Staff costs	*3.2*	*(4 480)*	*(4 168)*
Finance costs	*3.3*	*(8)*	*(91)*
Other expenses	*3.4*	*(3 931)*	*(4 421)*
Total expenses		**(335 522)**	**(229 889)**
ECONOMIC RESULT OF THE YEAR		**(335 440)**	**(229 819)**

Cash flow statement[69]

EUR '000

	2017	2016
Economic result of the year	*(335 440)*	*(229 819)*
Operating activities		
Depreciation and amortization	*40*	*86*
(Increase)/decrease in pre-financing	*11 708*	*7 058*
(Increase)/decrease in exchange receivables and non-exchange recoverables	*19 071*	*(26 298)*
Increase/(decrease) in payables	*(29 529)*	*(56 347)*
Increase/(decrease) in accrued charges	*30 950*	*(32 063)*
Increase/(decrease) in cash contributions	*126 599*	*209 265*
Increase/(decrease) in in-kind contributions	*176 618*	*128 166*
Investing activities		
(Increase)/decrease in intangible assets and property, plant and equipment	*(17)*	*(48)*
NET CASHFLOW	**-**	**-**
Net increase/(decrease) in cash and cash equivalents	*–*	*–*
Cash and cash equivalents at the beginning of the year	*–*	*–*
Cash and cash equivalents at year-end	*–*	*–*

[69] 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 2017. 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 31.12.2015	**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**
Allocation 2016 economic result	*–*	*(229 819)*	*229 819*	*–*
Cash contribution	*126 599*	*–*	*–*	*126 599*
Contribution in-kind	*176 618*	*–*	*–*	*176 618*
Economic result of the year	*–*	*–*	*(335 440)*	*(335 440)*
BALANCE AS AT 31.12.2017	**1 626 324**	**(1 290 548)**	**(335 440)**	**336**

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 that remain undetected and uncorrected does not exceed 2 % by the end of the research programmes (FP7 and H2020). 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.

Accordingly, the following considerations were taken into account:

- IMI programmes are multi-annual in nature thus the control strategy is designed for the whole programme duration. The holistic measure of control effectiveness must reflect the entirety of programme implementation at the time of reporting. The error rates are therefore calculated cumulatively for the entire programme period to date. This enables to continuously monitor the final control objective that is set to be achieved at the end of the programme. As the programme advances, the reliability of the control measure continues to improve.
- Furthermore, 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 on 14 December 2010 and the H2020 Ex-Post Audit Strategy (2016-2025), 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 in all samples in the programme up to the date of the drawing of the last sample from which audit results are available as of 31 December year N (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 JU 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 cumulative and provided as of a certain date.

Annex 11 – Media highlights

- eCancer (EU), 14 December 2017
  EAPM 2017 / The Innovative Medicines Initiative
- European Files (EU), 6 December 2017
  Several articles in the issue 'Public Private Partnerships Strengthening Innovation and Research in Europe'
- Horizon Magazine (EU), 23 November 2017
  We need a new way to pay for antibiotics – Dr David Payne
- Nordic Life Science (Sweden), 17 November 2017
  Antibiotic Advances from New Drugs 4 Bad Bugs
- European Biotechnology (EU), 16 November 2017
  Antibiotic Resistance: EU SME alliance calls for specific support to thrive AMR R&D
- Der Standard (Austria), 8 November 2017
  St.-Anna-Kinderkrebsforschung beteiligt sich an EU-Projekt (St Anna Children's Cancer Research takes part in EU project)
- Parliament Magazine (EU), 3 October 2017
  Research breakthroughs happen more easily when information is shared
- EUobserver (EU), 9 August 2017
  Holiday season means risk of tropical diseases in Europe
- Diario Medico (Spain), 28 July 2017
  'Big data' para mejorar el abordaje cardiovascular
- Horizon Magazine (EU), 27 July 2017
  Depression, schizophrenia may become redundant terms
- Technologist (EU), 10 July 2017
  How engineers and doctors are reinventing healthcare
- PharmaPhorum Deep Dive (UK), July 2017
  Healthcare in 2030: what role for pharma?
- Politico (EU), 29 June 2017
  Q and A with IMI Executive Director Pierre Meulien
- Daily Mail (UK), 15 June 2017
  UK researchers helping to create new whooping cough vaccine
- Daily Express (UK), 15 June 2017
  Whooping cough vaccine being developed by British researchers
- Corriere del Mezzogiorno (Italy), 5 June 2017
  Rivoluzione nel corso di formazione Così i pazienti diventano “esperti” (Revolution in training so patients become "experts")
- The Lancet Infectious Diseases (UK), June 2017
  Breaking up is hard to do: Brexit and European science
- Health Capital (Germany), 30 May 2017
  Big Data. Hope for patients
- Sunday Post (UK), 29 May 2017
  ‘Dementia research will suffer when we leave EU’: Top Alzheimer’s professor issues stark warning
- The Scientist (US), 24 May 2017
  Brexit will cost U.K. research funding, report indicates
- Health IT Central (Germany), 12 May 2017
  Pharmaceutical research goes big data
- Granada Hoy (Spain), 25 April 2017
  Genyo se afianza en la medicina personalizada y de precision (Genyo anchors its position in personalised and precision medicine)
- Regio 024 (Netherlands), 13 April 2017
  12 miljoen subsidie van IMI voor project TRISTAN (12 million subsidy from IMI for TRISTAN project)
- Cadureso (France), 11 April 2017
  Innovative Medicines Initiative – IMI
- EurActiv.com (EU), 7 April 2017
  IMI chief: ‘We need to learn how to share data in a safe and ethical manner’
- Photonics.com (US), 7 April 2017
  Multiple factors shape market for innovations
- SpringerMedizin (Austria), 7 April 2017
  Die Ethik der Daten (The ethics of data)
- Aarhus University News (Denmark), 6 April 2017
  The IMI is a sure path to an invaluable network

- PharmaBiz.com (India), 3 April 2017
  Text mining with automation becomes boon for ADR reporting
- Der Standard (Austria), 31 March 2017
  Konsortium will Standards bei Flüssigbiopsien verbessern (Consortium wants to improve standards for liquid biopsies)
- Malta Today (Malta), 21 March 2017
  Innovative Medicines Initiative: an opportunity for local researchers
- Manufacturing Chemist (UK), 17 March 2017
  Environment award for research on chemical contaminants
- Magyar Hírlap (Hungary), 6 March 2017
  Szócska Miklós: Magyarország egészségügyi adatnagyhatalom (Hungary health data superpower)
- PharmaVOICE (US), 1 March 2017
  Ebola research update
- Medical News Today (UK), 14 February 2017
  New biomarkers for bowel cancer treatment
- ZorgKrant (Netherlands), 7 February 2017
  Start internationaal onderzoek naar Personalized Medicine bij diabetische nierschade (Start of international research for personalised medicine for diabetic kidney damage)
- PharmaTimes (UK), 26 January 2017
  Liverpool Uni to run £14m drug safety study
- Ärzteblatt (Germany), 26 January 2017
  Leukämie: Internationale Datenbank für verbesserte Prognose und Therapie (Leukaemia: International database for improved prognosis and therapy)
- Pink Sheet (US), 24 January 2017
  EU mobile app for reporting ADRs to be tested in Burkina Faso and Zambia
- Mobi Health News (US), 23 January 2017
  Researchers developing smartphone-based microscope for low-cost DNA sequencing
- PharmaFile (UK), 23 January 2017
  Thinking big data
- Narod (Croatia), 19 January 2017
  Zagreb domaćin međunarodnog poslovnog umrežavanja prijavitelja EU projekata (Zagreb is hosting an international networking event for EU project applicants)
- Politico (EU), 12 January 2017
  Transforming health care through disruptive innovation: Will your data cure you?
- Der Standard (Austria), 10 January 2017
  Sensible Patientendaten: MedUni Wien entwickelt Richtlinien (Sensitive patient data: Medical University of Vienna develops guidelines)
- ITV (UK), 10 January 2017
  Newcastle University involved in £34.7m blood disorder project

Annex 12 – List of acronyms

Acronym	Meaning
AAR	Annual Activity Report
ABAC	Accrual Based Accounting System
AD	Alzheimer's disease
ADA	Anti-drug antibodies
ADCC	antibody-dependent cellular cytotoxicity
ADDIS	Aggregate Data Drug Information System
ADNI	Alzheimer's Disease Neuroimaging Initiative
ADR	Adverse drug reaction
AER	Average error rate
AIDS	Acquired immune deficiency syndrome
AMR	Antimicrobial resistance
API	Active pharmaceutical ingredient
ARLG	Antibacterial Resistance Leadership Group
ASD	Autism spectrum disorder
ATM-AVI	Aztreonam-avibactam
AWP	Annual Work Plan
BARDA	Biomedical Advanced Research and Development Authority
BCAA	Branched-chain amino acids
BD4BO	Big Data for Better Outcomes
BEL	Biological expression language
BfArM	Federal Institute for Drugs and Medical Devices (Germany)
BIT	Booking IT material
BMGF	Bill and Melinda Gates Foundation
BMI	Body mass index
BPs	Biopharmaceuticals
CA	Commitment appropriations
CA	Contract agent
CAS	Common Audit Service
CDR	Career development report
CE-IVD	European Conformity – *in-vitro* device
CEO	Chief Executive Officer
CEPI	Coalition for Epidemic Preparedness Innovations
CFS	Certificate on Financial Statements
CMI	Cell-mediated immunity
CMS	Content management system
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
CPO	Cellular Phenomics & Oncology
CRO	Contract research organisation
CRS	Common representative sample
CSA	Coordination and support action
CSC	Common Support Centre
CSF	Cerebro-spinal fluid
CSIRO	Commonwealth Scientific and Industrial Research Organisation (Australia)
CT	Computed tomography
CTC	circulating tumour cell
ctDNA	circulating tumour DNA
CV	Curriculum vitae
DAS	Declaration of Assurance
DAWBA	Development and Well-Being Assessment
DDS	Drug delivery system
DG BUDGET	European Commission Directorate-General for Budget
DG HR	European Commission Directorate-General for Human Resources and Security
DG RTD	European Commission Directorate-General for Research and Innovation
DGPML	Direction Générale de la Pharmacie, du médicament et des laboratoires (Burkina Faso)
DIA	Drug Information Association
DIVI	Drug-induced vascular injury
DKM	Data and knowledge management
DoA	Description of Action
DOI	Digital object identifiers
DORA	Document Registry Application
DoW	Description of Work
DPO	Data protection officer
DW	Data warehouse
EAPM	European Alliance for Personalised Medicine
EBO RT PCR	Ebola reverse transcriptase—polymerase chain reaction
EC	European Commission
ECA	European Court of Auditors
ECM	Endocrine cell mass
ECSEL JU	Electronic Components and Systems for European Leadership Joint Undertaking
EDPS	European Data Protection Supervisor

Acronym	Meaning
EFPIA	European Federation of Pharmaceutical Industries and Associations
EHDN	European Health Data Network
EHR	Electronic health record
ELISA	Enzyme-linked immunosorbent assay
EMA	European Medicines Agency
eMA	Electronic Missions Application
EP	European Parliament
EPF	European Patient Forum
EPO	Experimental Pharmacology & Oncology
ERM	Enterprise risk management
ERRIN	European Regions Research and Innovation Network
ERS	European Respiratory Society
EU	European Union
EULAR	European League Against Rheumatism
FAIR	Fraud and Irregularity in Research
FC	Financial contribution
FDA	US Food and Drug Administration
FG	Function group
FLC	Free light chains
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
GB	Governing Board
GBP	British pounds
GCP	Good clinical practice
GCPR	G-protein-coupled receptor
GWAS	Genome-wide association study
H2020	Horizon 2020
HA	hemagglutinin
HAI	haemagglutination inhibition
HES	Higher or secondary education establishments
HIV	Human immunodeficiency virus
HTA	Health technology assessment

Acronym	Meaning
HTS	High throughput screening
IaaS	Infrastructure as a Service
IAS	Internal Audit Service of the European Commission
ICF	Internal Control Framework
ICS	Internal Control Standards
ICT	Information and communication technology
ICU	Intensive care unit
IKC	In-kind contribution
IMI1 JU	Innovative Medicines Initiative 1 Joint Undertaking
IMI2 JU	Innovative Medicines Initiative 2 Joint Undertaking
IMPD	Investigational Medicinal Product Dossier
IP	Intellectual property
iPSC	Induced pluripotent stem cell
IR	Insulin resistance
ISA	Information System for Absences
ISARIC	International Severe Acute Respiratory and Emerging Infection Consortium
IT	Information technology
JAMA	Journal of the American Medical Association
JDRF	Juvenile Diabetes Research Funding and Advocacy
JTI	Joint Technology Initiative
JUs	Joint Undertakings
KPI	Key performance indicator
LAMP	Loop mediated isothermal amplification
LCI	Lung clearance index
LCS	Longitudinal Cohort Study
LEAP	Longitudinal European Autism Project
LFD-RPA	Recombinase polymerase amplification – lateral flow dipstick
LT	Long-term contract
MAPPs	Medicines adaptive pathways to patients
MBC	Metastatic breast cancer
MCI	Mild cognitive impairment
MCI	Multi-component intervention
MD	Major depression
MEP	Member of the European Parliament
MERS-CoV	Middle East respiratory syndrome coronavirus
MOOC	Massive open online course
MoU	Memorandum of Understanding
MRC	Medical Research Council

Acronym	Meaning
MRI	Magnetic resonance imaging
MS	Multiple sclerosis
NA	Neuraminidase
NAFLD	Non-alcoholic fatty liver disease
NASH	Non-alcoholic steatohepatitis
NCP	National Contact Point
ND4BB	New Drugs for Bad Bugs
NGS	Next-generation sequencing
NSCLC	non-small cell lung cancer
OICR	Ontario Institute for Cancer Research
OLAF	European Anti-Fraud Office
OPR&D	Organic Process Research & Development
ORR	Operating Risk Register
PA	Payment appropriations
PA	Physical activity
PAC	Patient Advisory Committee
PC	Parent cohort
PD	Parkinson’s disease
PHE	Public Health England
PK/PD	Pharmacokinetic / pharmacodynamic
PLoS	Public Library of Science
PMC	Portfolio Management Committee
PNAS	Proceedings of the National Academy of Sciences of the USA
PPI	Patient and public involvement
PPMI	Parkinson's Progression Markers Initiative
PPP	Public-private partnership
PRO	Patient reported outcome
pSS	Primary Sjögren’s Syndrome
PSWC	Pharmaceutical Science World Congress
R&D	Research and development
R&I	Research and innovation
RA	Rheumatoid arthritis
RACER	Relevant, accepted, credible, easy, robust
RAE	Risk assessment exercise
REC	Research organisations
RepER	Representative error rate
ResER	Residual error rate
RIA	Research and Innovation Action

Acronym	Meaning
RP	Reporting period
RSV	respiratory syncytial virus
RTO	Research and Technology Organisation
RVFV	Rift Valley fever
RWD	Real-world data
RWE	Real-world evidence
SBP / DBP	Systolic / diastolic blood pressure
SBV	Schmallenberg virus
SC	Scientific Committee
SC	Short-term contract
SEAB	Scientific and Ethical Advisory Board
SEP	H2020 IT tool for submission and evaluation of proposals
SFARI	Simons Foundation Autism Research Initiative
SGG	Strategic Governing Group
SIB	Swiss Institute of Bioinformatics
SLE	Systemic lupus erythematosus
SME	Small and medium-sized enterprise
SNE	Seconded national expert
SO	Scientific officer
SO	Scientific Officer
SOFIA	Submission of Information Application
SOP	Standard operating procedure
SP	Short proposal
SPR	surface plasmon resonance
SRA	Strategic Research Agenda
SRG	States Representatives Group
SRR	Strategic Risk Register
SSI	Surgical site infection
ST	Short-term contract
STOA	Science and Technology Options Assessment
SyGMA	H2020 IT tool for grant management
SZ	Schizophrenia
T2D	Type 2 diabetes
TA	Temporary agent
TB	Tuberculosis
TNF	Tumour necrosis factor
TTG	Time to Grant
TTI	Time to inform

Acronym	Meaning
TTP	Time to Pay
TTS	Time to sign
UK	United Kingdom
US	United States
USD	United States dollars
VAP	Ventilator-associated pneumonia
VN	Virus neutralisation
VSV-ZEBOV	Vesicular stomatitis virus-vectored Zaire Ebola vaccine
WHO	World Health Organisation
WP	Work package
ZAMRA	Zambia Medicines Regulatory Authority

Annex 13 – Table of IMI projects

(As of 31 December 2017)

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/about/about-combacte-care-detail/	antimicrobial resistance
COMBACTE-NET	Combatting bacterial resistance in Europe	www.combacte.com/about/about-combacte-net-detail/	antimicrobial resistance
COMBACTE-MAGNET	Combatting bacterial resistance in Europe - molecules against Gram negative infections	www.combacte.com/about/about-combacte-magnet-detail/	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

Project acronym	Full project title	Website	Subject area
DIRECT	Diabetes research on patient stratification	www.direct-diabetes.org	diabetes
DRIVE-AB	Driving re-investment in R&D and responsible antibiotic use	http://drive-ab.eu/	antimicrobial resistance
EBiSC	European bank for induced pluripotent stem cells	http://www.ebisc.org/	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.patientsacademy.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

Project acronym	Full project title	Website	Subject area
iABC	Inhaled antibiotics in bronchiectasis and cystic fibrosis	www.qub.ac.uk/sites/iABC	antimicrobial resistance
IMIDIA	Improving beta-cell function and identification of diagnostic biomarkers for treatment monitoring in diabetes	www.imidia.org	diabetes
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	www.mip-dili.eu	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	chronic obstructive pulmonary disease (COPD)

Project acronym	Full project title	Website	Subject area
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 sciences for medicines	www.safescimet.eu	education and training
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	asthma
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
BigData@Heart	Big data @ heart	www.bigdata-heart.eu	big data, cardiovascular disease
COMBACTE-CDI	Combatting bacterial resistance in Europe - clostridium difficile infections	www.combacte.com/about/combacte-cdi-understanding-of-the-epidemiology-and-clinical-impact-of-clostridium-difficile-infection/	antimicrobial resistance
DO>IT	Big data for better outcomes, policy innovation and healthcare system transformation	bd4bo.eu	big data
DRIVE	Development of robust and innovative vaccine effectiveness	www.drive-eu.org	vaccines
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

Project acronym	Full project title	Website	Subject area
EBOVAC2	Development of a prophylactic Ebola vaccine using an heterologous prime-boost regimen: Phase II	www.ebovac2.com	Ebola and related diseases
EQIPD	European quality in preclinical data	eqipd.org	data quality, neurodegenerative diseases
eTRANSAFE	Enhancing translational safety assessment through integrative knowledge management	etransafe.eu	safety
FILODIAG	Ultra-fast molecular filovirus diagnostics	www.filodiag.eu	Ebola and related diseases
HARMONY	Healthcare alliance for resourceful medicines offensive against neoplasms in hematology	www.harmony-alliance.eu	big data, cancer
IMPRiND	Inhibiting misfolded protein propagation in neurodegenerative diseases	www.imprind.org	neurodegenerative disease
INNODIA	Translational approaches to disease modifying therapy of type I diabetes: an innovative approach towards understanding and arresting type I diabetes	innodia.eu	diabetes
ITCC-P4	ITCC pediatric preclinical POC platform	www.itccp4.eu	paediatrics, cancer
LITMUS	Liver investigation: testing marker utility in steatohepatitis	www.litmus-project.eu	liver disease
MACUSTAR	Intermediate AMD: Development of novel clinical endpoints for clinical trials in patients with a regulatory and patient access intention	www.macustar.eu	eye disease
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
NGN-PET	Modelling neuron-glia networks into a drug discovery platform for pain efficacious treatments	www.phago.eu	pain
PERISCOPE	Pertussis correlates of protection Europe	www.periscope-project.eu	vaccines
PEVIA	Pan Ebola vaccine innovative approach	no website	Ebola and related diseases

Project acronym	Full project title	Website	Subject area
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	resc-eu.org	respiratory 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	roadmap-alzheimer.org	big data, Alzheimer's disease
RTCure	Rheuma tolerance for cure	www.rtcure.com	rheumatoid arthritis
TransQST	Translational quantitative systems toxicology to improve the understanding of the safety of medicines	transqst.org	safety
TRISTAN	Imaging biomarkers (IBs) for safer drugs: validation of translational imaging methods in drug safety assessment	www.imi-tristan.eu	safety
VAC2VAC	Vaccine lot to vaccine lot comparison by consistency testing	www.vac2vac.eu	vaccines
VSV-EBOPLUS	Systems analysis of adult and pediatric responses to the VSV-ZEBOV Ebola vaccine	no website	Ebola and related diseases
VSV-EBOVAC	Vaccine safety and immunogenicity signatures of human responses to VSV-ZEBOV	www.vsv-ebovac.eu	Ebola and related diseases

Annex 14 – Assessment of the consolidated Annual Activity Report 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 2017 (Authorising Officer's report) was presented to the IMI2 JU Governing Board at the end of February 2018 and it is planned to have it approved by the Governing Board in June 2018.

The Governing Board is of the opinion that the IMI2 JU AAR 2017 covers well the main activities and achievements of the IMI2 JU in 2017 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 2017 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 2017 together with the draft Budget 2017 was approved by the Governing Board on 23 December 2016 (Decision IMI2-GB-DEC-2016-32), first amended by the Governing Board on 11 July 2017 (Decision IMI2-GB-DEC-2017-13), and last amended by the Governing Board on 28 November 2017 (Decision IMI2-GB-DEC-2017-25).
- In 2017, the JU implemented the final stages of the IMI2 Calls for proposals 7, 9 and 10, initiated under the Horizon 2020 Framework Programme. The JU also implemented the evaluation steps for the next two cut-off dates of call 8 (16 March 2017 and 14 September 2017).
- In 2017, the JU launched 3 new Calls under Horizon 2020, IMI2 Calls 11, 12 and 13. Those Calls represent the commitment of: €185,498,000 of EU contribution; €162,349,000 of contribution from EFPIA companies; and €6,642,000 of contribution from Associated Partners to Call12 (topics 1 and 7) and Call 13 (topics 3, 4 and 5).
- In 2017, the JU signed 15 new grant agreements from IMI2 Calls 7, 8 and 9 initiated under Horizon 2020.
- As at 31 December 2017, the IMI portfolio of projects represented a total of 59 projects from the first phase of IMI (initiated under Framework Programme 7) of which 27 still running, as well as 40 Grant Agreements signed from IMI2 Calls 1 to 9 (initiated under Horizon 2020) of which 37 still running.
- 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.
- In 2017, IMI also continued organising meetings with coordinators and key partners of projects that have come to an end. IMI organised so called "close-out meetings" for 11 projects in 2017. This allowed

consortia to highlight the most significant results, share lessons learned and discuss impact and legacy of the projects in the longer term.

- 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: (a) New tools and resources for drug discovery and preclinical drug development; (b) Biomarkers and tools to predict clinical outcomes (efficacy and safety); (c) Improved protocols for clinical trial design and processes; (d) Biomarkers for the efficacy and safety of vaccine candidates; (e) New taxonomies of diseases and new stratifications of patient sub-populations; (f) Cohorts, registries and clinical networks for clinical studies and trials; (g) Data standards and big data solutions to leverage knowledge; (h) Education and training for new and existing R&D scientists and stakeholders.
- By 31 December 2017, IMI projects have led to 45 patents filled, and produced 3808 publications in peer reviewed journals, around 30% of which were published in year 2017. 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 (1.10). Also, 25% of IMI publications are published in top 10 % of publications. This confirms, like for previous year 2016, the scientific excellence of IMI projects.
- Impacts of projects on the regulatory framework start being demonstrated. Several project results are also implemented inside industries, and important resources generated by projects are now made available beyond consortia partners. Information on many of these can be found in the catalogue of project tools on the revamped IMI website.
- In 2017, a final evaluation of the Innovative Medicines Initiative Joint Undertaking (2008-2016), operating under the Seventh Framework Programme, as well as an interim evaluation of the Innovative Medicines Initiative 2 Joint Undertaking (2014-2016), operating under Horizon 2020, were carried out by the European Commission, with a panel of five independent experts. Two corresponding reports were published in October 2017 (ISBN 978-92-79-69299-4 and ISBN 8-92-79-69295-6). The experts concluded that the reasons to create a public-private partnership to strengthen the European pharmaceutical industry were valid and the goals were justified, and that the Joint Undertaking already delivered good results. The experts recommended that: (a) Stronger effort be made to attract and integrate other industries than pharmaceuticals in the collaborative projects; (b) Better Key Performance Indicators be developed; (c) More efforts be deployed to attract more SMEs; (d) Access to project outcomes be broadened, and sustainability of project results be improved, to increase impact; (e) IP policy be reviewed to make it more flexible to respond to the needs allowing negotiations on exclusive rights. In November 2017, the IMI2 JU Governing Board agreed on an Action Plan addressing these recommendations during the remaining years of IMI2 JU.
- In order to better capture the impacts of IMI2 JU, a new set of ten Key Performance Indicators (KPIs) was agreed by the Governing Board in November 2017 and formally adopted in 2018. These indicators are based on the RACER principles ("Relevant, Accepted, Credible, Easy, Robust"). This revision of the KPIs framework fulfils one of the recommendations from the interim evaluation of the IMI2 JU.
- In 2017, IMI2 JU mobilised the diagnostic companies notably for new antimicrobial resistance activities, mobilised the food and nutrition industries for future microbiome activities, and initiated synergies with the "Electronic Components and Systems for European Leadership" (ECSEL) Joint Undertaking.
- In 2017, the IMI2 JU States Representatives Group met 3 times. The IMI2 JU Scientific Committee held 4 meetings and 3 phone conferences. The 11th member of the Committee was appointed, as well as two new members in replacement of members who resigned. The mandate of the Strategic Governing Group for "Data and Knowledge Management" was revised end of 2017 into "Digital Health and Patient-Centric Evidence Generation". The 6 other Strategic Governing Groups (in the areas of Immunology; Diabetes and metabolic disorders; Neuro-degeneration; Translational safety; Oncology; and Infections control) regularly met and held teleconferences, each 3 to 4 times.
- In 2017, communication activities were focused on raising awareness of IMI2 JU, attracting the best researchers to apply for funding under IMI2 Calls, increasing the engagement of SMEs and patients in IMI activities, and gaining support from key groups of policymakers and opinion leaders.
- In October 2017, IMI launched a new IMI website with both new and updated content and a completely new look. The new website highlights the work and results of IMI’s projects, as well as tailored content for different stakeholder groups, including SMEs. In this respect it therefore responds to some of the recommendations of the independent evaluators of the IMI1 and IMI2 programmes.

- The 2017 edition of the Stakeholder Forum attracted more than 320 participants, plus 60 live web-streaming connections, compared to 300 in 2015 and 375 in 2016. 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 the IMI2 JU priorities for the two coming years, exchange views on new potential IMI2 JU actions in the domain of microbiome, and reflect on the patient engagement strategy of IMI2 JU.
- Upon recommendation from patient organisations, the Governing Board decided to establish mechanisms dedicated to strengthen patient engagement and input in the programme. The IMI2 JU Executive Director was tasked by the Governing Board to fully operationalise this in 2018.
- Overall, projects were managed well, including ex-ante and ex-post financial and scientific verifications. In 2017, as was expected, IMI2 JU conducted 16 interim reviews of projects from the IMI1 Calls 3, 6, 8, 10 and 11 initiated under Framework Programme 7 and from the IMI2 Calls 2, 3 and 4. Overall, the reviewers were satisfied with the progress made by these projects, and no major issue was identified with the reviewed projects.
- The “Time To Pay” is lower than in 2016 and below the maxima foreseen for the Horizon 2020 Programme, with 11 days for pre-financings, 64 days for interim payments, and 52 days for final payments.
- In total 234 ex-post audits of beneficiaries under Framework Programme 7 have been launched since 2011, out of which a total of 212 have been finalised, of which 23 during the year 2017. Twenty ex-post audits of beneficiaries under Horizon 2020 have been launched since 2016, out of which a total of 5 have been finalised in 2017. In 2017, the cumulative residual error rate from the finalised audits was 1.29% for operational expenditure under Framework Programme 7, and was 0.81% for operational expenditure under Horizon 2020 (although less representative considering the still limited number of audits), both below the materiality threshold of 2%.
- In addition, by the end of 2017, the declared in-kind contribution of 16 EFPIA companies participating in IMI projects (operating under Framework Programme 7) had been audited ex-post, altogether covering 93% of the total EFPIA contributions.
- 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 2016.
- In 2017, the Commission Internal Audit Service (IAS) issued a final audit report on "H2020 Grant Process (from the identification of the call topics to the signature of the grant agreement) in the IMI2JU", with four recommendations for improvements (one classified as very important and two 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 2017, as acknowledged by the IAS.
- Migration towards the Horizon 2020 IT tools progressed very significantly in 2017. IMI2 JU Calls are now all managed entirely using Horizon 2020 IT tools. In 2017, grant agreements started being prepared using the Horizon 2020 IT tools, and project reporting is expected to be carried out via the Horizon 2020 IT tools as of beginning 2018.
- In relation to the use of human resources, the IMI2 JU staff assigned to the activities carried out in 2017 has been used for their intended purpose. On 31 December 2017, 49 of the 54 positions as in the Staff Establishment Plan of the IMI2 JU were occupied. Eleven positions were filled during 2017 (8 to support project management and 3 to support other activities of the IMI2 JU Programme Office).

During 2017 the monitoring tools were fully operational and the IMI2 JU AAR 2017 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 2017 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 2017 in a realistic way.

The Governing Board considers that the following aspects require improvements:

- In 2017, the budget execution of commitment appropriations increased to 97.07%, from 94.08% in previous year. However the budget execution of payment appropriations reached only 71.96%, a similar level to the 69.60% in previous year.
- By the end of 2017, SMEs accounted for 17.9% of all EU beneficiaries, receiving 8.4% of the EU funding, as in the first 40 IMI2 JU signed grant agreements. SME participation should be improved, as was recommended in the interim evaluation of the IMI2 JU.
- Further efforts to attract and integrate other industries than pharmaceuticals are needed, as was also recommended in the interim evaluation of the IMI2 JU.
- With an average of 270 days in 2017, the "Time To Grant" is higher than in 2016 (average of 232 days) and higher than the requirement of maximum 243 days for the Horizon 2020 Programme.

Assessment

The declaration of the Executive Director and the IMI2 JU AAR 2017 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 2017.

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 recommended by the auditors are being implemented.

Therefore, the IMI2 JU Governing Board hereby adopts this analysis and assessment of the IMI2 JU AAR 2017 of the authorizing officer. This analysis and assessment will be included into the IMI2 JU AAR 2017.

Brussels, on 26/6/18.

For the Governing Board of the Innovative Medicines Initiative 2 JU

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