Annual Activity Report 2018

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 Governing Board of the Innovative Medicines Initiative 2 Joint Undertaking no. IMI2-GB-DEC-2019-11 approved on 21.06.2019

Document reference: IMI2/OUT/2018-06877

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)** Wolfgang Burtscher, Deputy Director-General of the Directorate-General for Research and Innovation Irene Norstedt, Head of the Innovative and Personalised Medicine Unit and Acting Director of the Health Directorate within the Directorate-General for Research and Innovation Carlo Pettinelli, Director for Consumer, Environmental and Health Technologies within the Directorate-General for Internal Market, Industry, Entrepreneurship and SMEs Andrzej Jan Rys, Director for Health Systems, Medical Products and Innovation within the Directorate-General for Health and Food Safety Maria Pilar Aguar Fernandez, Head of the Innovative Tools, Technologies and Concepts in Health Research Unit within the Directorate-General for Research and Innovation **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 Paul Stoffels, Chief Scientific Officer at Johnson & Johnson, Worldwide Chairman of Janssen Pharmaceutical Companies of Johnson & Johnson Jacky Vonderscher, CEO of Enyo Pharma S.A., member of the European Biopharmaceutical Enterprises Board
Other bodies	States Representatives Group (SRG): 28 European Union (EU) Member States and 16 Associated Countries to the Horizon 2020 Framework Programme Scientific Committee: 13 members including ad hoc members Stakeholder Forum: 386 registrations in 2018 Strategic Governing Groups (SGGs): 7 groups
Staff	Total posts: 56 (39 Temporary Agents, 15 Contract Agents, 2 Seconded National Experts) Posts filled: 48 (37 Temporary Agents, 10 Contract Agents, 1 Seconded National Experts)
2018 budget	Commitment appropriations: EUR 485 595 766 Payment appropriations: EUR 235 963 022
2018 budget implementation	Commitment appropriations: EUR 484 279 716 (99.73 %) Payment appropriations: EUR 203 518 634 (86.25 %)
Grants	20 grants signed in 2018 for a total value of EUR 546 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 2018.
Call implementation in 2018	Calls launched: 3 Proposals submitted under two-stage Calls: ▪ Short proposals submitted: 137 ▪ Eligible proposals submitted: 131 ▪ Full proposals submitted: 20 ▪ Proposals selected for funding: 20 Proposals submitted under single-stage Calls: ▪ Proposals submitted: 10 ▪ Eligible proposals submitted: 10 ▪ Proposals selected for funding: 6 Global project portfolio in 2018: 84 projects running during 2018 (27 under IMI1, of which 11 ended by 31 December 2018; and 57 under IMI2, of which 3 ended by 31 December 2018)
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. For beneficiaries receiving EU funding, the statistics on SME participation are: IMI2: 140 out of 912 participations (15.4 %) IMI1: 197 out of 1 234 participations (16.0 %)

Unless stated otherwise, all data in this factsheet reflects the situation as of 31 December 2018.

Foreword

In 2018, the Innovative Medicines Initiative (IMI[1]) celebrated the 10th anniversary of the very first IMI Call for proposals, and a series of events and other activities throughout the year showcased IMI's successes since its creation. These activities highlighted the breadth and depth of IMI's achievements, and demonstrated the impact of IMI project results in diverse areas.

While this report necessarily focuses on IMI's activities in 2018, it is nevertheless important to look at the bigger picture and bear in mind just how much IMI has achieved in its first decade. We have launched 119 projects with a combined budget in excess of EUR 3 billion coming from the EU (the Seventh Framework Programme and Horizon 2020), the pharmaceutical industry, and, for some IMI2 projects, Associated Partners. This represents a massive commitment to a new, more collaborative, open way of working with multiple stakeholder groups on some of the biggest health challenges facing society today. Indeed IMI has become a magnet for partnerships, attracting over 50 new contributing partners committing over EUR 180 million to the programme thus far.

And the results of these projects show the European added value of working in this way. One of IMI's biggest portfolios is antimicrobial resistance. In 2018, the European Centre for Disease Prevention and Control (ECDC) released figures showing that 33 000 people die every year in Europe from infections that prove resistant to treatment. At IMI, we launched our first projects in this field under the 'New Drugs for Bad Bugs' programme back in 2013 in response to the EU's action plan on AMR. Those investments are now bearing fruit. For example, the COMBACTE projects have set up a network of hundreds of hospitals and laboratories to facilitate the conduct of pan-European clinical trials and studies. The network is already being used extensively for a broad range of studies, including trials of potential new antimicrobials. Elsewhere, through our ENABLE project, we are helping small companies through the highly-challenging early stages of drug development. IMI's AMR story continues with the launch of the AMR Accelerator programme, which is set to make a difference in areas like tuberculosis, where there is a particularly urgent need for new treatments.

Another priority area in infectious diseases is Ebola, where we now have 12 projects working on vaccines, rapid diagnostics, and community engagement. Our first Ebola projects got underway in 2014-2015, during the outbreak in western Africa that left over 11 000 dead, mostly in Guinea, Liberia and Sierra Leone. Although that outbreak eventually subsided, in 2018 the disease re-emerged in two outbreaks in the Democratic Republic of the Congo. This shows that despite the end of the western-African outbreak, IMI's work in this area remains highly relevant.

Brain disorders represent an enormous healthcare and social burden – EUR 800 billion a year in Europe alone. There are currently limited treatment options for brain disorders, and IMI has many projects working to turn this around. For example, in Alzheimer's disease, we have the EPAD project, which is set to revolutionise the way we do clinical trials for Alzheimer's treatments. It will do this by studying multiple treatments at once and, crucially, by studying treatments designed to prevent or at least delay the onset of symptoms in people who are at a high risk of developing the disease. This is important because so far, efforts to treat people who already have clear symptoms have resulted in failure. In addition, IMI projects are delving into the underlying causes of Alzheimer's disease – information that is essential in the hunt for treatments.

On the medicines safety front, IMI projects have delivered a range of tools (both lab-based and computer-based) that are now being used in the medical research community. In the long term, this will help to make drug development far more efficient; previously, issues with toxicity were often only discovered late in the drug development process, once significant amounts of time and money had been invested in a compound. The new IMI tools allow researchers to identify toxicity issues much earlier in development, and this will allow them to either solve the issue if possible, or switch their efforts to an alternative compound.

[1] A note on nomenclature: to avoid confusion, we use the term 'IMI' throughout to refer to the IMI initiative in general. We only use the terms 'IMI1 JU' and 'IMI2 JU' when referring to the specific Joint Undertakings implementing the IMI initiative under (and funded by) FP7 and H2020 respectively.

More broadly, the results of our projects demonstrate how IMI has built a new ecosystem involving all the disciplines needed to enable accelerated and more efficient medicines development. As Research and Innovation Commissioner Carlos Moedas said in 2018 at one of our 10th anniversary events, IMI's product is 'radical collaboration'!

However, technology is moving extremely fast, and we need to integrate many aspects of what is happening in real time in our projects. The worlds of diagnostics and therapeutics are fusing due to personalised approaches to new medicine development. The digital revolution is providing new tools that have to be integrated at every step of the drug development process and can help redefine how we design clinical studies.

IMI is already moving in this direction, as we have attracted many new partners from the private, public and not-for-profit sectors. We are also launching projects that reflect this shift. For example, by the end of 2018, our 'Big Data for Better Outcomes' programme comprised six projects; some address broad questions on big data; others focus on testing solutions in major disease areas including cancer, Alzheimer's disease, and heart disease. Elsewhere, our RADAR ('Remote Assessment of Disease and Relapse') programme is investigating how wearable and smartphone technologies could help in the monitoring of people with certain diseases including multiple sclerosis and Alzheimer's disease.

Looking to the future, if we continue to reach out to other sectors and groupings, I am confident that IMI can be the vehicle through which change can be accelerated. At the same time, patients increasingly expect to be actively involved in all stages of research and drug development, and IMI supports this wholeheartedly.

I would like to close this foreword by thanking the vast numbers of people who make IMI a successful public-private partnership. The project partners, especially the coordinators, consistently deliver excellent science that will have an impact on drug development and, ultimately, patients' lives. IMI also benefits immensely from the input of its governance bodies – the Governing Board, Scientific Committee, States Representatives Group, and the Strategic Governing Groups, as well as the Stakeholder Forum. I would also like to thank our contacts in the European Commission and EFPIA for their dedication to IMI, as well as the many auditors and Members of the European Parliament (MEPs) who have helped us to improve our performance over the years.

I would also like to take this opportunity to pay tribute to Antoine Cuvillier, IMI's Head of Administration and Finance, who passed away in December 2018. Antoine joined IMI in 2011, and he played a vital role in helping the Programme Office to grow and develop over the years. He will be greatly missed.

Finally, I would like to thank my colleagues at the IMI Programme Office who often go above and beyond the call of duty to ensure IMI's success.

Pierre Meulien

IMI Executive Director

Executive summary

IMI highlights in 2018

- Launched three Calls for proposals with significant contributions from new Associated Partners and EFPIA Partners in Research, keeping IMI on track to commit its entire budget by the end of 2020.
- Signed 20 new Grant Agreements, bringing the total IMI project portfolio over the 100 mark.
- Celebrated the 10th anniversary of IMI's first Call for proposals with a highly successful communications campaign promoting IMI project results and impacts.
- Continued improving IMI's operational performance, resulting in strong budget execution and success hitting key targets such as time to grant.

The growing IMI community

In 2018, IMI launched 3 Calls for proposals with a total of 19 topics. These focused primarily on the areas of immunology; infectious diseases; digital health and patient-centric evidence generation; and neurodegeneration. As such, they are aligned with the priority areas identified in the Annual Work Plan (AWP) 2018.

These topics were created with significant input from organisations outside the pharmaceutical sector. For example, IMI's new Antimicrobial Resistance Accelerator programme features a topic on tuberculosis, where the TB Alliance joined IMI as an Associated Partner and helped to shape the topic. In total, IMI welcomed six new Associated Partners in 2018, and a further three existing Associated Partners decided to contribute to new topics launched in 2018.

In addition, 7 companies from the digital, medical technology, health IT and other sectors contributed to new Call topics as EFPIA Partners in Research.

All of this means that IMI remains on track to commit the entire IMI2 budget by the end of 2020.

IMI also continued to forge links with the ECSEL Joint Undertaking on electronic components and systems, which has projects in the health field.

IMI's project portfolio hits the 100 mark

In 2018, IMI achieved an important milestone with the launch of the 100th project. The project in question, Hypo-RESOLVE, focuses on diabetes, a condition for which there is still no cure, and as such, it exemplifies the benefits of a public-private partnership approach to

IMI in 2018 at a glance

New projects

20 Grant Agreements signed launching new projects with a combined budget of **EUR 546 million** from…

EU: EUR 274 million

EFPIA:
EUR 211 million

Associated Partners:
EUR 61 million

Ebola and related diseases
EBOVAC3
VHFMODRAD

Alzheimer's disease
RADAR-AD

addressing unmet medical needs. One major worry for people with diabetes is hypoglycaemia, which occurs when blood sugar levels become too low. Symptoms of hypoglycaemia include behavioural changes, memory loss and confusion, and in the worst cases, it can result in hospitalisation or death.

Despite its seriousness, little is known about hypoglycaemia. Hypo-RESOLVE aims to change that by adding to our understanding of the underlying causes of the condition, as well as its predictors and consequences. Ultimately, the hope is that the project will pave the way for new, better treatments for people with diabetes that will help them to maintain healthy blood sugar levels.

By the end of the year, IMI had signed a total of 20 new Grant Agreements, bringing the total project portfolio to 119 (59 IMI1 projects + 60 IMI2 projects).

Meanwhile, IMI's ongoing projects continued to deliver exciting results that further highlight the added value of the PPP model.

Antimicrobial resistance

- The COMBACTE projects' antibacterial clinical development network grew to over 900 hospitals in 42 countries (including many in central and eastern Europe) with over 10 000 patients enrolled in clinical studies on some of the most dangerous resistant infections.
- ENABLE, which has set up a platform to facilitate the earlier stages of antibiotic development, has selected its first clinical candidate; the next step is to prepare for a Phase 1 clinical trial.

Diabetes

- A study funded partly by the BEAT-DKD and RHAPSODY projects identified five new subtypes of diabetes; if confirmed in a larger group, this paves the way for personalised treatments.
- INNODIA identified some of the molecules that trigger the immune system in people with type 1 diabetes; the project will use this knowledge to develop vaccines to prevent and treat the condition.

Brain disorders

- EMIF created a panel of proteins that can be detected via a blood test and indicate which patients have a build-up in their brains of amyloid plaques, one of the hallmarks of Alzheimer's disease.

Impacts on the regulatory framework

- MACUSTAR received a letter of support from regulators for its approach to clinical studies on dry age-related macular degeneration (AMD), a leading cause of blindness.
- ADVANCE published the blueprint of a framework to rapidly provide scientific evidence of the benefits and risks of vaccines that are on the market.
- ADAPT SMART brought together relevant stakeholders and delivered a wide range of resources on the implementation of medicines adaptive pathways to patients (MAPPs). MAPPs seek to foster timely patient access to medicines, starting with small

Autism spectrum disorder
AIMS-2-TRIALS

Pain
IMI-PainCare

Diabetes
Hypo-RESOLVE

Sjögren's syndrome
NECESSITY

Paediatric clinical trials
c4c

Patient involvement in medicines development
PARADIGM
EFOEUPATI

Big Data for Better Outcomes
PIONEER (prostate cancer)
EHDEN (health data network)

Drug discovery & development
ReSOLUTE
ESCULAB

Drug delivery
IM2PACT

Vaccines
VITAL

Manufacturing technologies
iConsensus

Relative effectiveness
GetReal Initiative

Pharmacovigilance
WEB-RADR 2

Knowledge management
FAIRPlus

groups (e.g. those with no alternative), and extending access to other groups as evidence accumulates.

Tools and resources that are available to researchers outside the project

- iPiE released an online tool that summarises the properties, environmental toxicity and characteristics of drugs.
- COMBACTE launched a platform that allows users to explore and visualise data on antibiotic resistance in humans and animals across Europe.
- A new start-up is making the outputs of three IMI projects – eTOX, K4DD and Open PHACTS – available to the research community.
- Ebola+ project EBODAC produced an online handbook on running clinical trials during disease outbreaks.

More information on IMI project results and impacts in 2018 can be found in section 1.2 and annex 3 of this report, and via projects and results section of the IMI website.

Celebrating 10 years of IMI

30 April 2018 marked the 10th anniversary of the very first IMI Call for proposals. To celebrate this, and to tell the story of IMI's achievements, the Programme Office ran a multi-channel communications campaign spanning several months with the theme 'IMI – carrying the torch of medical innovation'.

Events

The campaign featured high-level events on 27 June and 22-23 October, which attracted almost 700 attendees between them. The first, organised jointly by IMI, the European Commission, and EFPIA, showcased some of the most exciting results from IMI projects through fast-paced, interview style panel discussions and an interactive exhibition. Speakers included Research and Innovation Commissioner Carlos Moedas (who described IMI's work as 'radical collaboration'), and Merck CEO Stefan Oschmann.

The second event was a two-day scientific symposium during which young scientists from the projects shared their findings with the scientific community. The presenters were selected by a Programme Committee following a call for abstracts. The best presenters (as judged by the Programme Committee and the public) were awarded prizes.

Videos

In a series of six videos, representatives of different stakeholder groups (including the academic, SME and patient communities) talk about their involvement in IMI and why it matters to them. The videos were published on YouTube and the IMI website and promoted through all channels.

IMI in 2018 at a glance

New Call topics

3 Calls for proposals launched with a total of **19 topics** and a budget of:

EU: EUR 301 million

EFPIA: EUR 228 million

Associated Partners: EUR 71 million

Immunology

Better control of immune-mediated diseases

Non-invasive imaging of immune cells

A better understanding of immune-mediated diseases

Safer immune therapies

Digital health and patient-centric evidence generation

Remote, decentralised clinical trials

Digital clinical trials

Machine learning for drug discovery

Research platforms for patient-centric drug development

Bringing the blockchain into healthcare

Social media

Social media, and Twitter in particular, were an integral part of the campaign. In order to amplify the message and reach new audiences, IMI ran a series of promoted tweets at key points in the year. This, coupled with regular, carefully prepared content, resulted in strong social media metrics as well as an increase in the number of visitors to the IMI website.

Tracking IMI's progress

The IMI2 objectives are far reaching and ambitious and with that come inherent challenges in order to ensure that project deliverables can be measured in a manner that is in line with these objectives. In 2016 the IMI office initiated a plan which had the goal of creating (albeit retrospectively) a performance framework for IMI2 based on a logic model which strives to graphically represent how IMI's objectives and activities would eventually lead to the expected outcomes and impacts given the input investments made.

The logic model therefore tracks inputs, in terms of investments and other resources made available to enable the programme implementation, the strategic focus of the activities, outputs during the implementation of the programme, outcomes which result on the completion of the action and, finally, impacts - which may take some years after the programme has finished to be realised.

It is important therefore that the indicators that are measured during the programme implementation are clearly positioned on a trajectory which can deliver the expected impact. This is the philosophy behind the creation of a series of 10 key performance indicators (KPIs) that have been approved by the IMI Governing Board and are tracked and reported on for the first time in this AAR 2018. As the report shows, IMI is on track to meet its objectives as set out through these KPIs.

A focus on sound financial management

In all its activities, IMI adheres to sound financial management principles and strives to achieve and maintain operational excellence. In 2018, IMI took further steps to improve budget execution, and this resulted in an execution rate of 86.69 % for operational payment appropriations. This represents a significant improvement over previous years, when the figure was around 70 %.

On Call and grant management, IMI achieved the official targets for:

- Time to inform (TTI): 75 days out of a target of 153 days
- Time to grant (TTG): 232 days out of a target of 245 days
- Time to pay (TTP) pre-financing: 9 days out of a target of 30 days
- TTP interim payments: 59 days out of a target of 90 days
- TTP final payment: 54 days out of a target of 90 days.

IMI carefully monitors all cost claims from beneficiaries both before making the payment (ex ante controls) and afterwards (ex post controls). If errors are spotted during ex post controls, these are

Neuroscience and neurodegeneration

Joining the dots on brain disorders (synaptopathies)

Antimicrobial Resistance (AMR) Accelerator programme

Pillar A: Capability Building Network to accelerate and validate scientific discoveries

Pillar B: Tuberculosis drug development network to accelerate and validate scientific discoveries and advance the R&D pipeline of new and innovative agents to address the global tuberculosis epidemic

Pillar C: Portfolio Building Networks to advance the R&D pipeline of new and innovative agents to address AMR Topics

corrected. At the end of 2018, the error rate (after corrections and recoveries) for both IMI1 and IMI2 programmes was below the materiality threshold of 2 %.

IMI's improvements in operational efficiency have been recognised by the European Court of Auditors, which again issued an unqualified ('clean') opinion on the reliability of the accounts for 2017, as well as on the legality and regularity of revenue and payments underlying the annual accounts.

1 Implementation of the Annual Work Plan 2018

1.1 Key objectives in 2018

The key objectives for IMI in 2018 were set out in the Annual Work Plan (AWP) 2018 and were based on the overall objectives of IMI2 JU as set out in Article 2 of Council Regulation (EU) No 557/2014. A summary of the progress made against them is given below. More information on all points can be found throughout the report.

Objective: Initiate competitive Calls for proposals within the Strategic Research Agenda priorities bringing together the different stakeholders involved in drug development (including SMEs, regulators and patient organisations) and foster cross-project collaboration through proactive outreach strategies and conducive Call design.

- Launched three Calls for proposals:
  - IMI2 – Call 14 (two stages, 4 topics, launched 15 March) covered the AWP priorities immunology and digital health and patient centric evidence generation.
  - IMI2 – Call 15 (two stages, 8 topics, launched 18 July) covered the AWP priorities neurodegeneration and other neuroscience priorities; immunology; infection control including vaccines; and digital health and patient centric evidence generation.
  - IMI2 – Call 16 (one stage, 7 topics, launched 18 July) covered the AWP priority infection control including vaccines.
- Promoted all Calls through all communication channels (website, webinars, events, newsletter, social media, etc.) as well as multipliers such as the States Representatives Group (SRG) and National Contact Points (NCPs). Opportunities for SMEs, regulators and patient groups were flagged up, particularly during the webinars.

Objective: Ensure sound budget implementation through the efficient management of Calls for proposals, grant award process and close monitoring of ongoing projects, ensuring the completion and close-out.

- Implemented steps to improve budget execution, for example by sticking to a strict schedule of two Call launch dates per year.
- For the operational payment appropriations, achieved an execution rate of 86.69 %, an improvement over previous years, where the figure was around 70 %.
- On Call and grant management, IMI achieved the official targets for:
  - Time to inform (TTI): 75 days out of a target of 153 days
  - Time to grant (TTG): 232 days out of a target of 245 days
  - Time to pay (TTP) pre-financing: 9 days out of a target of 30 days
  - TTP interim payments: 59 days out of a target of 90 days
  - TTP final payment: 54 days out of a target of 90 days.

  This was achieved thanks to the full implementation of the Horizon 2020 IT management tools, the appointment of a grant coordinator in IMI, and enhanced management supervision and regular monitoring.
- IMI also maintained a low error rate for ex post audits (below the 2 % materiality threshold), demonstrating the effectiveness of IMI's control procedures.
- During 2018, IMI held close-out meetings on 11 projects that had finished. The results and impacts were summarised on the IMI website and promoted.

Objective: Demonstrate the EU added value of IMI2 JU through assertive communication to target audiences of the openness, transparency, relevance, effectiveness, efficiency and coherence of IMI2 JU activities.

- Used the 10th anniversary of the first IMI Call for proposals as the basis for a large-scale communications campaign to promote IMI's achievements and impact so far. The campaign was built around two major events (one targeting the policy community, and one targeting the scientific community), videos, success stories, and social media. The campaign resulted in high levels of visibility for IMI on social media and triggered a rise in the number of visitors to the IMI website

from an average of around 12 000 visitors per month in previous years to over 14 000 visitors per month in 2018.
- Increased the transparency of the Call topic development process by publishing indicative information on topics under consideration for future Calls in the long term.
- The Stakeholder Forum and other events provide stakeholders with the opportunity to learn about and provide their own input on IMI's activities.

Objective: Involve industry from related sectors other than the pharmaceutical industry (diagnostics, medical technologies industry, imaging, digital industry, etc.) in IMI2 JU projects through proactive outreach strategies.

- IMI continued to attract new Associated Partners from other sectors, such as diagnostics company Cepheid Europe (contributes to the VHFMoDRAD project on diagnostics for Ebola and related diseases); patient organisation Parkinson UK (which extended its association by joining the IMI2 – Call 15 topic on digital endpoints in neurodegenerative and immune-mediated diseases); and SpringWorks Therapeutics, which will contribute to the IMI2 - Call 15 topic on integrated research platforms enabling patient-centric drug development.
- A number of companies from other sectors opted to contribute to IMI by becoming EFPIA Partners in Research. In total, 7 companies committed EUR 7.98 million to IMI Calls for proposals in 2018, including mobile and digital company Nokia; medical technology company Medtronic; and health IT company IQVIA.
- IMI continued to work closely with ECSEL, the joint undertaking on electronic components and systems, to exploit obvious synergies. Both IMI and ECSEL have presented at each other's strategy meetings.

Objective: Ensure IMI2 JU internationalisation and build productive linkages to major international efforts to address Global Challenges (AMR, Alzheimer's, autism, cancer, emerging infectious diseases, etc.).

- The IMI platform is becoming a magnet for partners wanting to leverage their own investments through more open collaboration models.
- Through its Associated Partners, IMI is forging new links and strengthening existing ones with initiatives elsewhere in the world, primarily in the US.
- On AMR and infectious diseases, the Bill and Melinda Gates Foundation and the TB Alliance are Associated Partners for the IMI2 - Call 15 topic on a tuberculosis drug development network. Meanwhile the Antibacterial Resistance Leadership Group (ARLG) became the first US consortium to take part in clinical studies run by IMI's COMBACTE programme on antimicrobial resistance. Two new Ebola+ projects, VHFModRAD and EBOVAC3, include partners from Senegal and Sierra Leone respectively.
- On autism, 2018 saw the launch of the AIMS-2-TRIALS project, whose Associated Partners include Autism Speaks and the Simons Foundation Autism Research Initiative (SFARI).
- On Alzheimer's disease, IMI attended the World Dementia Summit where IMI projects EMIF, AETIONOMY and EPAD featured in the presentations.
- On cancer, IMI met the US National Cancer Institute (NCI) to explore synergies between their Cancer Moonshot programme and IMI's oncology portfolio.
- More broadly, IMI used its presence at major international events such as BIO to raise awareness of IMI's activities among a global audience and to meet with key opinion leaders from relevant organisations.

1.2 Research & 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.

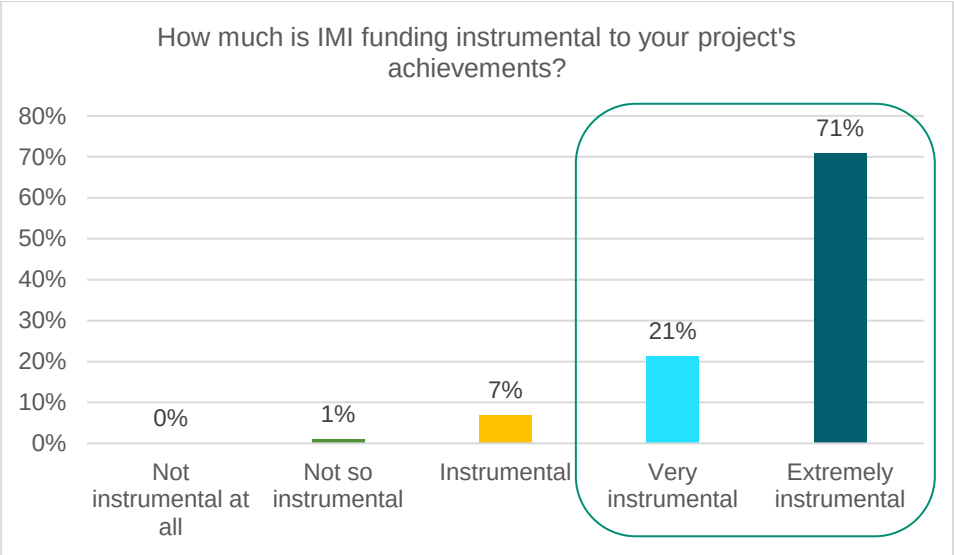
These categories are aligned with the new IMI KPIs, which were approved by the Governing Board in March 2018. They were selected due to their alignment with the goals of IMI, and because they allow IMI to assess projects' actual impact on drug development. A detailed list of achievements for both IMI1 and IMI2 projects in these categories can be found in Annex 3 of this report. Figures on the KPIs can be found in Annex 8.

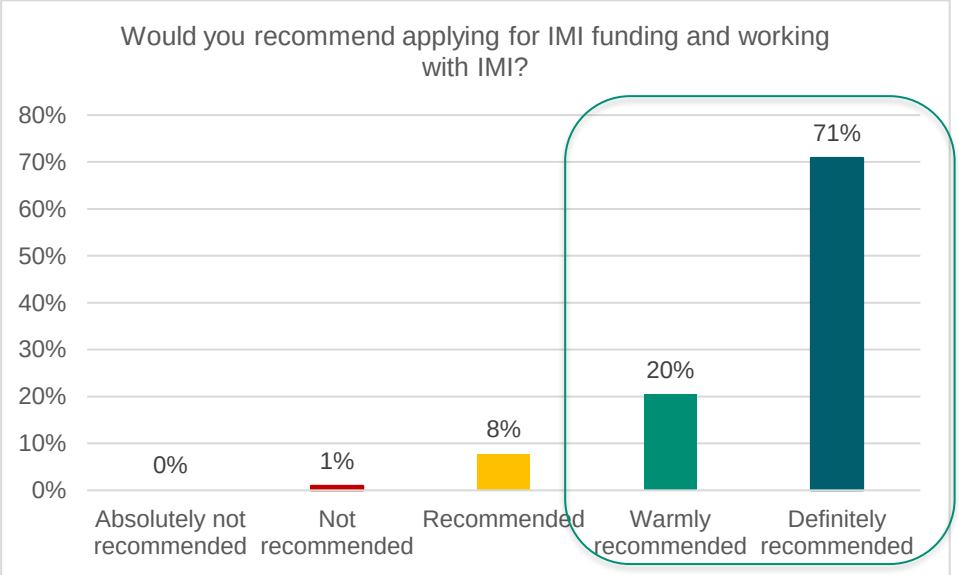
Here, a selection of success stories demonstrates how IMI projects are:

- delivering results in disease areas with high unmet medical and social needs (such as diabetes, antimicrobial resistance, and brain disorders);
- having an impact on regulatory frameworks;
- delivering tools and resources that are accessible to the wider scientific community.

Meanwhile the IMI Programme Office carried out a survey[2] of IMI project coordinators, which revealed that over 90 % feel that IMI funding is very or extremely instrumental in achieving their project's objectives. Furthermore, when asked if they would recommend applying for IMI funding and working with IMI, over 90 % of respondents replied that they would warmly or definitely recommend it.

[2] The survey was sent to 111 coordinators; 103 answered the questions highlighted in this section.





1.2.1 IMI projects are delivering results in disease areas with high unmet medical and social needs

Recent years have seen dramatic advances in medicine, yet in some disease areas, such as brain disorders, antimicrobial resistance, and diabetes, progress remains slow. In all three cases, the sheer complexity of the challenges mean that no single organisation, country or sector can hope to make progress alone. For progress to be made, leading experts from pharmaceutical companies, companies in other sectors, universities, small and medium-sized enterprises (SMEs), patient organisations, and regulatory authorities must work together, and that is where IMI comes in. As a neutral public-private partnership, IMI is ideally placed to build large-scale, international, multi-stakeholder consortia capable of delivering results in these challenging areas.

Tackling the scourge of antimicrobial resistance

According to figures released by the European Centre for Disease Prevention and Control (ECDC) in 2018, an estimated 33 000 people die each year in the EU / European Economic Area (EEA) as a direct consequence of an infection due to bacteria resistant to antibiotics. IMI's New Drugs for Bad Bugs programme was set up as part of the European Commission's action plan on antimicrobial

resistance and now counts eight projects tackling the scientific, regulatory and economic challenges of developing new treatments for resistant infections.

The early stages of antibiotic discovery and development are extremely difficult. To address this challenge, The IMI1 project ENABLE has created a drug discovery platform for testing and optimising molecules that are still in the earlier stages of drug discovery but have the potential to become future drug candidates. Researchers in universities and SMEs with promising potential antibiotics that are in the early stages of drug discovery can apply to access the platform created by the project. Organisations selected to join ENABLE have the opportunity to collaborate with experts in all areas of antibacterial drug discovery, such as microbiology, pharmacology and chemistry, to help advance their molecule through the drug development process, through to clinical testing.

In 2018, the project achieved a major milestone when it selected one potential antibiotic it has worked on, apramycin, as a clinical candidate. The clinical potential of apramycin was discovered by researchers at the University of Zurich who set up a spin-out company, Juvabis, to develop it further. Juvabis joined ENABLE in 2016. Thanks to the collaboration with the project, the Juvabis team has now been able to demonstrate the safety and efficacy of apramycin in animal models for various infections, including infections caused by some of the more dangerous drug-resistant bacteria. This prompted ENABLE to select apramycin as a clinical candidate; the next step is to prepare for a Phase I clinical trial application.

Running clinical trials on new antibiotics is difficult due to regulatory requirements and the large numbers of patients required – put simply, a lot of patients have to be recruited to the studies to be sure of having enough patients with the resistant bacteria under investigation and to demonstrate that the new antibiotic is not inferior to comparable antibacterial drugs. These issues mean that the costs of carrying out a clinical trial on a new antibiotic are also extremely high.

IMI's COMBACTE family of projects (IMI1: COMBACTE-NET, COMBACTE-CARE and COMBACTE-MAGNET; IMI2: COMBACTE-CDI) is building a self-sustaining, pan European antibacterial development network and using it to run high-quality clinical studies of new antibiotics for multi-drug resistant bacteria. In 2018, COMBACTE achievements included:

- A white paper with recommendations for improving the design and analysis of clinical trials of drugs to treat resistant infections, which was published in the journal Clinical Infectious Diseases. The paper assesses different ways of finding enough patients for a study, scoring each one on its alignment with regulatory frameworks; its technical feasibility; ease of data interpretation; ease of practical implementation; and the strength of the evidence base for the recommendation. The authors note that although not all recommendations will be applicable to all trials, they are all relevant to the debate supporting change.
- Strengthening the CLIN-NET network of more than 900 hospitals & 2 900 hospital contacts across 42 European countries. As of June 2018, 116 hospitals in 18 European countries were actively recruiting patients for clinical studies, and over 10 000 patients had been enrolled in clinical studies. In addition, the projects provided training on good clinical practice (GCP) for 800 investigators from 28 countries.
- Consolidation of the LAB-Net network (>750 labs) and development activities focusing on implementing the LAB-Net quality assurance programme including training for laboratories.
- Completed recruitment for a number of studies, including the EURECA study (2 266 patients) on infections that are resistant to antibiotics called carbapenems. Cases of infections caused by bacteria known as carbapenem-resistant enterobacteriaceae (CRE) are on the rise, and are most common in healthcare settings. They are extremely hard to treat and can be fatal. The EURECA study is investigating the risk factors for CRE infection and things that influence treatment outcomes. The samples collected during the study were sent to a central site for analysis.

There is a contradiction at the heart of antibiotic development. On the one hand, we urgently need new antibiotics to treat resistant infections. At the same time, the use of new antibiotics should be restricted, so as to minimise the risk of bacteria developing resistance to them. As a result of this situation, the potential return on investment is much lower than in most other medical fields. The IMI1 project DRIVE-AB set out to generate recommendations for economic models that would address this contradiction; it published its final report in 2018. In the report, the project explains that a mix of economic drivers and incentives is needed to stimulate antibiotic development. The report, based on

input from diverse stakeholders, highlights four incentives that could be the most effective in stimulating the antibiotic pipeline while also ensuring that critical antibiotics are used sustainably and are accessible to all who need them. The incentives picked out by the report are grants; pipeline coordinators; market entry rewards; and a long-term supply continuity model.

Towards personalised treatments for diabetes

Figures from the International Diabetes Federation (IDF) show that approximately 425 million adults worldwide are living with diabetes, and just over 1 million children have type 1 diabetes. It kills 4 million people every year. Although there are treatments for diabetes (such as insulin injections), there is no cure. Patients play an important role in IMI's diabetes projects; patient organisations JDRF and the IDF are IMI Associated Partners, and many projects have patient committees to ensure the patient voice is heard.

In 2018, scientists funded in part by the IMI2 projects BEAT-DKD and RHAPSODY revealed that they had identified five subtypes of diabetes. The research was published in The Lancet Diabetes and Endocrinology. Currently, two main types of diabetes are recognised, and diagnosis is through a measurement of a patient's blood sugar levels. In this study, scientists monitored over 13 000 newly-diagnosed diabetes patients, analysing blood sugar levels, insulin resistance, insulin secretion, and age of onset among other things. This revealed five distinct groups of patients with different risk levels for certain complications associated with diabetes. For example, patients in group 2 ('severe insulin-deficient diabetes') are at greatest risk of eye disease, while patients in group 3 ('severe insulin-resistant diabetes') had the highest incidence of kidney damage. According to the researchers, current diagnostics and classification of diabetes are insufficient and unable to predict future complications or choice of treatment. This study is the first step towards personalised treatment of diabetes. The study only included people in Sweden and Finland; they now plan to carry out similar studies in China and India, to see if their findings apply in different ethnic groups.

Further results that pave the way towards personalised treatments for diabetes came from the IMI1 project DIRECT. Here, the project found that people with altered ARRB1 and GLP-1R genes respond better to certain injectable anti-diabetic drugs. Around 5 % of the population has been found to have one or more copies of the altered ARRB1 gene. They show a much better response to GLP-1RA drug treatments, equivalent to an extra 0.6mg of Liraglutide or 10µg of Exenetide. The study suggests that in future, doctors may need to test patients' genetic make-up before prescribing these drugs.

Another important result in 2018 came from the IMI2 project INNODIA, which identified the molecules that trigger the immune system in people with type 1 diabetes. Type 1 diabetes is an autoimmune disease. It occurs when immune cells called T lymphocytes attack the pancreatic beta cells, which are responsible for the production of the hormone insulin. To make up for the loss of these cells, people with type 1 diabetes have to inject themselves with insulin to manage their blood sugar levels. In this study, the researchers analysed the molecules on the surface of the pancreatic beta cells and how the T lymphocytes respond to them. They found that in both healthy people and diabetes patients, T lymphocytes recognised these molecules when they encountered them in the blood. However, in diabetes patients, the immune cells also recognised them in the pancreas. The team will use this new-found knowledge to develop vaccines to prevent and treat type 1 diabetes. However, while conventional vaccines seek to boost the immune response, the aim here will be to neutralise it. The research was published in the journal Cell Metabolism.

IMI and brain disorders

Some 179 million Europeans are living with brain disorders including neurological diseases such as Alzheimer's disease as well as mental health conditions like depression, according to the European Brain Council. The total annual cost of brain disorders in Europe stood at almost EUR 800 billion in 2010. There is still no cure for most brain disorders, and the best patients can hope for is a treatment to alleviate their symptoms or slow the progression of their disease. Unfortunately, for many patients, the limited treatments on offer do not work or come with severe side effects. Part of the problem is that developing new drugs is a slow, costly process, and this is especially true for drugs for brain disorders.

IMI has projects addressing a wide range of brain disorders, including Alzheimer's disease, autism spectrum disorders, pain and depression, to name a few. By bringing together leading researchers

from the public and private sectors as well as patients, they are well placed to make progress in this most challenging of areas.

There are over 35 million people worldwide living with Alzheimer's disease, yet there is no cure and the treatments available only address some symptoms but do not slow the progress of the disease. IMI has a large portfolio of projects under both the IMI1 and IMI2 programmes working to turn this situation around. One of the many challenges in Alzheimer's disease research is identifying people who are at risk of developing the disease. Among other things, the lack of a simple test in this area means it is hard to identify people who could take part in a clinical trial.

The IMI1 project EMIF has created a panel of seven proteins which can be detected via a blood test and which indicate which patients may have a build-up of amyloid plaques in their brains. Tangled 'plaques' of amyloid proteins are considered to be a hallmark of Alzheimer's disease. The proteins were identified through detailed analyses of up to 1 000 people including healthy elderly people, people with mild cognitive impairment, and people with mild Alzheimer's disease. The project is now working to develop the test further so that it can be used in clinical trials.

1.2.2 IMI projects have an impact on the 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.

Tackling a leading cause of blindness

For example, the IMI2 project MACUSTAR aims to develop and validate tests that are capable of accurately detecting subtle changes over time in the eye disease dry age-related macular degeneration (AMD). People with dry AMD gradually lose their central vision, usually in both eyes. It is already a leading cause of blindness worldwide, and as the population ages, the number of cases is likely to rise. The project embarked on a parallel advice procedure on its proposed approach with the European Medicines Agency, US Food and Drug Administration, and the UK's health technology assessment body. In 2018, the project received a letter of support from the EMA. By the end of the year, the project had launched its study across 20 clinical sites and recruited a quarter of the patients needed.

Analysing the safety and efficacy of vaccines

Only medicines and vaccines that have been demonstrated to be safe and effective (through clinical trials) are allowed onto the market. Once a medicine or vaccine is on the market and being used by the general public, manufacturers and regulators continue to monitor safety and efficacy.

The IMI1 project ADVANCE focused on the safety and efficacy of vaccines that are already on the market. Vaccinations are a highly successful public health intervention. However, as they are used primarily in healthy people (often children), expectations on their safety and effectiveness are particularly high. In 2018, ADVANCE published a blueprint of a framework to rapidly provide scientific evidence of the benefits and risks of vaccines that are on the market. The document is the culmination of the project's work and it underwent a comprehensive consultation process with representatives of the main stakeholders interested in the assessment of benefits and risks of vaccines, as well as a public consultation.

The document sets out the steps needed to use the framework, the tools that can be used, and how to disseminate the results. The hope is that it will help health professionals, regulatory agencies, public health institutions, vaccine manufacturers and the general public make more informed decisions on the benefits and risks of vaccines.

Advancing discussions on MAPPs

Elsewhere, the IMI2 project ADAPT SMART has delivered a wide range of resources for people interested in the implementation of medicines adaptive pathways to patients (MAPPs). MAPPs refers to a concept that seeks to provide patients with timely access to beneficial medicines, starting from a small group of well-identified patients (e.g. those with no alternative treatments). As evidence accumulates on the benefits and risks of a medicine, access may be extended to other groups of patients. As such, MAPPs relate to a flexible pathway covering the entire life cycle of a medicine. However, implementing MAPPs involves diverse stakeholders and raises difficult questions.

By bringing together representatives from key European stakeholder groups – regulatory agencies, health technology assessment (HTA) bodies, pharmaceutical companies, payers, patients and health care professionals – ADAPT-SMART created a platform where the conditions and feasibility of MAPPs implementation within the EU regulatory/legal context could be discussed openly. As a result, the project contributed to an improved understanding among stakeholders of the issues promoting early access of medicinal products to patients.

Thanks to ADAPT-SMART, there is now a wide acceptance among different stakeholders that medicines development should take the lifespan approach. Whereas in the past the prevailing idea was that a drug should be developed for 5 to 10 years, then launched and left out there for patients to use, this project reinforced the idea of continuous evaluation and use. The project came up with recommendations on how the system could be improved at the various decision points in the product lifespan, including before and after licencing. This means that patients who are running out of time could get access to new drugs more quickly, and that evaluation continues even after the product launch.

ADAPT SMART's outputs are available on the project website via an infographic that guides users to the information they require.

1.2.3 IMI projects are delivering tools and resources that are accessible to the wider scientific community

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 IMI website includes a catalogue of accessible results, including a brief description of each resource and a link for more information.

A database on environmental aspects of drugs

The IMI1 project iPiE has released an online tool that summarises the properties, environmental toxicity and characteristics of active pharmaceutical ingredients (APIs). Dubbed, iPiE*SUM ('iPiE Summary Database Search'), the tool is designed to allow public and regulatory bodies to obtain a high-level overview of what studies were collected during the iPiE project and what eco-toxicity data and studies are available. APIs can be released into the natural environment during the manufacturing process, following use by patients, or when unused medicines are disposed of inappropriately. The goal of iPiE is to develop a framework that will provide methodologies to prioritise new and existing medicinal compounds for a comprehensive environmental risk assessment. As such it will support and inform regulatory activities designed to assess and reduce the environmental impact of medicines.

COMBACTE launches platform on antimicrobial resistance in Europe

The IMI1 COMBACTE projects have launched a unique European platform that allows users to explore and visualise data on antibiotic resistant infections in humans and animals across Europe. The website, which is freely accessible, brings together epidemiology data from 32 European countries on the priority list of pathogens released by the World health Organization in 2017. It also includes data on more recent outbreaks and emerging cases of resistance to newly-developed antibiotics. Data is displayed via colour-schemed maps that allow users to easily track things like the setting, resistance rates, sample sizes and data sources. If users register, they can also select and download data. In a statement, the project explains: 'The goal is to give industry, policy makers, and public an easy tool to

use in order to understand the trends and the epidemiology of antimicrobial resistant infections across Europe using a One Health approach. The platform provides an interactive space, which combines multiple sources and allows users to overcome language barriers.'

New start up facilitates access to IMI project outputs

Publicly-available outputs of three IMI1 projects – eTOX, K4DD and Open PHACTS – are now available through a newly-launched start-up company called Phenaris. The projects delivered a wealth of tools and resources in the areas of toxicology (eTOX); the analysis of interactions between a drug and its target (K4DD); and data management across diverse sources (Open PHACTS). The start-up is the brainchild of an IMI project coordinator, and it provides researchers with data, models, and decision support in all aspects of *in silico* (i.e. computer-based) toxicology.

A handbook on running clinical trials during a disease outbreak

One of the IMI projects launched in response to the devastating Ebola outbreak in western Africa in 2014 focused on working with local communities in Sierra Leone on clinical trials of a new vaccine regimen. When the IMI2 project EBODAC started, the outbreak was still very much ongoing; fear and anxiety were rife, and rumours spread rapidly through communities. The project deployed a combination of methods, including radio and drama shows, public meetings and house-to-house visits. A social sciences team listened to the community and took note of any rumours or concerns as soon as they arose, allowing the project to respond rapidly. Thanks to EBODAC and the communities, the project succeeded in setting up and running the trial. Many of the project's methods could be applied to other disease outbreaks elsewhere in the world. To facilitate this, the project is sharing its experience through an online handbook entitled 'Community engagement, communications, and technology for clinical trials in outbreak settings'. It includes chapters on ethics, the social context, engagement, rumours, and enabling technologies.

1.2.4 Collaboration among consortia and with external bodies and other sectors

IMI patient engagement projects sign memorandum of understanding

Two IMI2 projects focusing on patient engagement, PARADIGM and PREFER, signed a memorandum of understanding (MoU) in 2018 to enhance collaboration between the projects and to maximise results. The MoU outlines how the projects will work together and share ideas. While PARADIGM is broadly focused on patient engagement at three points in the research and development process, PREFER looks at how and when it is best to perform and include patient preferences in decision making during the medical product life cycle. Through the MoU, the two projects hope to identify areas of mutual interest; identify any gaps that are hindering progress; establish collaborative activities to address these gaps; and share knowledge and data. The projects will also mutually participate in project events and use each other's communications channels to promote news and results. In a joint statement, the projects write: 'There is an ample opportunity to leverage the work of these projects, to avoid duplicate efforts as well as maximise results.'

US Antibacterial Resistance Leadership Group joins COMBACTE studies

In 2018, the Antibacterial Resistance Leadership Group (ARLG) became the first US consortium to take part in clinical studies run by the IMI1 COMBACTE programme on antimicrobial resistance. In a statement, the project described the news as a 'major milestone' that 'clearly demonstrates the benefits of public-private collaboration and international collaboration between COMBACTE and ARLG'. The ARLG joined two studies on treatments design to prevent pneumonia in people in intensive care who require a ventilator to help them breathe. The SAATELLITE study focuses on pneumonia caused by *Staphylococcus aureus*, while EVADE focuses on infections caused by *Pseudomonas aeruginosa*. When the news was announced, 15 US sites were slated to participate in the trials; the first, in Detroit, was activated in January. The ARLG's participation in the studies is supported by the US National Institute of Allergy and Infectious Diseases (NIAID).

Collaboration with ECSEL

IMI continues to build strategic links with ECSEL JU. These links are important because ECSEL projects are developing technologies that could be implemented in the health sector, while at the same time IMI projects need technology to accelerate innovative solutions. However, these need to be connected so that we are not developing technologies that cannot be used or that we are reinventing technologies that already exist and are implemented in other sectors (automotive, etc.)

In 2018, IMI and ECSEL strengthened their ties by participating in each other's governing bodies – IMI is represented in ECSEL's e-health Lighthouse initiative, and ECSEL is represented in IMI's Strategic Governing Group on Digital Health and Patient Centric Evidence Generation. In addition, the Executive Directors of IMI and ECSEL took part in at each other's Governing Board meetings, and representatives from both JUs presented at each other's events.

Collaborations and connections with other EU initiatives in the health cluster

IMI has forged many additional collaborations and connections with several existing EU initiatives for synergistic and/or sustainability purposes. These include:

- JPIND (Joint Programme – Neurodegenerative Disease Research), the Human Brain Project, and the European Brain Council in the area of neurodegeneration;
- JPIAMR (Joint Programming Initiative on Antimicrobial Resistance) in the area of antimicrobial resistance;
- ELIXIR, ECRIN (European Clinical Research Infrastructure Network), and BBMRI (Biobanking and BioMolecular Resources Research Infrastructure), in order to optimise the sustainability of IMI project's data assets, clinical research networks and bio-resources respectively;
- EIT (EIT European Institute of Innovation & Technology) Health – especially in the area of digital enabling technologies.

1.3 Stakeholder engagement

1.3.1 SME involvement

The IMI small and medium-sized enterprise (SME) engagement strategy focuses on three pillars: 1) explicitly embedding expected SME participation in Call topics; 2) preparing tailored SME communications for different stakeholders; and 3) disseminating these communications as widely as possible.

- **Call topics:** In 2018, the review of all Call texts to ensure expected SME participation is highlighted was continued. All Strategic Governing Groups (SGGs) were also informed of the importance of embedding SME participation in all IMI topics.
- **Communications:** As in 2017, dedicated communications targeting SME participation were developed for each Call launched in 2018. The importance of SME participation was also emphasised during the topic webinars accompanying each Call launch. In addition, specific webinars for SME participants were held for each Call launched in 2018, attracting a total of 182 registrants. Following the webinars, a list of SMEs interested in each topic was disseminated via the IMI website to allow coordinators to easily find relevant SMEs for their applicant consortia. In addition, an SME representative was the subject of one of IMI's 10th anniversary videos.
- **Outreach:** The programme of outreach established in 2016 was continued and enhanced. This included updating the dedicated SME webpage; giving presentations at SME events including BIO-Europe 2018; the Nordic Life Science Days partnering event; and the Spanish Digital Health event. Opportunities in IMI were also promoted at the European Biopharmaceutical Enterprises (EBE), and via the IMI States Representatives Group, Scientific Committee & European SME clusters / umbrella organisations.

In addition to the direct involvement of SMEs as IMI beneficiaries, several IMI projects support the activities of other SMEs. For example, the IMI1 projects European Lead Factory (ELF) and ENABLE provide open platforms that allow SMEs to progress interesting drug targets and candidate molecules. In 2018, one spin-off SME, Keapstone Therapeutics, received additional funding to continue research into its potential Parkinson's disease drug. In addition, ScandiCure partnered with Servier to advance its novel compounds through preclinical development.

Furthermore, a compound for the treatment of critical systemic infections caused by Gram-negative bacteria from Swiss start-up company Juvabis was selected as the first clinical candidate of the ENABLE project.

In November 2018, the EHDEN project was launched. This project has allocated EUR 16 million to support the harmonisation of electronic health record (EHR) data to a common format. It is expected that this harmonisation will be carried out by SMEs, starting in 2019.

For the IMI2 programme, SMEs account for 18.7 % of 2018 stage 1 applications, 15.4 % of EU funding beneficiaries (by participations), 20.3 % of EU funding beneficiaries (by participants), and receive 9.45 % of EU funding so far.

1.3.2 Patient involvement

Including patients' perspectives in IMI activities and facilitating patient participation in projects is a top priority for IMI, and in 2018, the Programme Office demonstrated its commitment to this by recruiting a Seconded National Expert (SNE) to work full time on patient engagement. Patients are a core third pillar in many of IMI's projects. As of the end 2018, close to 60 % of ongoing IMI projects have patient organisations either as partners in the consortium or represented on advisory boards, ethics advisory boards, or being consulted for topics of relevance.

Patient-centricity was a focal point of two major events organised by IMI in 2018. The IMI 10th Anniversary Scientific Symposium included a session entitled 'Patient-centric approaches in drug development', with presentations covering issues such as patient education; patient preference information; and patient-centred views in health decision-making. One presentation, by a patient representative from the EUPATI project, won 2nd prize for the best oral presentation as selected by the event's Programme Committee. The poster session also included a track on 'Patient engagement along the value chain'.

Patient representatives were also present at the IMI Stakeholder Forum, where they participated in two panels, providing valuable input to the discussion on how to steer and apply technology convergence to optimise health research and delivery.

IMI was also invited to attend BioFIT in Lille, France, where an IMI staff member participated in a panel together with academia and patient organisations discussing the added value of having patient organisations in existing pharma-biotech-academia alliances.

Furthermore, the Programme Office held numerous consultations and meetings with patient representatives and patient organisations. The interaction with patients and the feedback they provided will feed in to further developments of IMI's patient engagement strategy.

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 continued to maintain a close collaboration with regulators, mainly the European Medicines Agency (EMA) and FDA (US Food and Drug Administration) in 2018. 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.

The summary of the key messages of the 5th IMI-EMA-FDA Regulatory Science Summit held in December 2017 were made public in 2018 to encourage wider discussion in the scientific and regulatory communities. These address the value of collaboration, the evolution of science and its impact on regulatory science, the existing gaps to be addressed, and the need for tangible and impactful outputs.

Interaction with the EMA and other national regulatory agencies in the EU occurred also through the Scientific Committee, and via participation in workshops / meetings (e.g. IMI's workshop on disease interception, and the EMA workshop Regulatory Science to 2025).

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 the EMA. This year a number of projects benefited from these services, in particular through briefing meetings for input on the project plan, and the EMA's qualification advice of novel methodologies for drug development. This resulted in the EMA issuing a qualification opinion for PROactive patient reported outcomes (PROs) in chronic obstructive pulmonary disease (COPD), and Letters of Support to the project MACUSTAR for intermediate age related macular degeneration (AMD) biomarker and novel clinical endpoint development.

1.4 Calls for proposals and grant information

1.4.1 Launch and management of Calls in 2018

In 2018, three Calls for proposals were launched (IMI2 - Calls 14, 15 and 16) and three Calls were at various stages of the evaluation and granting process (IMI2 - Calls 8, 12 and 13). The evaluations for IMI2 - Calls 8 (third cut-off date), 10 and 11 were completed in 2017 but grant preparation and Grant Agreement signature were completed in 2018. Each single stage and stage 2 evaluation encompasses ethics screening of the full proposals performed by a separate ethics experts' panel. In 2018, the following evaluations were concerned: IMI2 Call 8 (5th cut-off) single stage, IMI2 Call 12 - stage 2, IMI2 Call 13 - stage 2, IMI2 Call 16 - single stage.

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 2018 (AWP 2018) were addressed through Calls launched in 2018.

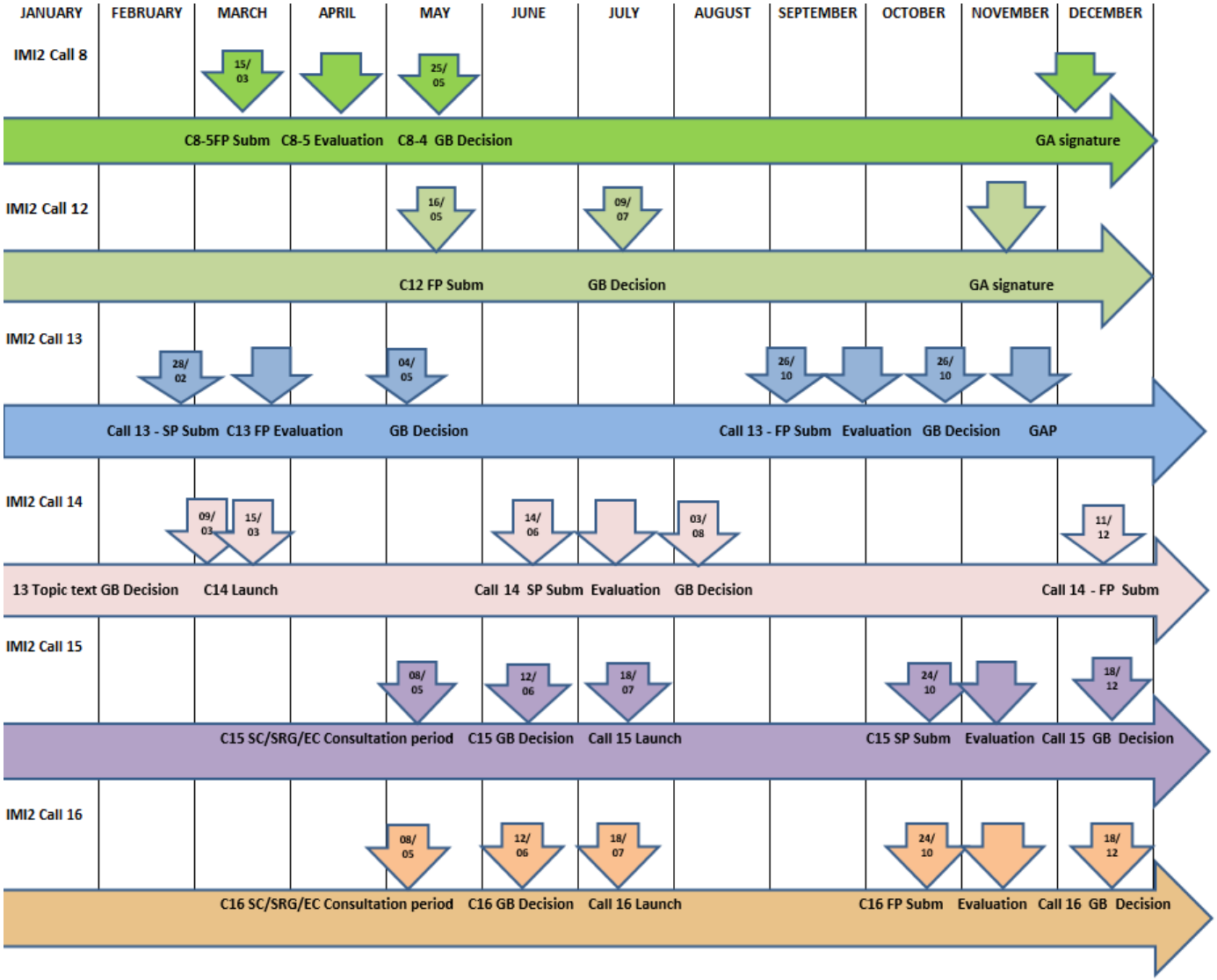
The key points in the submission and evaluation process are highlighted as follows:

- 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 States Representatives Group – the SRG, and the Scientific Committee – the SC), as well as of the European Commission (EC).

There was one redress case following the evaluation of Calls in 2018. The review committee evaluated the complaint and found no grounds to re-evaluate the proposal.

Chart showing overview of Call processes in 2018



Note: IMI2 – Call 8 was an open Call with a number of cut-off dates. C8-4 and C8-5 refer to the 4th and 5th cut-off dates respectively.

Table summarising key information related to IMI2 Call launches, submission deadlines and Grant Agreements signed in 2018

IMI2 Call	Topic title	Call pro-cess	Launch date	Deadline for sub-mission of SPs	SPs received	Particip-ants in eligible SPs, FPs	SPs selected to prepare a FP	FPs selected for funding	GAs signed in 2018
8	▪ 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	1
8	▪ Ebola and other filoviral haemorrhagic fevers (Ebola+) programme: future outbreaks (two year Call with multiple cut-off dates)	Single stage	18/12/2015	Fifth cut-off date:	4	34	1	1	1
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	8

IMI2 Call	Topic title	Call pro-cess	Launch date	Deadline for sub-mission of SPs	SPs received	Particip-ants in eligible SPs, FPs	SPs selected to prepare a FP	FPs selected for funding	GAs signed in 2018
11	▪ Exploitation of IMI project results	Single stage	19/07/2017	24/10/2017	6	39	3	3	3
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	7	7	7
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)	Two stage	30/11/2017	28/02/2018	38	500	13	13	open

IMI2 Call	Topic title	Call pro-cess	Launch date	Deadline for sub-mission of SPs	SPs received	Particip-ants in eligible SPs, FPs	SPs selected to prepare a FP	FPs selected for funding	GAs signed in 2018
	▪ A sustainable European induced pluripotent stem cell platform ▪ 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								
14	▪ Targeted immune intervention for the management of non-response and relapse ▪ Non-invasive clinical molecular imaging of immune cells ▪ Development of a platform for federated and privacypreserving machine learning in support of drug discovery	Two stage	15/03/2018	14/06/2018	28	384	7 [3]	open	open

[3] Topic 1 of IMI2 - Call 14 had 4 subtopics that merged at stage 2.

IMI2 Call	Topic title	Call pro-cess	Launch date	Deadline for sub-mission of SPs	SPs received	Particip-ants in eligible SPs, FPs	SPs selected to prepare a FP	FPs selected for funding	GAs signed in 2018
	▪ Centre of excellence – remote decentralised clinical trials								
15	▪ Integrated research platforms enabling patient-centric drug development ▪ Blockchain Enabled Healthcare ▪ Microenvironment imposed signatures in tissue and liquid biopsies in immune-mediated diseases ▪ Emerging translational safety technologies and tools for interrogating human immuno-biology ▪ Development and validation of translational platforms in support of synaptopathy drug discovery ▪ Digital endpoints in neurodegenerative and immune-mediated diseases ▪ AMR Accelerator programme Pillar A: Capability Building Network to accelerate and validate scientific discoveries ▪ AMR Accelerator programme Pillar B: Tuberculosis drug development network to accelerate and validate scientific discoveries and advance the R&D pipeline of new and innovative agents to address the global tuberculosis epidemic	Two stage	18/07/2018	24/10/2018	42	570	8	open	open
16	▪ Progress new assets (one pre-new molecular entity (preNME) and one first-time-in-human (FTIH) start) for tuberculosis (TB) that act synergistically with bedaquiline, cytochrome bc or cytochrome bd inhibitors ▪ Progress novel assets (one FTIH start) for non-tubercular mycobacteria (NTM) that may act synergistically with bedaquiline and cytochrome bc drugs	Single stage	18/07/2018	24/10/2018	6	42	5	5	open

IMI2 Call	Topic title	Call pro-cess	Launch date	Deadline for sub-mission of SPs	SPs received	Particip-ants in eligible SPs, FPs	SPs selected to prepare a FP	FPs selected for funding	GAs signed in 2018
	▪ Discover and progress novel assets with new mechanisms of action (one preNME for TB and one preNME for NTM) and biomarkers for TB and NTM infection ▪ Determination of gepotidacin levels in tonsils and prostatic tissue ▪ Infection site targeting, antibiotic encapsulated in nanoparticles for treating extracellular bacterial infections ▪ Functional Ethionamide boosters: a novel combination for tuberculosis therapy ▪ Intravenous treatments of serious infections (urinary tract infections (UTI), intra-abdominal infections (IAI) & hospital-acquired pneumonia/ventilator associated pneumonia (HAP/VAP)) caused by Gram(-) bacteria (Enterobacteriaceae +/- Pseudomonas and/or Acinetobacter)								

Table summarising IMI2 Calls for proposals launched in 2018, highlighting the priorities of Annual Work Plan 2018 implemented, the date of Call launch and budget available per Call

IMI2 Call	Call type	Number of topics	Annual Work Plan 2018 Priorities implemented	Launch date	Budget (in EUR)		
					EU	EFPIA	Associated Partners
14	Two stage	4	▪ Immunology ▪ Digital health and patient centric evidence generation	15/03/2018	82 357 000	84 832 860	87 500
15	Two stage	8	▪ Neurodegeneration and other Neuroscience Priorities ▪ Immunology ▪ Infection control including vaccines ▪ Digital health and patient centric evidence generation	18/07/2018	171 875 862	143 595 500	71 251 500
16	Single stage	7	▪ Infection control including vaccines	18/07/2018	46 900 000	*See note*	*See note*

Note re IMI2 – Call 16: As this was a single-stage Call for proposals, no EFPIA / Associated Partner contributions were indicated at Call launch. However, this Call is expected to attract EFPIA / Associated Partner contributions.

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

Evaluation experts

In 2018, IMI used 219 experts from 35 countries in the evaluation of IMI2 - Calls 8, 12, 13, 14, 15 and 16. Most of the experts (89.05 %) came from EU and Horizon 2020 (H2020) associated countries. Almost half of the experts (104) came from academia (86), and research organisations (18). Other experts came from private for-profit entities (36), public bodies (28), and other types of organisations (51).

Call	Total no. experts	Science evaluation	Ethical screening	Observers	Gender Female	Gender Male
IMI2 - Call 8, 5th cut-off	9	5	3	1	4	5
IMI2 - Call 12, stage 2	46	38	6	2	18	28
IMI2 - Call 13, stage 1	70	68	0	2	30	40
IMI2 - Call 13, stage 2	73	59	12	2	32	41
IMI2 - Call 14, stage 1	22	21	0	1	8	14
IMI2 - Call 15, stage 1	59	57	0	2	27	32
IMI2 - Call 16, single stage	17	11	4	2	7	10

IMI2 – Call 8

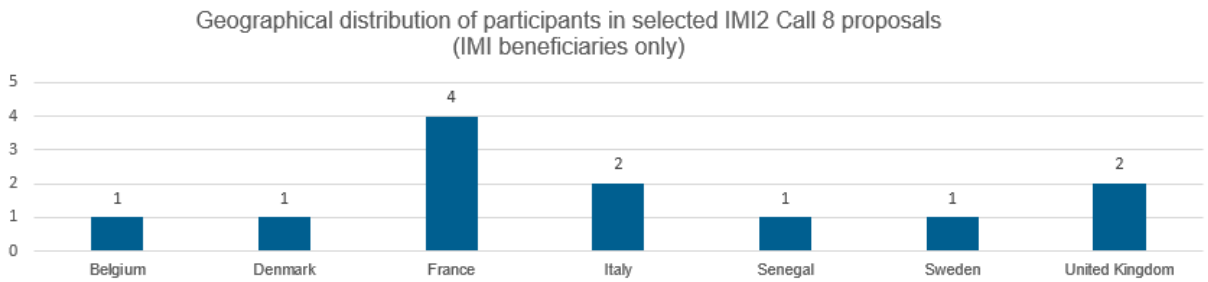
Progress in 2018: 4th cut-off date – GA signature. 5th (final) cut-off date: from FP submission and evaluation to GA.

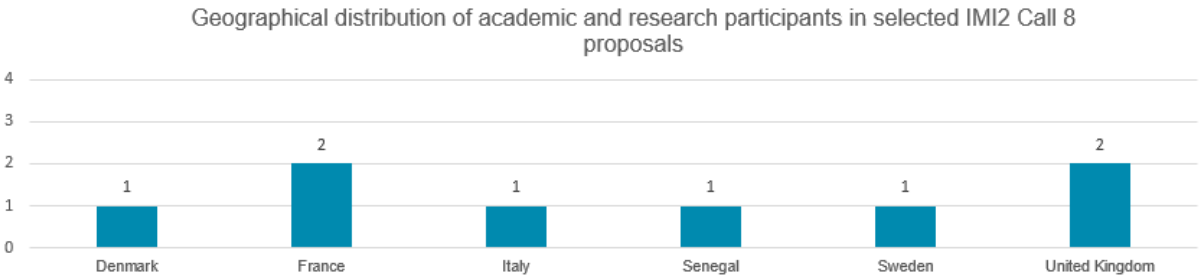
IMI2 - Call 8 (H2020-JTI-IMI2-2015-08-single stage) on Ebola and other filoviral haemorrhagic fevers (Ebola +) programme: future outbreaks consists of a single topic with multiple cut-off dates. The Call was launched on 18 December 2015 with deadlines for submission of FPs of 16 March 2016, 15 September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

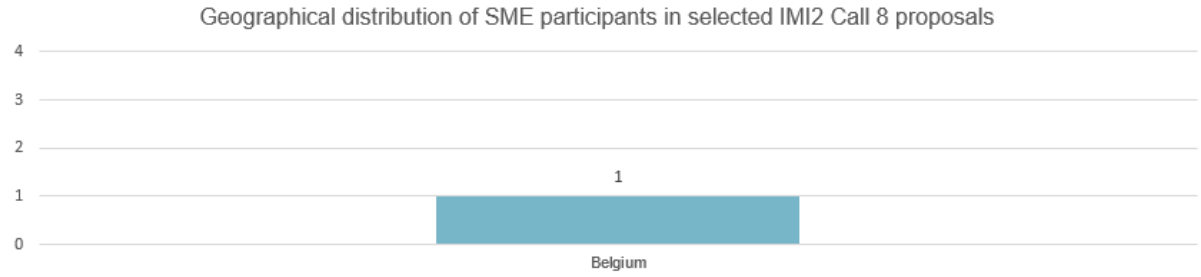
The GA for the EBOVAC3 project, which resulted from the proposal submitted in response to the 4th cut-off date was signed in the first part of 2018.

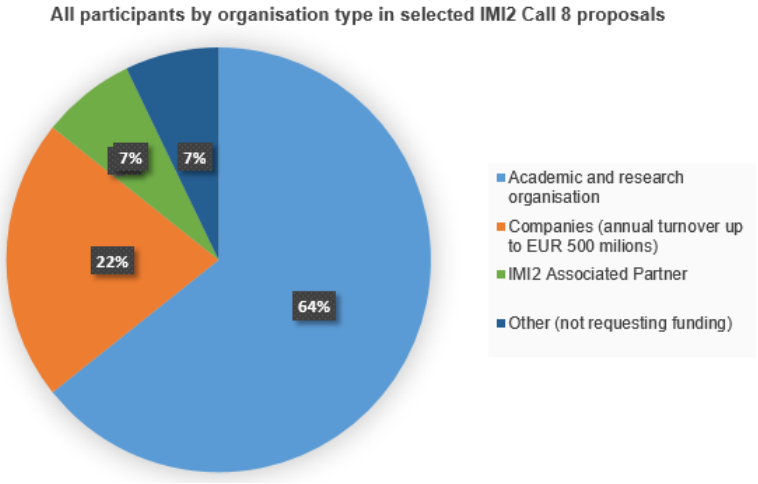
The proposals submitted in response to the 5th (and final) cut-off date were evaluated according to the IMI rules and procedures. The Governing Board approved the evaluation results on 25 May 2018. The winning consortium was invited to start GAP and the GA was signed before the end of 2018.

IMI2 – Call 8, 5th cut-off date: Participant details









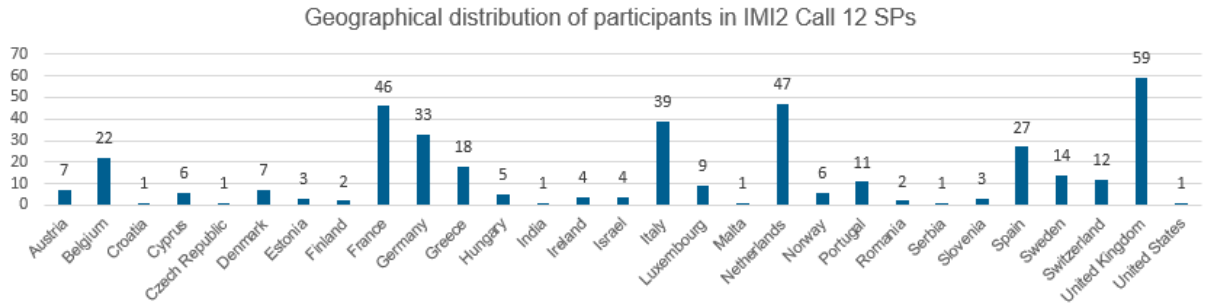
IMI2 – Call 12

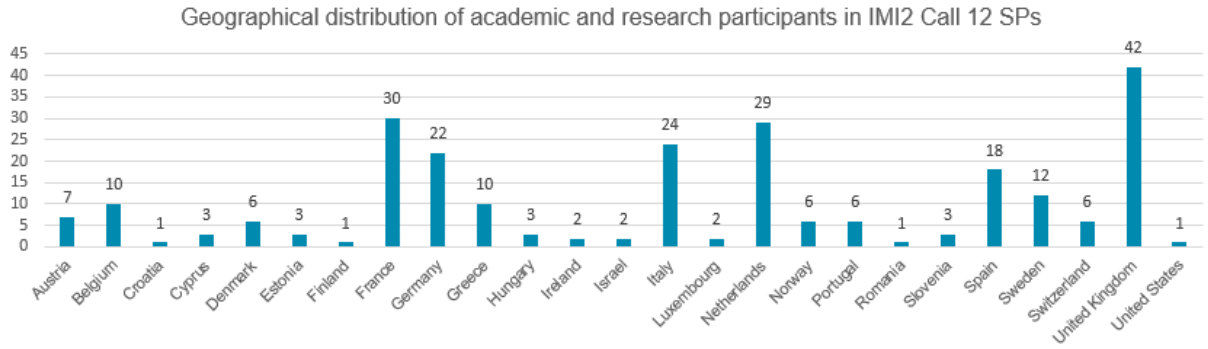
Progress in 2018: from informing the applicants about the stage one evaluation results to GA signature.

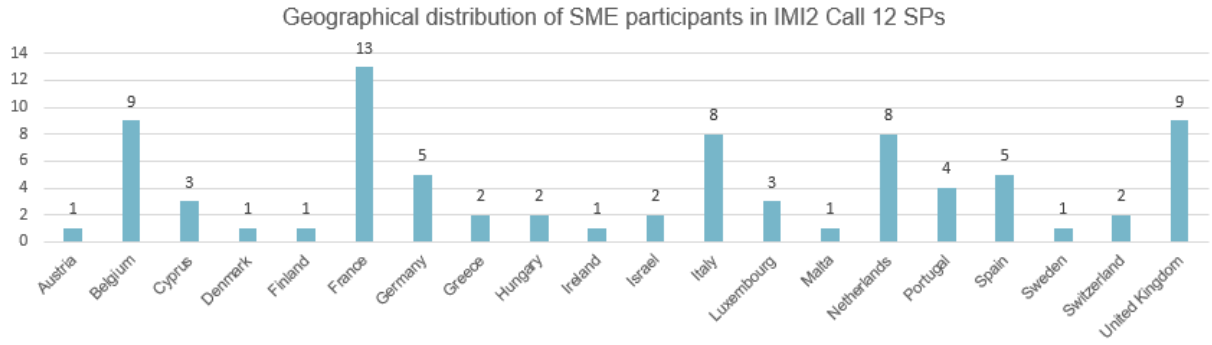
IMI2 Call 12 (H2020-JTI-IMI2-2017-12-two-stage) was launched on 19 July 2017 with seven topics and a submission deadline of 24 October 2017 for SPs. The evaluation of the SPs was completed successfully according to the IMI rules and procedures in 2017. In February 2018, following Governing Board approval of the evaluation results, the first-ranked SPs were invited to prepare a FP together with the pre-defined industry consortium. The submission deadline for FPs was 16 May 2018.

The stage-two evaluation was successfully concluded and the IMI Governing Board approved the evaluation results on 9 July 2018. The applicants were invited to start GAP and the seven grants were signed before the end of 2018.

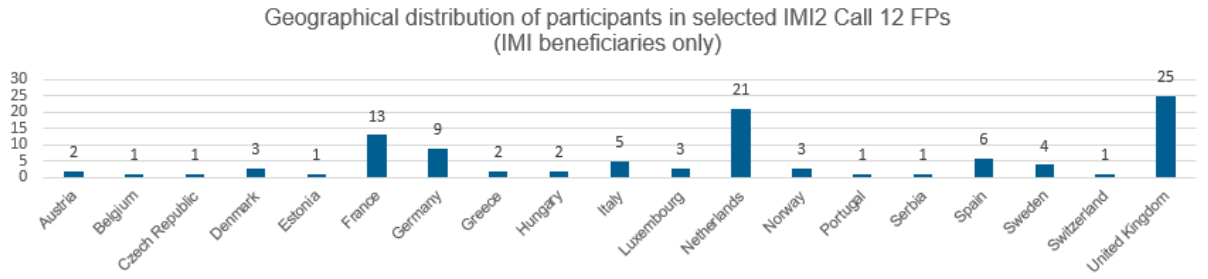
IMI2 – Call 12: Short proposal participant details

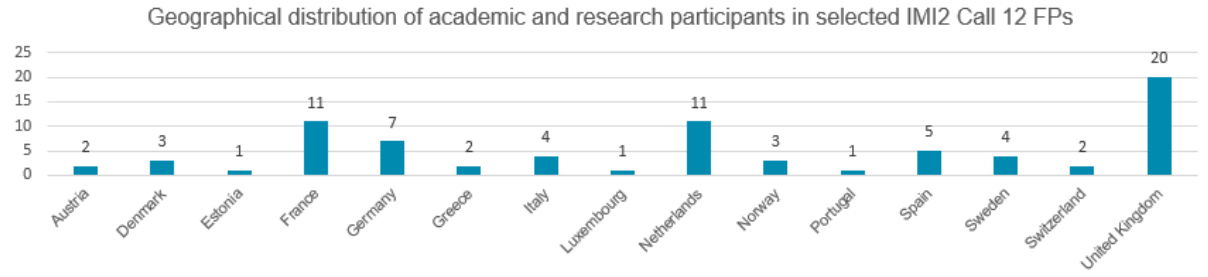


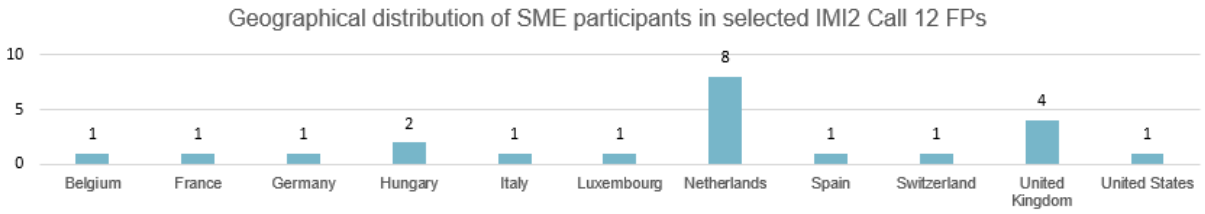


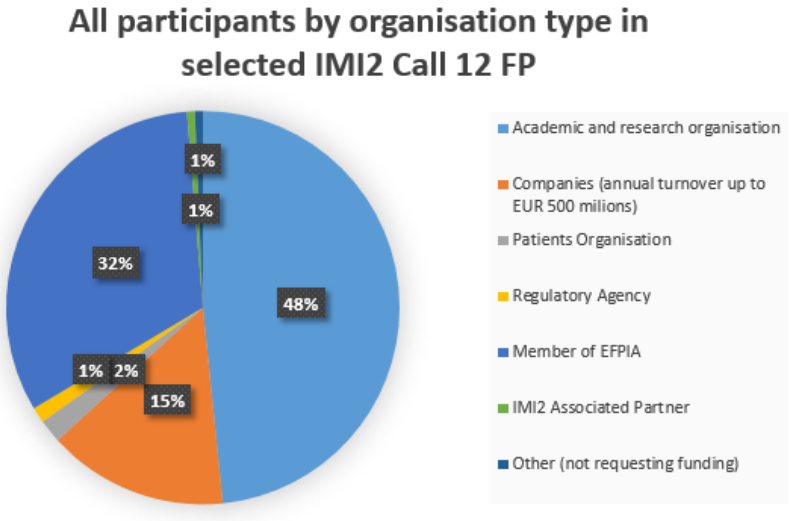


IMI2 – Call 12: Full proposal participant details









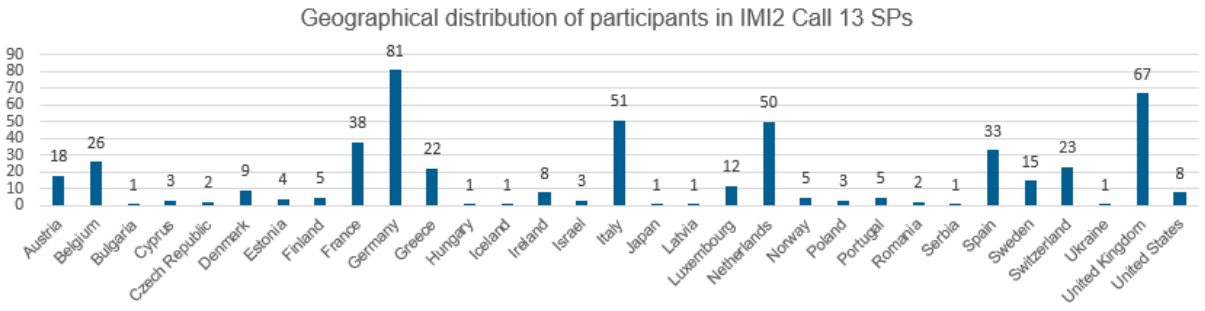
IMI2 – Call 13

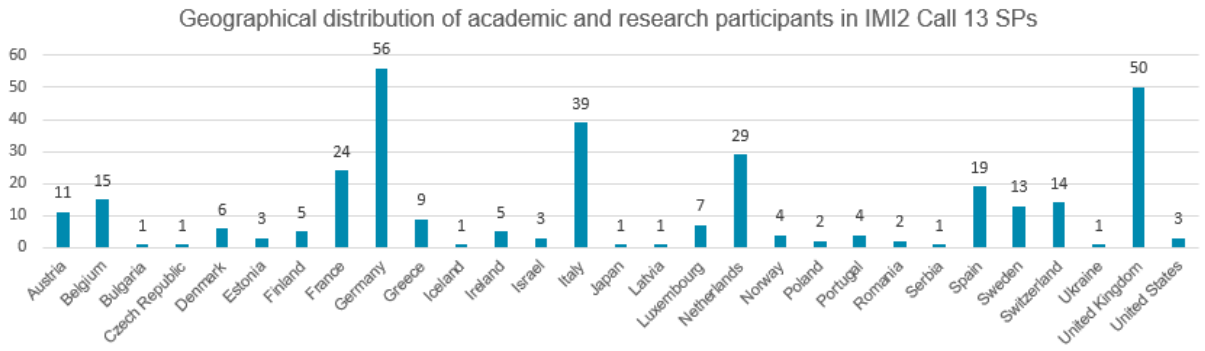
Progress in 2018: from stage one evaluation of SPs to the sending of the invitation letters to start GAP.

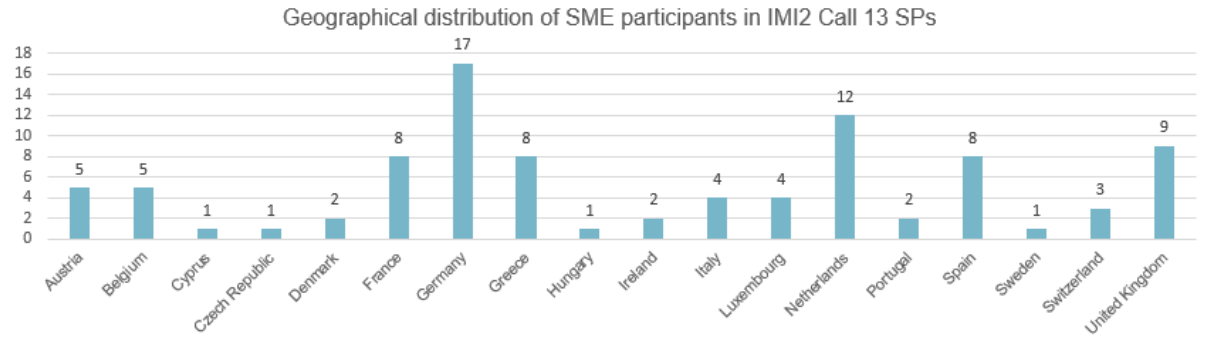
IMI2 – Call 13 (H2020-JTI-IMI2-2017-13-two-stage) was launched on 30 November 2017 with a submission deadline of 28 February 2018. The submission of SPs at the stage one was completed successfully according to the IMI rules and procedures and the Governing Board approved the evaluation results on 4 May 2018. The first-ranked SP in each of the 13 topics was invited to prepare an FP together with the pre-defined industry consortium, with a submission deadline of 6 September 2018.

The stage two evaluation was successfully concluded and the IMI Governing Board approved the evaluation results on 26 October 2018. The applicants were invited to start GAP, with the aim of having the GAs signed in the first part of 2019.

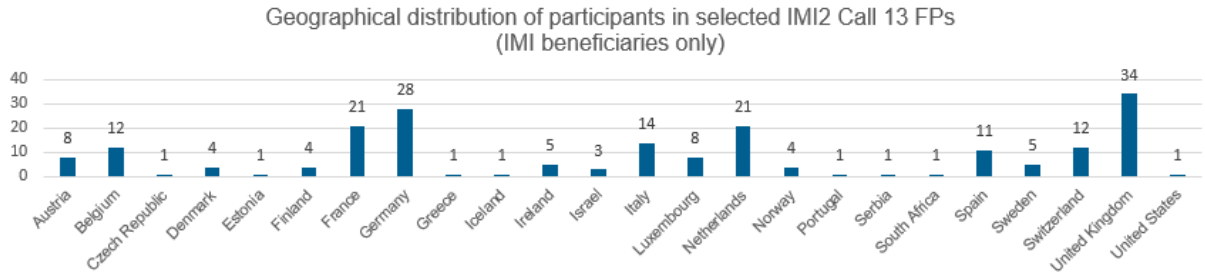
IMI2 – Call 13: Short proposal participant details

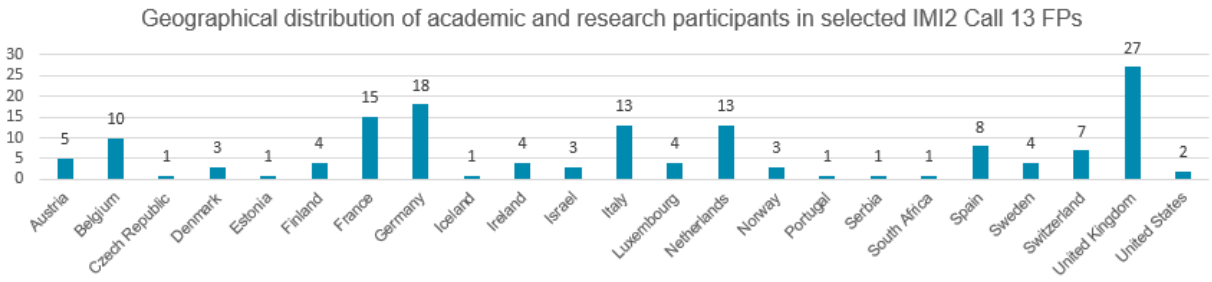


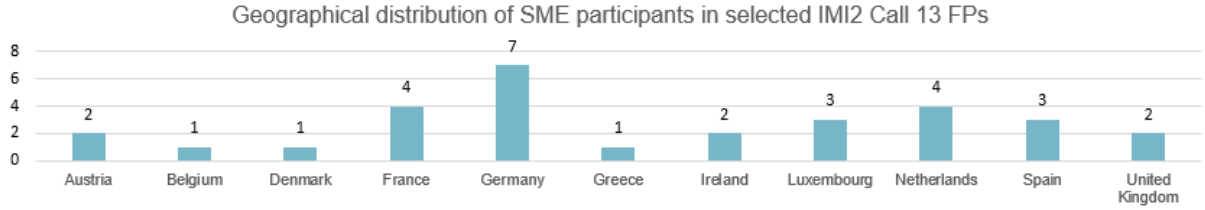


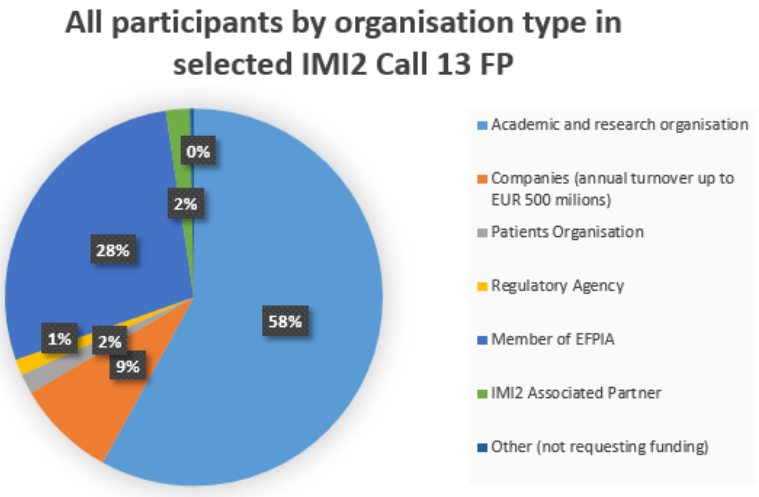


IMI2 – Call 13: Full proposal participant details









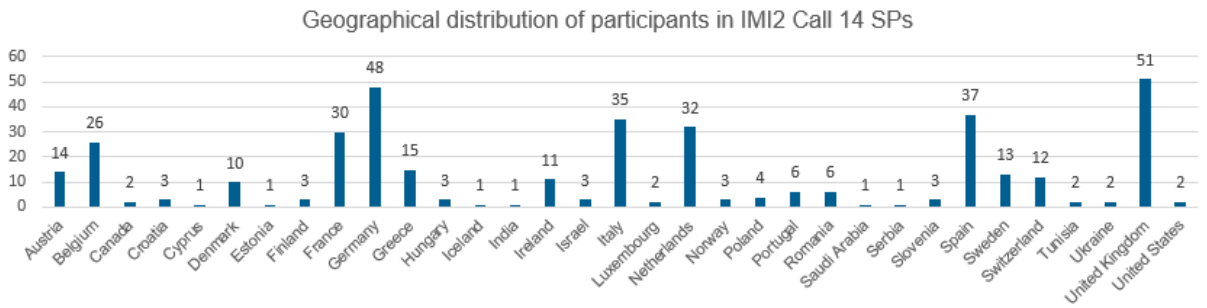
IMI2 – Call 14

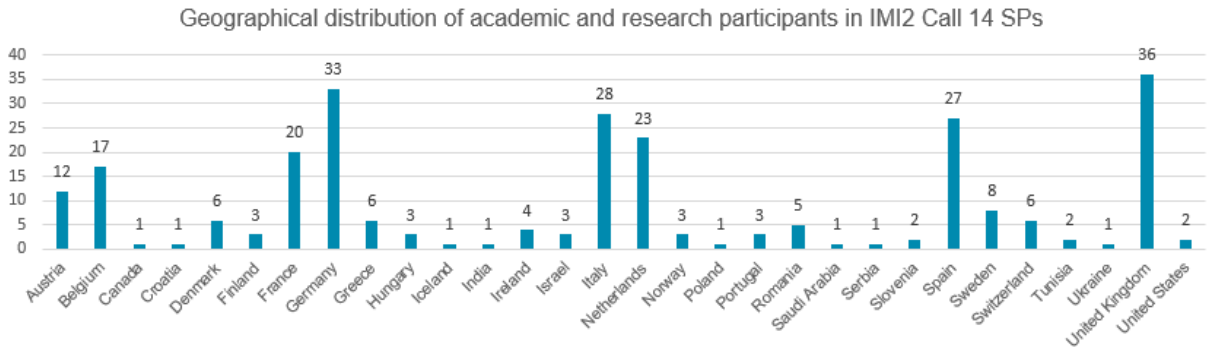
Progress in 2018: from Call launch to the opening of the remote evaluation of FPs.

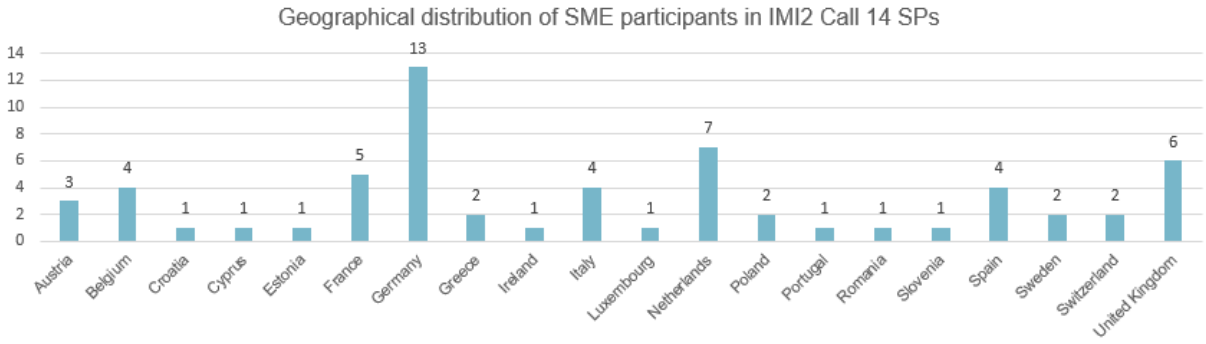
IMI2 – Call 14 (H2020-JTI-IMI2-2018-14-two-stage) was launched on 15 March 2018 with four topics and a submission deadline of 14 June 2018 for SPs. The evaluation of the SPs was completed successfully according to the IMI rules and procedures. In August 2018, following the approval of the evaluation results by the Governing Board, the first-ranked proposal in each topic (or subtopics in topic 1, which had 4 subtopics) was invited to prepare an FP together with the pre-defined industry consortium.

The submission deadline for stage two was 11 December 2018. The remote evaluation for the four FPs submitted started on 14 December 2018.

IMI2 – Call 14: Short proposal participant details





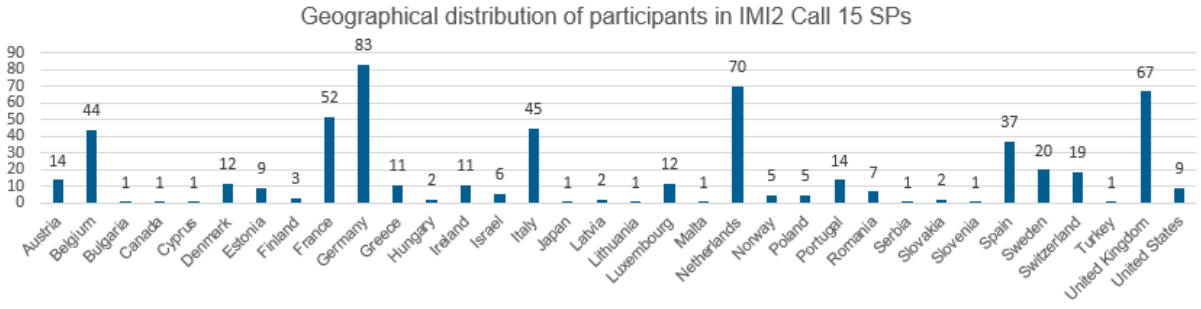


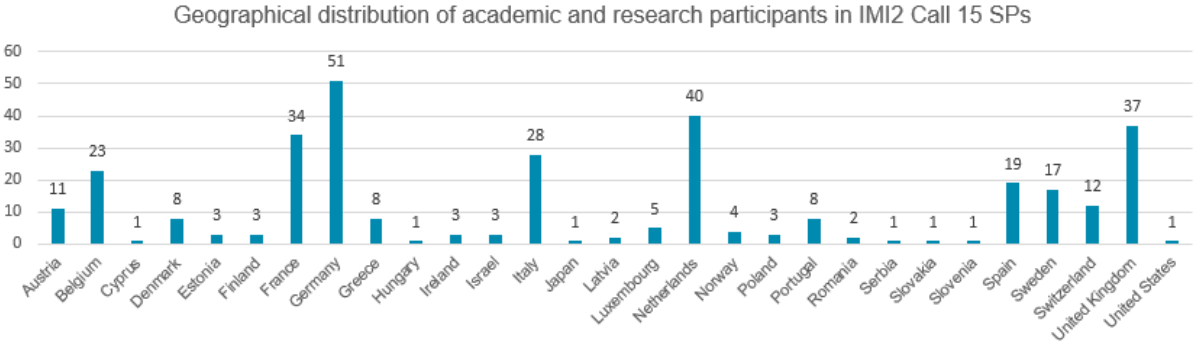
IMI2 – Call 15

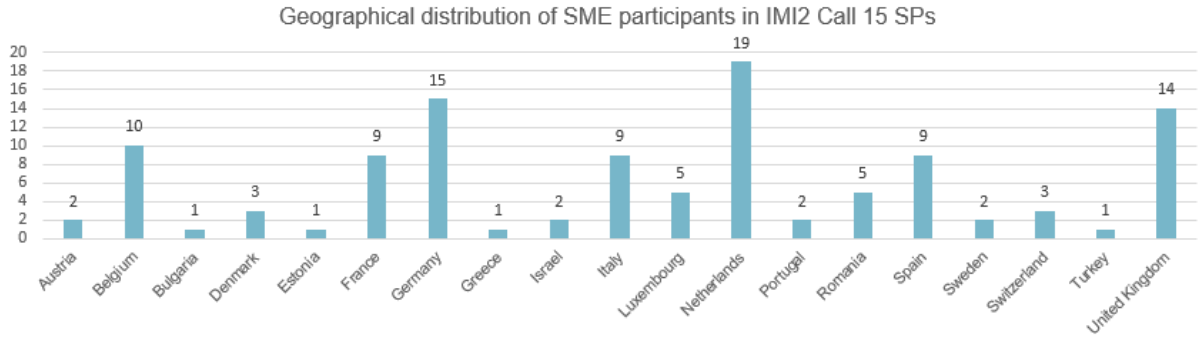
Progress in 2018: from Call launch to approval of the SP evaluation results by the Governing Board.

IMI2 – Call 15 (H2020-JTI-IMI2-2018-15-two-stage) was launched on 18 July 2018 with eight topics and a submission deadline of 24 October 2018 for SPs. The evaluation of the SPs was completed according to the IMI rules and procedures and the Governing Board approved the evaluation results on 18 December 2018. The first-ranked SPs will be invited to prepare a FP together with the pre-defined industry consortium in January 2019.

IMI2 – Call 15: Short proposal participant details





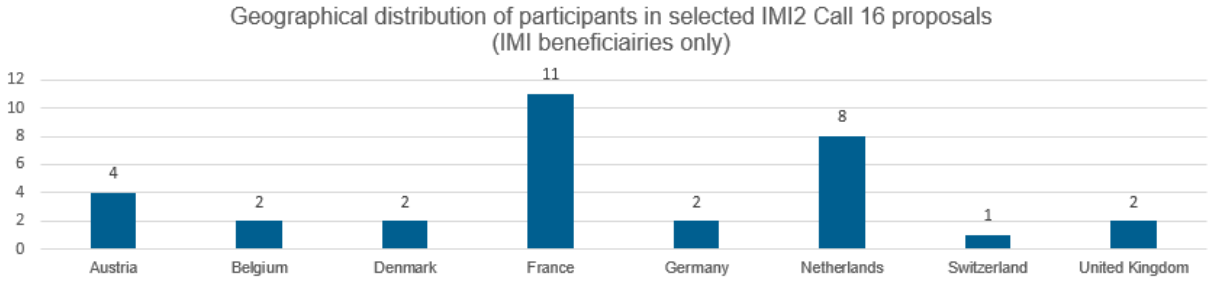


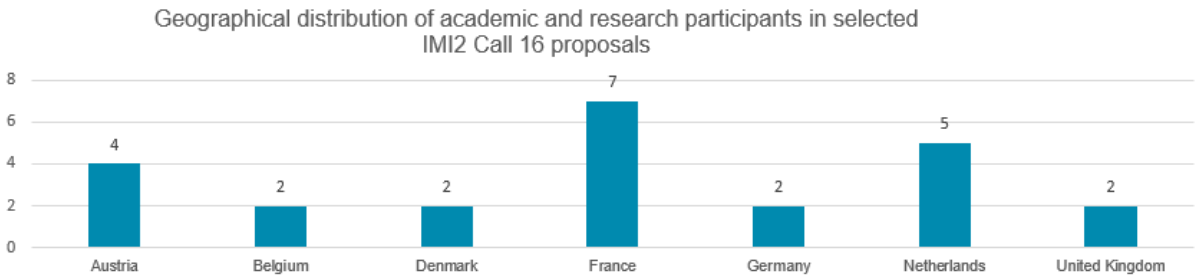
IMI2 – Call 16

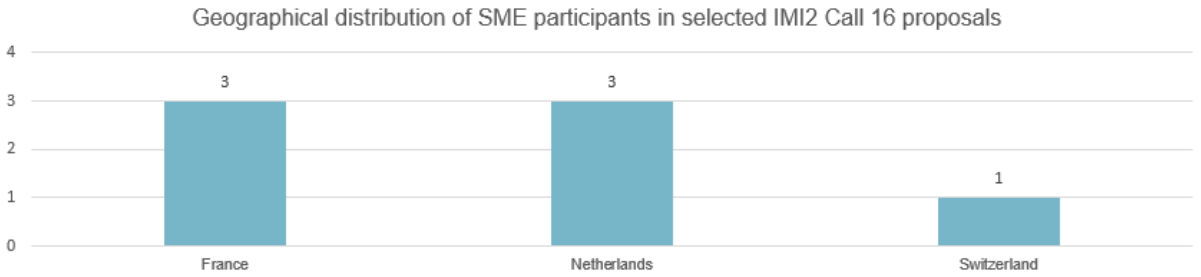
Progress in 2018: from Call launch to approval of the evaluation results by the Governing Board.

IMI2 – Call 16 (H2020-JTI-IMI2-2018-16-single-stage) was launched on 17 July 2018 with a submission deadline of 24 October. The evaluation of the proposals submitted in response to six out of the seven topics was completed successfully according to the IMI rules and procedures in November 2018. On 18 December 2018, the Governing Board approved the evaluation results. The consortia of the five selected proposals will be invited to start GAP in January 2019.

IMI2 – Call 16: Participant details







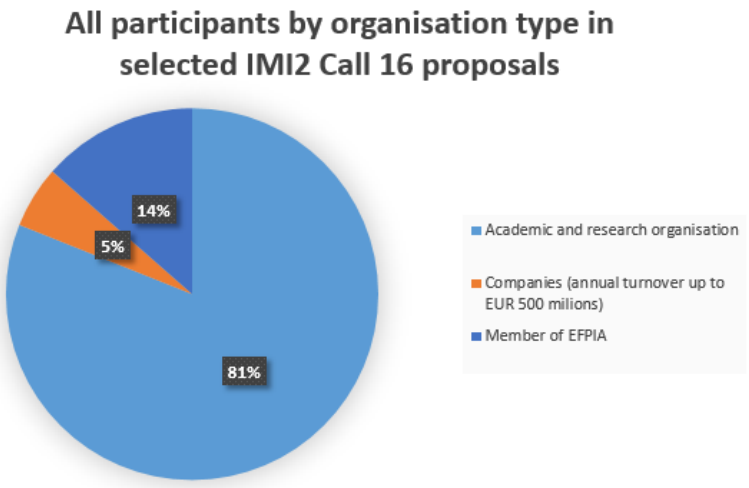

All participants by organisation type in selected IMI2 Call 16 proposals
14%
5%
81%
Academic and research organisation
Companies (annual turnover up to EUR 500 milions)
Member of EFPIA

Table summarising the number of beneficiaries and budgets for projects with GAs signed in 2018

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)
8	EBOVAC3	7	1	0	29 402 656			0	29 402 656	21 335 376		50 738 032
8	VHFMODRAD	13	0	1	2 448 763	575 220		292 030	3 316 013	0	1 574 000	4 890 013
10	AIMS-2-TRIALS	41	5	3	47 159 381	1 136 869		6 703 749	54 999 999	2 654 856	55 620 060	113 274 915
10	c4c	37	10	0	59 196 500	573 750	1 677 250	5 552 500	67 000 000	73 496 816		140 496 816
10	Hypo-RESOLVE	14	5	4	11 917 182	502 125		1 030 750	13 450 057	10 316 000	3 008 525	26 774 582
10	iConsensus	12	7	0	2 416 500	2 283 500		0	4 700 000	4 700 000		9 400 000
10	IMI-PainCare	34	6	0	9 901 436	1 187 555	22 530	113 750	11 225 271	12 030 000		23 255 271
10	PARADIGM	13	21	0	1 437 240	1 017 328	1 796 363	248 000	4 498 931	4 601 344		9 100 275
10	PIONEER	24	8	0	4 448 756	1 411 250	79 994	60 000	6 000 000	6 402 174		12 402 174
10	ReSOLUTE	7	6	0	10 858 750	1 141 250		0	12 000 000	11 600 000		23 600 000
11	EFOEUPATI	5	7	0	3 750		249 578	111 915	365 243	238 800		604 043
11	GetReal Initiative	7	9	0	918 200	411 800	90 000	330 000	1 750 000	1 350 688		3 100 688
11	WEB-RADR 2	7	4	0	87 500			1 081 250	1 168 750	615 629		1 784 379
12	EHDEN	11	11	0	10 409 563	2 849 938	236 250	610 000	14 105 750	14 811 607		28 917 357
12	ESCULAB	11	8	1	8 876 599	8 495 594		877 800	18 249 993	17 669 327	810 000	36 729 320
12	FAIRPlus	16	7	0	3 278 266	717 884		0	3 996 150	4 232 500		8 228 650
12	IM2PACT	20	7	0	8 045 249	954 751		0	9 000 000	8 410 136		17 410 136

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)
12	NECESSITY	22	4	0	7 850 000	300 000	50 000	0	8 200 000	7 225 020		15 425 020
12	RADAR-AD	11	4	1	3 815 598	903 659	230 500	50 000	4 999 757	2 327 402	223 132	7 550 291
12	VITAL	17	7	0	5 022 531	477 351		0	5 499 882	6 927 335		12 427 217

1.4.2 Interim reviews for IMI projects

In 2018, IMI conducted 10 reviews of projects from IMI1 - Calls 6, 9 and 11, and IMI2 - Calls 3, 5 and 6, as shown in the table below. The expert reviewer panels consisted of at least three experts, one from each of the IMI Scientific Committee and the full project proposal evaluation panel, and one selected from suggestions by the consortium.

Interim Reviews for IMI1 – Calls 6, 9 and 11

IMI project acronym	Full project name	Call #	Interim review
APPROACH	Applied public-private research enabling osteoarthritis clinical headway	IMI1 - Call 11	24/04/2018
COMBACTE-MAGNET	Combatting bacterial resistance in Europe - molecules against Gram negative infections	IMI1 - Call 11	26/06/2018
COMBACTE-CARE	Combatting Bacterial Resistance in Europe - Carbapenem Resistance	IMI1 - Call 9	27/06/2018
COMBACTE-NET	Combatting Bacterial Resistance in Europe	IMI1 - Call 6	28/06/2018
iABC Programme	Inhaled antibiotics in bronchiectasis and cystic fibrosis	IMI1 - Call 11	30/11/2018

APPROACH

The reviewers reported that the overall objectives of the project as defined in the Description of Work (DoW) are still valid and that efforts should be continued to reach them in the time frame of the project. The majority of the planned milestones and deliverables have been achieved within each work package. The delay in some of them was justified and should not affect the final outcome of the project. The reviewers strongly recommend that the partners start to plan funding applications now to ensure that the resource is sustained and used in the future.

COMBACTE-MAGNET – COMBACTE-CARE – COMBACTE-NET

A panel of experts carried out the interim reviews of COMBACTE-MAGNET, COMBACTE-CARE and COMBACTE-NET in one go. By reviewing all three projects one after another, the reviewers had an opportunity to appreciate the ambition of the clinical work carried out by these three projects within the New Drug for Bad Bugs programme and the synergies among the projects.

COMBACTE-MAGNET aims to give antibiotic drug development a much-needed boost for the development of novel antibiotics against Gram-negative bacteria. COMBACTE-CARE is dedicated to meeting the challenge of carbapenem-resistant bacteria. COMBACTE-NET, for which this was the second review, aims to give antibiotic drug development a much-needed boost by pioneering new ways of designing and implementing efficient clinical trials for novel antibiotics.

Overall, the three projects showed significant progress, despite challenges faced in particular with delays in several clinical trials, with the development of the compounds that are in the projects. The delays were due in large part to the sheer complexity of the trials.

Among the achievements, the panel noted the conduct of the epidemiological studies, and the development of epidemiologic network EPI-Net. The experts considered the associated surveillance

dedicated EPI-Net website platform as a powerful and useful tool that should be developed further in collaboration with other groups undertaking similar work and should be sustained beyond the lifetime of the project.

They acknowledged the progress in COMBACTE-CARE of the EURECA observational study looking at clinical management and outcomes of hospitalised patients with serious carbapenem resistant Enterobacteriaceae (CRE) and carbapenem-resistant *Acinetobacter baumannii* (CRAB) infections; the completion of the Phase II study (REJUVENATE) evaluating the pharmacokinetics, safety and tolerability of aztreonam-avibactam (ATM- AVI) for complicated intra-abdominal infections in hospitalised adults; and the progress in setting up the global phase III study of ATM-AVI, a complementary IMI-BARDA (Biomedical Advanced Research and Development Authority) effort.

For COMBACTE-NET, the panel appreciated that the consortium responded to most of the recommendations from the initial review held in 2017 and recognised among the major achievements the expansion and maturation of the infrastructures: CLIN-NET, with increased capability and clinical research capacity as documented by enrolment in clinical studies, especially in Eastern Europe; LAB-NET, with additional training and improved external quality assessment and quality indicators across the lab network; STAT-NET, whose work will impact the design of new antibiotics for antibiotic resistant bacteria, with inclusion of some of their findings into recent PK/PD guidance from the EMA.

By reviewing the three projects, the reviewers could better assess the impact of the COMBACTE networks, CLIN-Net, LAB-Net, STAT-Net and EPI-Net, in particular through the work in the individual clinical trials; the pharmaceutical companies were positive about the tremendous benefits of having the clinical trials conducted by the consortia through the networks. They emphasised that these four networks represented an enormous potential value for present and future clinical trials in the area of antimicrobial resistance, and encouraged the teams to continue in further consolidating and sustaining these networks. The experts also made some recommendations with respect to strengthening risk management considering the complexity and challenges associated with these projects. Considering the importance of sharing with the community the valuable results generated by the projects, the panel encouraged also the three consortia to maximise the potential of open access to data, results and information.

iABC Programme

The iABC Programme aims to advance the development of inhaled antibiotics for patients with cystic fibrosis (CF) and bronchiectasis (BE). The panel noted that the project faced several changes that affected the overall scientific and technical achievements, in particular with the termination of the development of the compound from Basilea and the addition of early development activities for a new antibiotic from Polyphor. The panel considered nonetheless that the iABC project has provided a variety of assets that are beneficial for drug development in both patient populations. In particular the panel appreciated the excellent partnering activities that have led to the foundation of a huge international patient registry (EMBARC, European Bronchiectasis Registry) that will provide a significant resource to enable research and clinical studies in BE. The panel made some recommendations to the consortium on how to maximise the impact of the project results.

Interim Reviews for IMI2 – Calls 3, 5 and 6

IMI project acronym	Full project name	Call #	Interim review
ADAPTED	Alzheimer's disease apolipoprotein pathology for treatment elucidation and development	IMI2 - Call 5	12/04/2018
MOPEAD	Models of patient engagement for Alzheimer's disease	IMI2 - Call 5	15/05/2018
TransQST	Translational quantitative systems toxicology to improve the understanding of the safety of medicines	IMI2 - Call 6	14/06/2018
VAC2VAC	Vaccine lot to vaccine lot comparison by consistency testing	IMI2 - Call 3	27/11/2018
AMYPAD	Amyloid imaging to prevent Alzheimer's disease	IMI2 - Call 5	04/12/18

ADAPTED

The ADAPTED project aims to boost the development of new medicines by investigating an area of Alzheimer's disease (AD) research which has previously received little attention – the APOE gene. The APOE gene is a well-known risk factor for developing the disease, but precisely how this gene contributes to the risk of developing AD is not known. In light of the potential risks linked to the highly exploratory area and the short duration of the action (36 months), the project underwent interim review at the end of the first year of activities. The reviewers found that ADAPTED, which started in October 2016, has made significant progress during the first year. Collaborative relationships have been successfully established between all partners, in a harmonious public and private partnership, and the first tangible results are emerging. It is expected that this initial work will lead to substantially increase our knowledge about APOE biology and its fundamental impact on cognitive dysfunction in the context of Alzheimer's disease. The reviewers recommended the work to continue overall as planned, with some specific technical recommendations. In particular, specific legal and technical issues were or are being resolved, but have created delays. The reviewers asked the consortium to put in place a robust strategy and action plan to ameliorate the current delays and avoid similar issues in the future.

MOPEAD

MOPEAD aims to identify and test different models for engaging with individuals in the early stages of Alzheimer's disease (AD) in the general population ('hidden AD'), and determine which models work best in different contexts / European countries. As well as adding to our understanding of the earliest stages of dementia, the project will facilitate recruitment for clinical trials and, most importantly, ensure that patients are able to access support from early on in their disease. The reviewers found that MOPEAD is very ambitious given the complex construct of the project, which comprises four different models of patient engagement with different types of health care practitioners (HCPs) in five different countries. Overall progress is good. The project's most innovative approach is RUN 1, the Citizen Science Web Application. Because of the delay due mostly to ethical issues, some critical issues remain such as the recruitment rate and the referrals rate, with a potential negative impact on the amount and quality of the data to be analysed. The reviewers recommended that the duration of the project be extended from 33 to 39 months to allow the analysis of the data to be completed, to prepare educational and dissemination material and give enough time for the dissemination of the results.

TransQST

TransQST is orientated towards the development of translational quantitative systems-based toxicological models for four organs (liver, kidney, cardiovascular and gastro-intestinal system). Most interestingly, it will be built on existing pharmacokinetic/pharmacodynamic (PK/PD models) that have a physiological basis aiming to define systemic, as well as specific organ/cell exposure to drug and metabolites in a holistic fashion.

In the first year of the TransQST project assessed by the reviewers, two main foundations to support more accurate and predictive decision-making tools for quantitative human drug safety assessment were put in place:

- a data management platform to centralise the modelling data;
- a tool in the R-Shiny package to visualize and analyse toxicogenomic weighted correlation network analysis (WGCNA) module data has been developed. The tool is available to the broad scientific community (https://wgcna-lacdr-dds.nl) and dissemination activities are underway to raise awareness.

In addition, some important methodological work has also been initiated in all the relevant work packages. The panel of reviewers concluded that the project has achieved in general the objectives for the reported period, as shown by the accomplishment of the corresponding deliverables. To maximise the impact of the project result, the panel made some recommendations to the consortium on the methodology and including stakeholders' point of view.

VAC2VAC

The project brings together scientists from both the human and veterinary pharmaceutical industry along with academia and regulators to develop and validate non-animal tests; generate vaccine specific toolkits of consistency tests; increase our scientific understanding of vaccine quality; and contribute to the regulatory acceptance and routine use of non-animal tests during vaccine quality control testing.

This project has the potential to reduce greatly *in vivo* animal use for vaccine testing and the reviewers congratulated the consortium for their work to date. Whilst several problems have been encountered, the panel was satisfied that these have been adequately addressed and alternatives have been proposed. However while there has been a great deal of positive work done and progress made, there are still delays that need to be addressed and the reviewers requested the consortium to consider a relevant action plan.

AMYPAD

Deposits of beta amyloid protein in the brain are a common sign of Alzheimer's disease. AMYPAD is studying the value of using positron emission tomography (PET) imaging to scan people's brains for beta amyloid deposits. AMYPAD will carry out beta amyloid PET imaging on an unprecedented number of people suspected to be in the early stages of Alzheimer's disease. The goal is to determine the clinical added value of PET imaging in diagnosis and patient monitoring, and to develop data to establish its usefulness in clinical trials. The reviewers found that the scientific and medical objectives of AMYPAD are relevant, ambitious and address urgent medical issues posed by an aging population with increasing prevalence of Alzheimer's disease and related cognitive and neurodegenerative disorders. However, the reviewers expressed concerns for some activities being significantly behind schedule and asked the consortium for an aggressive action plan to address and correct the delays. The reviewers also had recommendations for enhancing the regulatory strategy of the project and the safety and ethics processes.

1.4.3 Progress against key performance indicators (KPIs) and statistics

The IMI2 objectives are far-reaching and ambitious and with that come inherent challenges in order to ensure the IMI2 project deliverables can be measured in a manner that is in line with these objectives.

In 2016 the IMI office initiated a piece of work which had the goal of creating (albeit retrospectively) a performance framework for IMI2 based on a logic model which strives to graphically represent how IMI's objectives and activities would eventually lead to the expected outcomes and impacts given the input investments made.

The logic model therefore tracks inputs - in terms of investments and other resources made available - to enable the programme implementation, the strategic focus of the activities, outputs during the implementation of the programme, outcomes that result in the completion of the action, and, finally, impacts - which may take some years after the programme has finished to be realised.

It is important therefore that the indicators that are measured during the programme implementation are clearly positioned on a trajectory which can deliver the expected impact. This is the philosophy behind the creation of a series of 10 key performance indicators that have been approved by the IMI Governing Board and tracked and reported on for the first time in this AAR 2018 in Annex 8.

The new set of 10 IMI key performance indicators focus on performance in the following strategic areas:

(1) the coverage of the research portfolio, showing adequate implementation of the annual scientific priorities;
(2) the achievements of the assets during the course of the IMI programmes;
(3) the impact of the IMI programmes on the regulatory framework;
(4) the ability of the IMI programs to set new standards (i.e. new taxonomies, new stratifications)
(5) the rate of contribution of non-pharma actors to the IMI programmes (e.g. non-pharma industries, foundations, charities, professional organisations);
(6) the accessibility of the resources/outputs beyond the IMI consortia partners;
(7) the level of co-authorships and cross-sector publications between European researchers;
(8) the adoption of the novelty generated by the IMI programmes by the industrial partners;
(9) the level of involvement of patients groups or healthcare professional association;
(10) the level of collaboration and SME participation so far.

The Programme Office has published the new set of 10 key performance indicators specific to IMI on its web site (www.imi.europa.eu/about-imi/mission-objectives) to ensure transparency, clarity and visibility of the new IMI performance indicators, communicating that these new indicators will be monitored yearly as part of the Annual Activity Reports for the year 2018 and beyond.

In 2018 the progress and achievements of the IMI1 and IMI2 programmes were measured against this new set of 10 KPIs specific to IMI activities. To enable the monitoring of these, the Programme Office has been working to redefine its performance evaluation methodology, to identify appropriate sources of information, to streamline the way information is collected, and to strengthen the consistency of internal processes and tools.

The analysis of the data collected up to 31 December 2018 shows that almost all the relevant priority areas in the IMI2 Strategic Research Agenda (SRA) are addressed by IMI2 projects (11 out of 12).

The data examination displays that the IMI2 projects have generated 16 assets that completed a significant milestone during the project lifecycle, and if we look at both IMI1 and IMI2 programmes together, the analysis shows that IMI2 projects have generated 57 assets that completed a significant milestone so far (versus an overall target of 50). The definitions of 'projects' asset' and 'significant milestone' were meticulously defined. Examples of assets are tools, methodologies, processes, services, training materials, etc.; examples of significant milestones are key clinical trial phases, animal models, prototypes, commercialisation, patents, publications, etc.

A subset of IMI projects managed to impact the regulatory framework and received acceptance by regulatory authorities: in IMI2 there are 7 completed procedures and if we look at both IMI1 and IMI2 programmes together there are 15 complete procedures (versus an overall target of 15).

Several new tools and processes generated by IMI2 projects have been implemented by the industry participants (examples of implementations are animal models, standards, biomarkers, SOPs, use of screening platforms, clinical trial networks, etc.). The data shows 19 implementation results in IMI2 and 122 implementation results if we consider both IMI1 and IMI2 programmes together (versus an overall target of 50).

Additionally, more than half of the projects involve patient organisations and healthcare professionals' associations as consortium partners, members of advisory boards, members of stakeholder groups etc. (63.46 %), and this trend increases year on year towards an ambitious target that was set at 80 %.

This analysis reveal a dynamic in which IMI projects are on track to meet the pre-defined targets. Nevertheless, it is clear that the number of outputs identified will rise over time, as many outputs arise in the later phases of the project lifecycle and very often even beyond the end date (after projects have been completed). This dynamic is in line with the nature of IMI projects, which involve research in the healthcare space, multi-stakeholder partnerships and cross-sector collaboration.

The Programme Office also continues 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.

In addition, with the goal of tracking IMI’s contribution to achieving the H2020 objectives, the Programme Office also collects data to report against the relevant standard H2020 key performance indicators. This allows 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.

1.5 Dissemination and information about project results

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

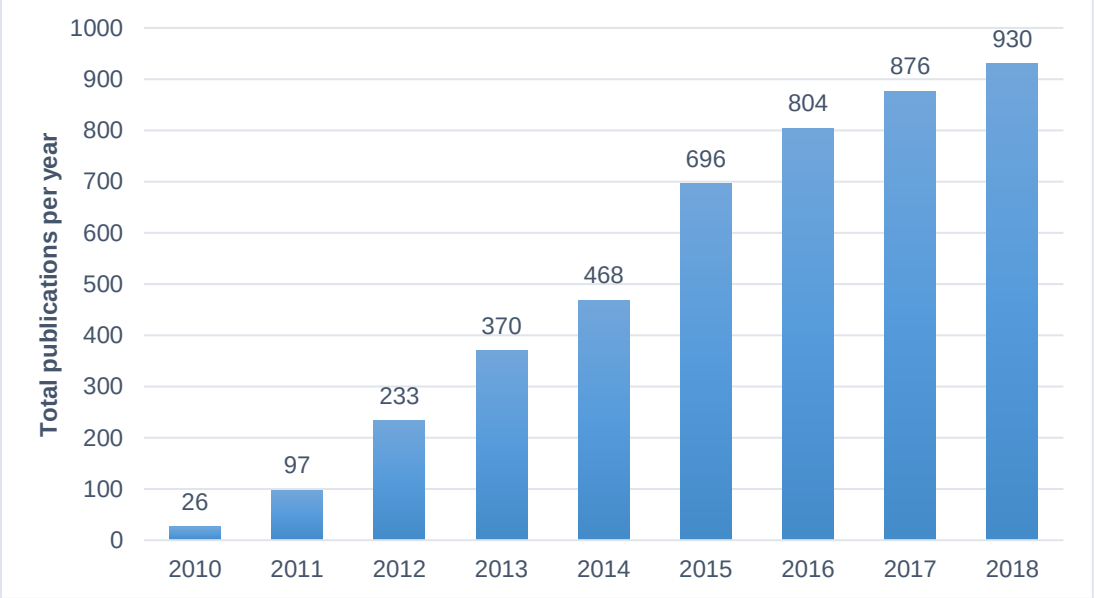
IMI consistently reminds its projects of the importance of dissemination, and in 2016 issued a practical guide on this which remains valid to date.

Publications from IMI projects

IMI has been monitoring and analysing the papers coming out of its projects since 2012. The analyses, carried out by Clarivate Analytics (formerly Thomson Reuters) have consistently demonstrated both the sheer volume and high quality of research taking place in IMI projects.

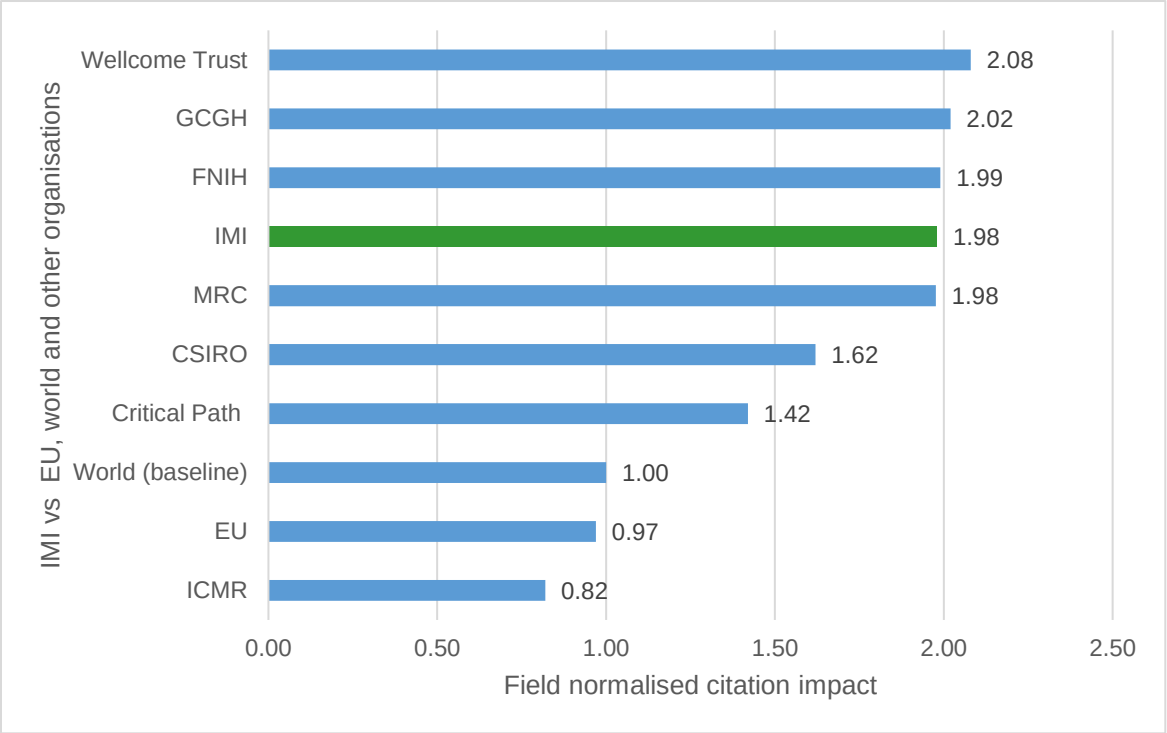
As the graph below shows, the number of publications is increasing year-on–year. In 2018 alone, IMI projects produced nearly **1 000** publications (930), bringing the total number of publications produced by IMI projects from 2010 to 2018 to **4 500**. With the number of IMI projects on the rise, this trend is set to continue for the coming years.

The number of IMI publications per year is increasing



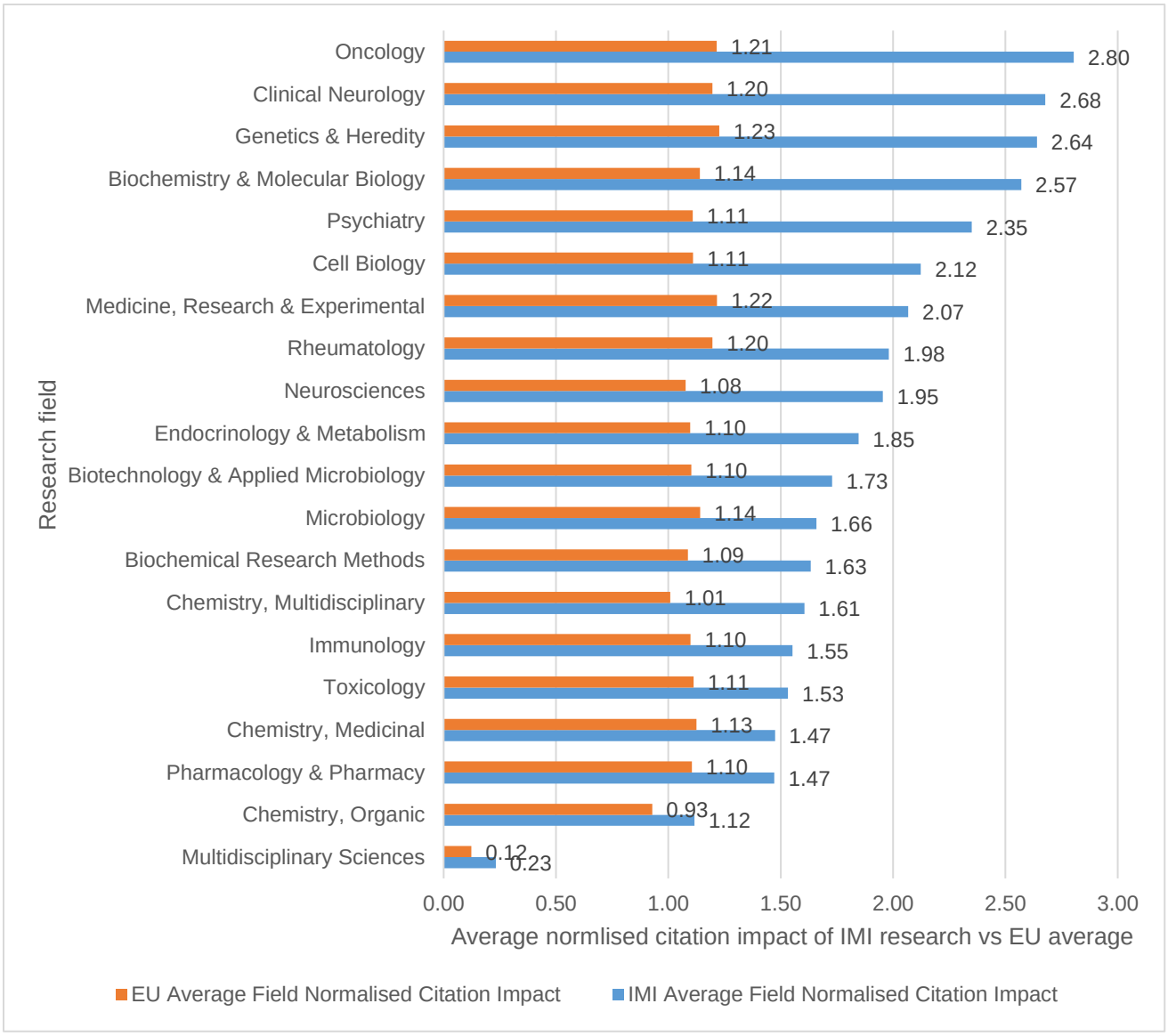
The citation impact of IMI research is higher than EU and world averages

The field-normalised citation impact for all IMI papers is **1.98** (compared to 0.97 for the EU and the baseline of 1 for the world). IMI is also compares favourably with similar organisations such as the Wellcome Trust, the Medical Research Council (MRC) and the Foundation for the National Institutes of Health (FNIH). This is similar to the result in previous years and shows that IMI is maintaining a high standard even as its output increases.



In all fields, IMI research has a higher citation impact than the EU average

As the graph on the following page shows, IMI research is published in a range of fields within the biomedical sector. In all fields, IMI research has a higher citation impact than the EU average. This is most notable the case in the fields of Oncology, Clinical Neurology, Genetics and Heredity, Biochemistry & Molecular Biology where the IMI citation impact is between 2.5 and 3.



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

- 24.64 % of papers from IMI projects are ‘highly cited’, meaning they are in the top 10 % of papers by journal category and year of publication.
- IMI projects have published in 1 052 journals to date, and the average journal impact factor for IMI research is 6.24.
- Journals with a particularly high impact factor that have published IMI research include the New England Journal of Medicine, Lancet, Nature (and other Nature journals e.g. Nature Drug Discovery, Nature Cancer, Nature Immunology, Nature Genetics), Science, Chemical Reviews and the Journal of the American Medical Association (JAMA).
- The collaborative nature of IMI is reflected in the authorship of the papers, with over half of papers (60.58%) recording authors from more than one country.

Project snapshot

Going by the number of papers produced, the most prolific projects are unsurprisingly the older ones. The table below shows the top 10 projects, ranked by number of papers produced. As the figures show, most have citation impacts between 1.5 and 2.

Top 10 IMI projects producing the highest number of publications

Project	Total publications	Mean field normalised citation impact
BTCure	645	1.89
EU-AIMS	346	2.13
EMIF	229	2.65
NEWMEDS	187	2.27
ULTRA-DD	177	1.89
EUROPAIN	166	2.33
IMIDIA	137	1.66
ORBITO	130	1.64
CHEM21	117	1.78
TRANSLOCATION	115	1.52

Between 2010 and 2018, IMI published papers in **1 052 different journals**.

The tables below shows the top 10 journals in which IMI projects are published, ranked by number of IMI publications and by journal impact factor (JIF).

Top 10 journals by number of IMI publications

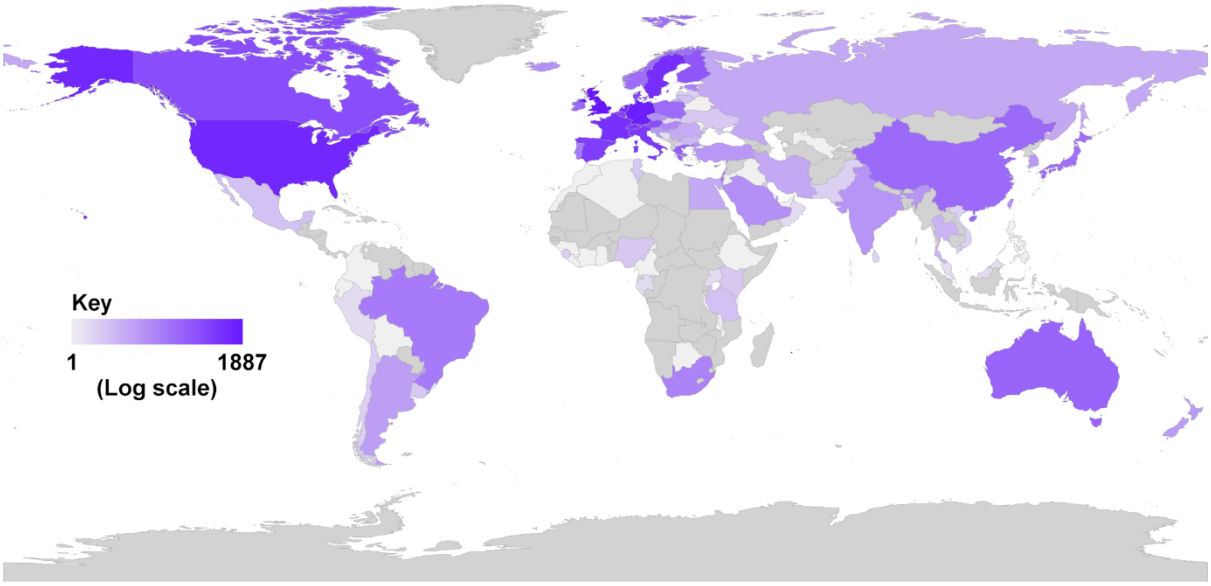
Rank	Title	JIF	IMI papers
1	PLoS One	2.77	163
2	Annals Of The Rheumatic Diseases	12.35	106
3	Scientific Reports	4.12	104
4	Diabetologia	6.02	50
4	Arthritis Research & Therapy	4.27	50
6	Nature Communications	12.35	49
7	Pain	5.56	47
8	European Journal Of Pharmaceutical Sciences	3.47	42
9	Psychopharmacology	3.22	42
10	Journal Of Alzheimer’s Disease	3.48	42

Top 10 journals by JIF

Rank	Title	JIF	IMI papers
1	New England Journal Of Medicine	79.26	1
2	Lancet	53.25	2
3	Chemical Reviews	52.61	2
4	Nature Reviews Drug Discovery	50.17	3
5	JAMA-Journal Of The American Medical Association	47.66	6
6	Nature Reviews Cancer	42.78	1
7	Nature Reviews Immunology	41.98	2
8	Nature	41.58	11
9	Nature Reviews Genetics	41.47	2
10	Science	41.06	8

The analysis also reveals the global reach of IMI's research activities. In total, **98 countries** have at least one paper funded by IMI.

Countries with at least one paper funded by IMI



The log scale shows countries having from 1 publication to 1 887 publications (UK being the top end with 1 887 publications).

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[4]. 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 2018

The total operational budget approved for 2018 was EUR 475.2 million in commitment appropriations (CA) and EUR 224.1 million in payment appropriations (PA). In 2018, the operational commitment and payment appropriations reached a level of 99.98 % and 86.69 % respectively.

The commitment appropriations related to H2020 were consumed by Grant Agreements implementing IMI2 - Calls 8 (fourth cut-off date), 10, 11 and 12, and by launching IMI2 – Calls 14, 15 and 16.

The payment appropriations related to H2020 were used by pre-financing for projects of IMI2 - Calls 10, 11 and 12 and by intermediate payments for projects of IMI2 – Calls 1, 2, 3, 4, 5, 6, 7 and 8.

On operational commitment appropriations, IMI has fully executed its annual budget (99.98 %).

As regards operational payment appropriations, execution reached 86.69 %. This is a significant increase and a rising trend in the absorption of operational payment appropriations in comparison to the previous years (69.39% in 2016, 71.96% in 2017). This result is due to a number of corrective measures applied in the budgetary planning and monitoring process.

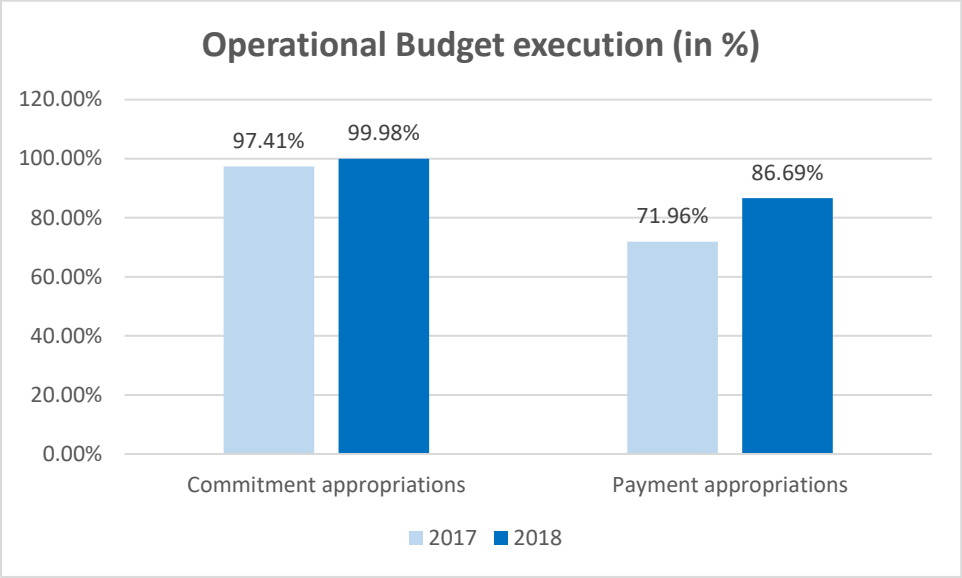
In order to break the cycle of low operational budget execution, the following actions were taken:

- As part of the Annual Work Plan, a fixed schedule of two Calls for proposals per year with a fixed launch time has been set out so as to ensure better operational planning of tasks and related financial transactions.
- In preparation of the 'Fiche Financière' for 2019 in January 2018, a very detailed forecast was prepared and the claim for new payment appropriations (C1 credits) was significantly reduced up front (to EUR 185 million) in order to integrate into the total budget envelope the carryover estimates between 2018 and 2019.
- Following the GB adoption of 2018 budget amendment No 3 , the Commission services reduced 2018 payment appropriations by EUR 35 million (Bourlange procedure).

Moreover, on the operational side, the slower implementation of the PERISCOPE project and some underspending triggered a temporary reduction of EUR 1 354 000 in the contribution of IMI2 JU Associated Partners (in 2018). However, as the project will run until 2021, the Associated Partner contribution will be disbursed in the coming years.

[4] 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 2018 operational budget execution compared with 2017.



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

	Execution of commitment appropriations in EUR Total		
	Appropriations	**Execution**	**%**
IMI1 (FP7) *	*204 875.37*	*149 036.58*	*72.74%*
IMI2 (H2020)	*475 055 530.82*	*475 010 686.05*	*99.99%*
Title 3 Implementing the research agenda of IMI	**475 260 406.19**	**475 159 722.63**	**99.98%**

**IMI1 (FP7) appropriations - amount recovered during 2018 from projects (assigned revenue)*

	Execution of payment appropriations in EUR Total		
	Appropriations	**Execution**	**%**
IMI1 (FP7)	66 850 254.71	58 886 630.36	88.09%
IMI2 (H2020)	157 327 880.74	135 461 705.62	86.10%
Title 3 Implementing the research agenda of IMI	**224 178 135.45**	**194 348 335.98**	**86.69%**

The commitments carried forward from 2017 to 2018 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 13, was de-committed at the end of 2018 and, based on the N+3 rule as set out in the IMI2 Financial Rules, the unused appropriations were carried over to the 2019 budget.

The table below shows the summary of commitments outstanding for operational expenditure per programme at the end of 2018.

Commitments carried forward from previous year 2017	Commitment appropriations in EUR				
	Carry forward	Commitments made during 2018	De-commitments	Payments	Commitments outstanding at the end of 2018
IMI1 (FP7)	246 089 317	149 037	817	58 886 630	187 350 906
IMI2 (H2020)	324 789 527	475 010 686	31 615	135 461 706	664 306 892
Total Title 3	**570 878 844**	**475 159 723**	**32 432**	**194 348 336**	**851 657 798**

EU funds committed under IMI1 and IMI2

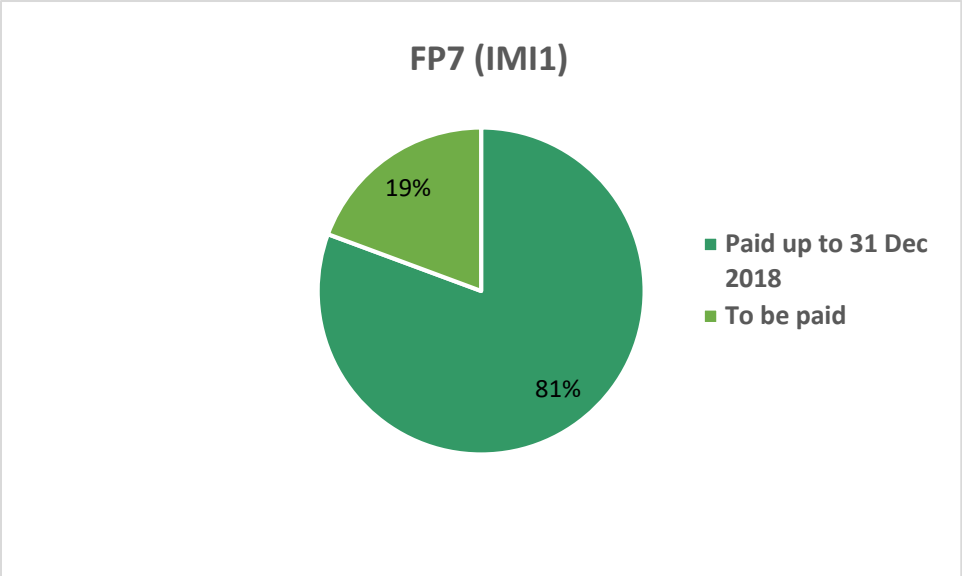
The table below outlines the breakdown per Call of EU committed funds for IMI1 (FP7).

EUR '000

FP7 (IMI1)	Committed (budget)	Paid up to 31/12/2018	To be paid
Call 1	116 082	114 641	1 441
Call 2	85 765	85 226	539
Call 3	112 840	109 230	3 610
Call 4	97 944	91 701	6 243
Call 5	79 999	79 355	644
Call 6	125 417	56 058	69 359
Call 7	13 000	11 699	1 301
Call 8	98 733	86 241	12 492
Call 9	56 441	37 311	19 130
Call 10	6 100	4 431	1 669
Call 11	173 410	102 490	70 920
Other	149	149	0
Total FP7 (IMI1)	**965 880**	**778 532**	**187 348**

At the end of 2018, 81 % of the commitment appropriations had been paid out. EUR 125 million were paid as advances (pre-financing) and EUR 653 million were paid for cost claims submitted by the projects. 16 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.

The graph below shows the percentage of what has been paid and what remains 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

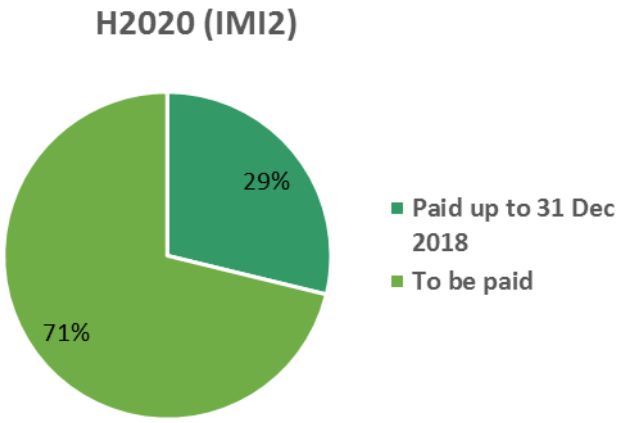
H2020 (IMI2)	Committed	Paid up to 31/12/2018	To be paid
Call 1	17 630	8 515	9 115
Call 2	114 090	86 588	27 502
Call 3 *	56 060	35 855	20 205
Call 4	1 130	1 078	52
Call 5	47 477	21 652	25 825
Call 6 *	46 696	21 762	24 934
Call 7	46 795	20 975	25 820
Call 8	47 462	15 900	31 562
Call 9 *	57 606	21 602	36 004
Call 10	173 874	56 576	117 298
Call 11	3 284	2 627	657
Call 12	64 052	21 978	42 073
Call 13 **	114 152	0	114 152
Call 14	82 357	0	82 357
Call 15	171 876	0	171 876
Call 16 ***	35 184	0	35 184
Other (late interests)	4	4	0
Total H2020 (IMI2)	1 079 728	315 112	764 616

** The Call 3 commitment includes a financial contribution from the Bill and Melinda Gates Foundation (BMGF), an IMI2 Associated Partner. The commitment for Calls 6 and 9 includes a financial contribution from EFPIA companies.*

*** The IMI2 - Call 13 level 1 commitment was de-committed at the end of 2018 and the amount carried over to 2019 because the Grant Agreements will be concluded and committed in January and February 2019. Therefore, the difference between total to be paid for H2020 and commitments outstanding for H2020 refers to the IMI2 - Call 13 amount.*

**** The IMI2 – Call 16 level 1 commitment was created for the amount of EUR 46 900 000. However, following evaluations that took place in December 2018, the total amount approved is EUR 35 184 000.*

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[5], the total IMI2 JU budget (in commitments) is up to EUR 1.638 billion, of which up to EUR 1.425 billion to match EFPIA in-kind contributions and up to EUR 213 million to match IMI2 Associated Partners' contributions.

As stated in Article 13 of the statutes, the part of IMI2 JU budget (in commitments) for administrative costs is EUR 85.2 million, shared equally between EC and EFPIA.

The IMI2 JU budget (in commitments) for operational costs is EUR 1.595 billion.

At the end of 2018, 67.7 % of the operational IMI2 JU budget in commitments had been committed (EUR 1.079 billion out of EUR 1.595 billion).

[5] 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[6].

On the one hand, in IMI projects, legal entities eligible for JU funding (beneficiaries receiving funding from IMI) receive financial support from IMI to fund their activities[7].

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[8], 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 JU funding.

This chapter presents the contributions of EFPIA companies and (for IMI2) IMI Associated Partners, including commitments made at Call and project launch, and actual contributions made during the lifetime of the projects. The equivalent EU commitments / contributions are also provided throughout this chapter to facilitate comparison; for both IMI1 and IMI2, the public and private contributions should match by the end of the programmes.

EFPIA companies and Associated Partners are contractually obliged to report to IMI all costs 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: EU funding up to EUR 966 million, to match the equivalent contributions from EFPIA.
- IMI2: EU funding up to EUR 1.425 billion, to match the equivalent contributions from EFPIA companies.
  An additional EUR 213 million in EU funding may be provided to match additional contributions from other Members, Associated Partners, or from their constituent entities or their affiliated entities.

IMI1 programme

This section highlights the commitments pledged by EFPIA companies. EFPIA's commitment to the IMI1 programme totalled EUR 965 million as of 31 December 2018, representing an increase of EUR 6.1 million from the previous year following amendments of existing projects. The EU commitment remained unchanged at EUR 965.7 million. There are 59 projects in the IMI1 portfolio.

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

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

[8] 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'.

IMI1 (EUR million)	Up to 31.12 2017	2018	TOTAL
EU commitment	965.7	N/A	**965.7**
EFPIA commitment	958.9	6.1	**965.0**

IMI1 EU and EFPIA contributions - comparison by year

As of 31 December 2018, EFPIA contributions of EUR 633.3 million had been formally validated (i.e. checked by IMI staff and / or audited by external auditors – see section 4.3). The table below gives an overview of validated IMI1 contributions for every year since the start of the programme.

IMI1 (EUR million)	Validated cost claims from beneficiaries *	Validated EFPIA in kind contributions
2010	0.5	
2011	15.2	
2012	33.5	52
2013	59.4	58
2014	80.5	132.2
2015	80.4	65.4
2016	141.9	80.9
2017	129.2	141.3
2018	112.5	103.5
TOTAL	**653.1**	**633.3**

(*) excluding pre-financing

For the IMI1 programme, there is currently a small imbalance (EUR 19.7 million) between the contributions from the EU and EFPIA; this is because in some projects, the tasks of EU-funded beneficiaries are carried out before the tasks of EFPIA companies. In 2018, the IMI Programme Office continued to closely monitor the overall commitments of industry participants. At the end of 2018, 16 of the 59 IMI1 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 planned.

IMI1 EU and EFPIA contributions - comparison by Call

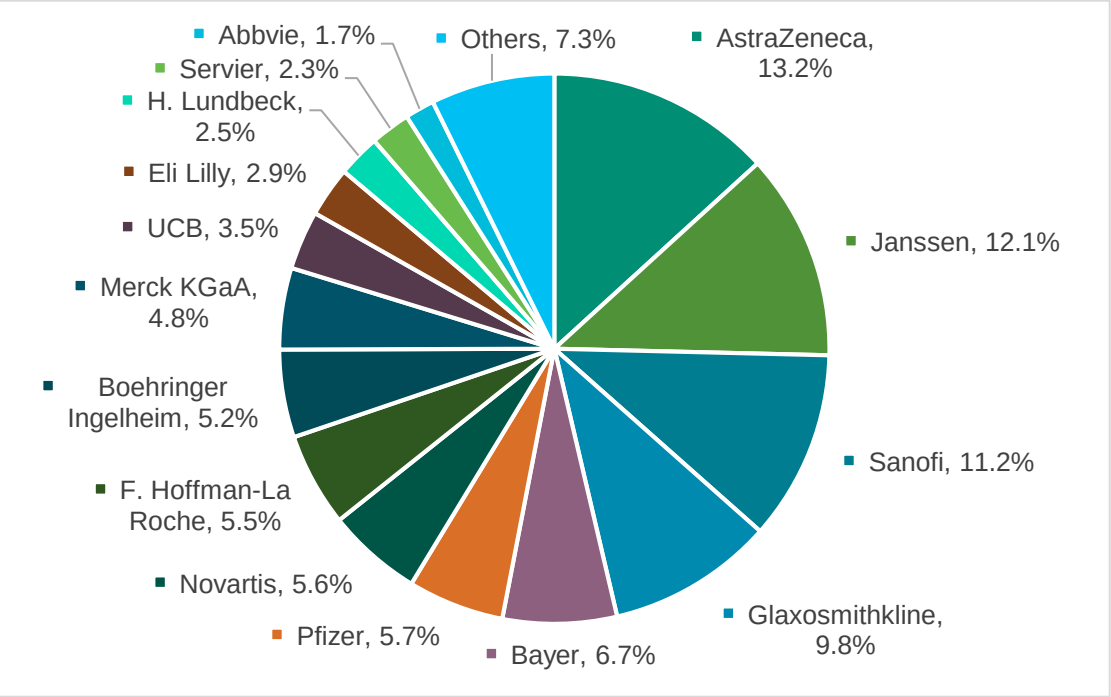
The following table provides a breakdown by Call of both EU funding (cost claims only excluding pre-financing) and validated EFPIA contributions for the whole IMI1 programme:

IMI1 Call	Projects	EU funding (EUR million)		%	EFPIA in kind (EUR million)		%
		Committed	Validated		Committed	Validated	
1-2008	15	116.1	114.3	98.5 %	149.9	150.3	100.2 %
2-2008	8	85.8	84.1	98.0 %	73.8	67.8	91.8 %
3-2010	7	112.8	102.3	90.7 %	73.8	63.7	86.4 %
4-2011	7	97.9	86.9	88.7 %	108.5	103.7	95.6 %
5-2012	1	80	79.3	99.2 %	91.7	90.9	99.2 %
6-2012	2	125.4	44.1	35.2 %	110.1	29.0	26.4 %
7-2012	2	13	8.3	63.5 %	11.9	7.0	58.3 %
8-2013	4	98.7	53.6	54.3 %	48.0	36.4	75.7 %
9-2013	4	56.4	22.0	39.0 %	89.1	27.3	30.7 %
10-2013	1	6.1	2.5	40.5 %	6.1	2.0	32.0 %
11-2013	8	173.4	55.7	32.1 %	202.1	55.3	27.3 %
Total	**59**	**965.7**	**653.1**	**67.6 %**	**965.0**	**633.3**	**65.6 %**

Note: for public (EU) funding, actual payments cannot exceed the commitments; eligible costs in excess of the grant amount are capped. However, for private funding, the EFPIA in-kind contribution may exceed the initial commitment; this explains why the validated in-kind contribution for Call 1 exceeds the initial commitment.

IMI1 EFPIA contributions - by company

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



Companies listed under 'Others' are: Abbott, AC Immune, AiCuris, Almirall, Amgen, Astellas, Basilea, Biogen Idec, Bristol Myers Squibb, Chiesi Farmaceutici, Da Volterra, Eisai, Esteve, Farmaindustria, Grünenthal, INFARMA, Ipsen, Menarini, Merck Sharp & Dohme, Novo Nordisk, Orion, Seqirus, Sigma-Tau, Takeda, Teva, VFA, Vifor

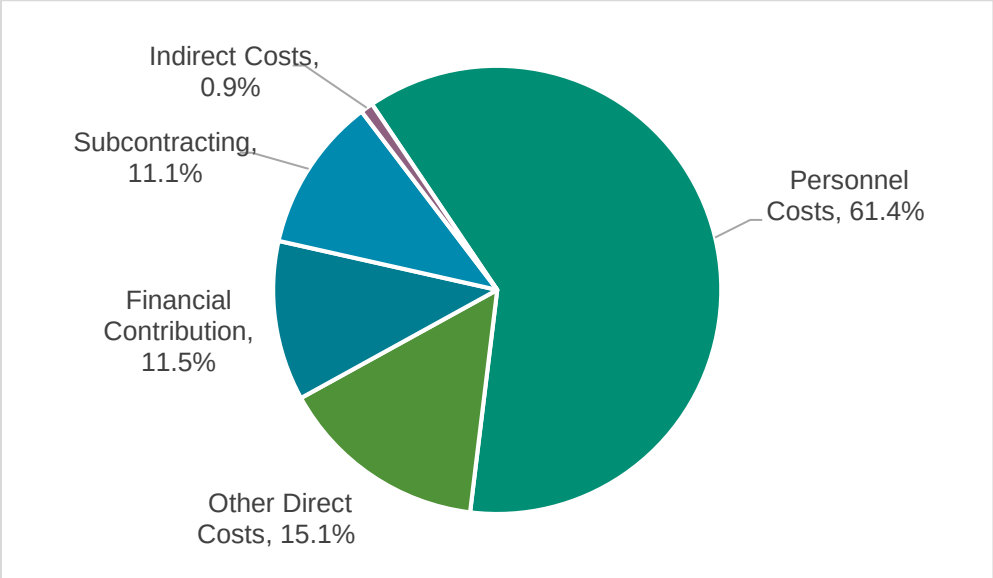
IMI1 EFPIA contributions - by cost category

The validated 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.

In addition, EFPIA contributions can also be provided through financial contributions (FC), i.e. 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 cover project costs, such as the purchase of consumables or equipment.

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



IMI2 programme

During 2018, 20 grant agreements were signed, bringing the total number of IMI2 projects to 60. The total budget of the IMI2 portfolio is:

- EUR 664.9 million in EU funding;
- EUR 655.6 million commitments from EFPIA companies (EUR 579.9 million) and Associated Partners (EUR 75.7 million).

Both EFPIA and Associated Partner commitments include in-kind contributions, as well as financial contributions directly to the IMI2 JU operational costs[9], or at project level to beneficiaries receiving EU funding.

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

IMI2 (EUR million)	Up to 31.12 2017	2018		TOTAL
		Amend-ments to existing grants	New grants	
EFPIA commitment (1)	366.6	2.4	210.9	579.9
Associated Partner commitments (2)	14.4		61.3	75.7
Total EFPIA and Associated Partner commitments [= (1) + (2)]	381.0	2.4	272.2	**655.6**
EU funding commitment	391.0		273.9	**664.9**

Of the EUR 655.6 million committed by EFPIA and Associated Partners as of 31 December 2018, 27.8 % 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

On 31/12/2018, EFPIA companies and Associated Partners had contributed EUR 135.5 million to the IMI2 programme (amount certified by external auditors and validated by IMI).

For comparison, at the same time, accepted cost claims for JU funding from beneficiaries stood at EUR 89.7 million.

[9] In accordance with Article 13.4.b of the Statutes of IMI2 JU annexed to Council Regulation (EU) No 557/2014 (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).

EUR millions	Up to 31.12.2017	2018	TOTAL
1. EFPIA companies – certified and validated contributions	81.3	46.7	128.0
2. Associated Partners —certified and validated contributions[10]	1.2	1.3	2.5
3. EFPIA & Associated Partner financial contributions paid directly to IMI2 operational costs[11]	3.9	1.0	5.0
Total EFPIA and Associated Partner contributions (in kind and financial)	**86.4**	**49.0**	**135.5**

Both EFPIA and Associated Partners 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 (EUR millions)	Validated cost claims from beneficiaries receiving JU funding *	Validated EFPIA & Associated Partner contributions
2015		
2016	13.0	50.2
2017	26.3	36.3
2018	50.4	49.0
TOTAL	**89.7**	**135.5**

(*) excluding pre-financing

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

Call	Projects	Commitments (EUR million)			
		EFPIA	Associated Partners	TOTAL EFPIA + AP	EU
1	1	12.7	5.7	18.4	17.6
2	8	103.1	0.0	103.1	114.1
3	5	46.0	7.0	53.0	49.0
4	1	2.2	0.0	2.2	1.1
5	6	45.8	1.9	47.7	47.5
6	4	46.0	0.0	46.0	46.5

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

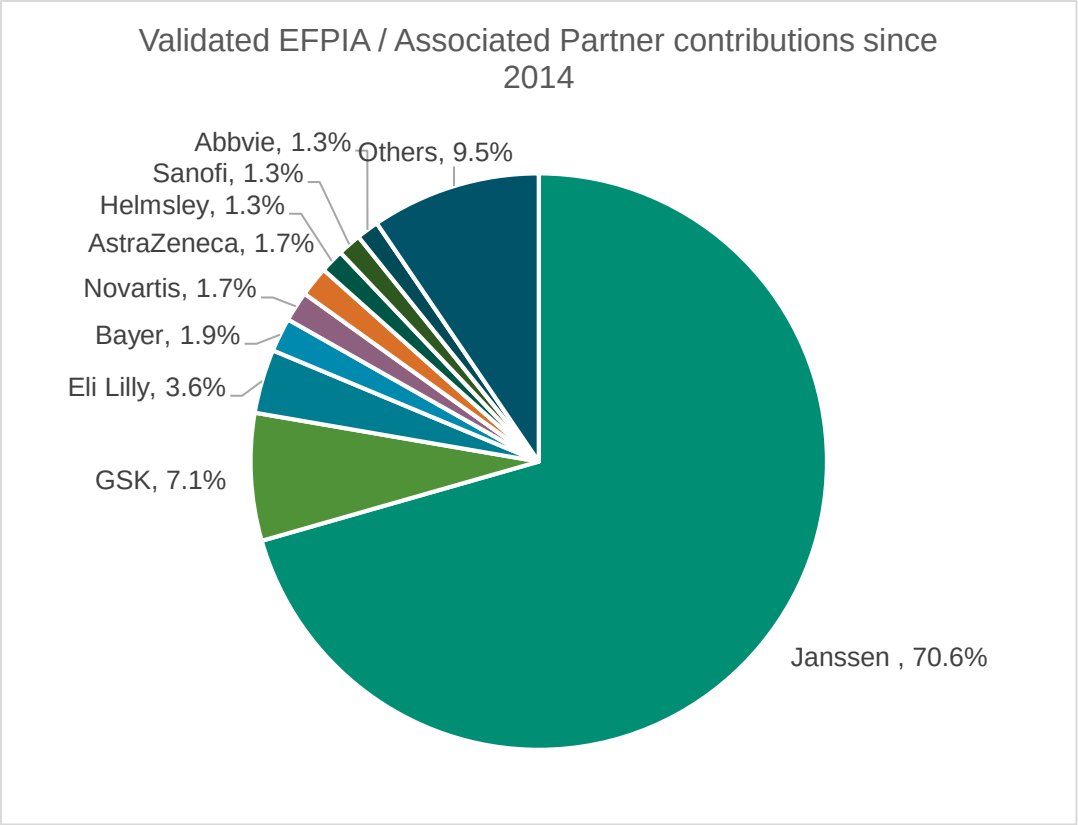
[11] Article 13.4.b of the IMI2 Council regulation (financial contribution of BMGF to IMI for the PERISCOPE project, plus the contribution of four EFPIA companies to IMI for the DRIVE project).

Call	Projects	Commitments (EUR million)			
		EFPIA	Associated Partners	TOTAL EFPIA + AP	EU
7	7	48.2	0.0	48.2	46.8
8	4	32.2	1.5	33.7	47.4
9	6	54.1	0.0	54.1	53.6
10	8	125.8	58.6	184.4	173.9
11	3	2.2	0.0	2.2	3.3
12	7	61.6	1.0	62.6	64.0
Total	**60**	**579.9**	**75.7**	**655.6**	**664.9**

The table above of committed contributions, as stipulated in individual Grant Agreements, 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 since 2014 up to the end of 2018

As the organisational breakdown below shows, 70 % of the total validated IMI2 contribution is provided by one European company, Janssen. This is mainly due to the fact that Janssen was the only contributor to the first IMI projects (four Ebola+ projects which started in 2014 in response to the Ebola virus epidemic in western Africa). The remaining 30 % comes from other EFPIA companies and Associated Partners (The Leona M. and Harry B. Helmsley Charitable Trust and JDRF). The remaining IMI2 projects are in their start-up phase and it is expected that the breakdown by organisation will be more balanced as the number of IMI2 projects increases. This is already evident in the second graph below which shows the reported contributions for the calendar year 2018, where the contribution of other EFPIA companies increases significantly.



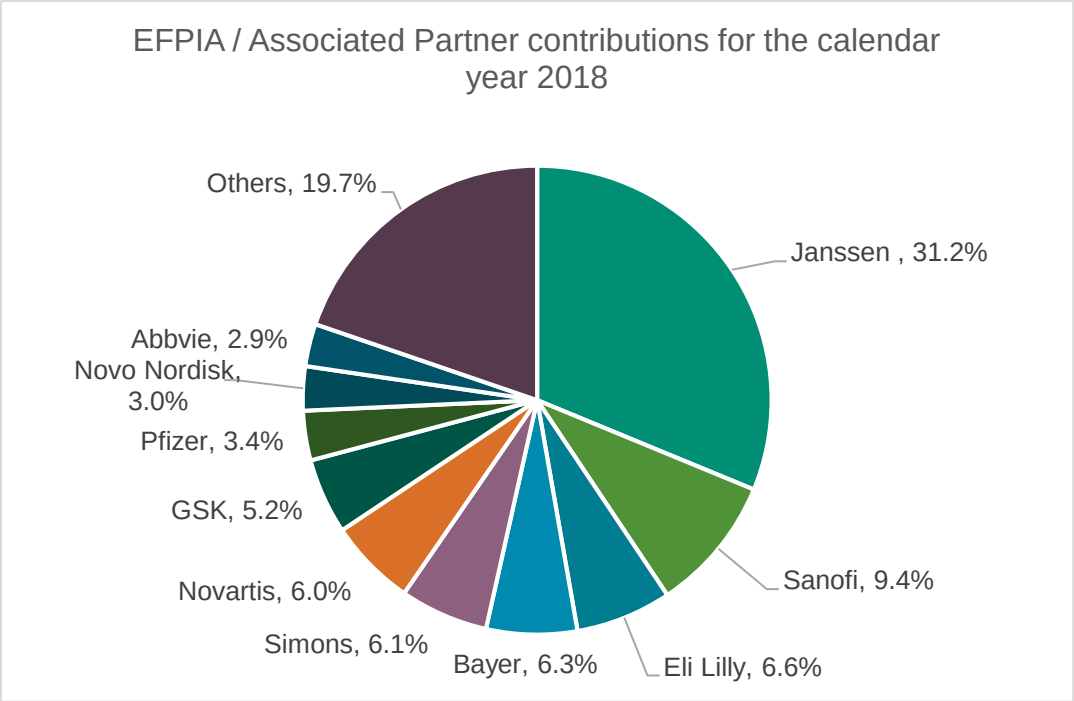
Companies listed under 'Others' are: Abbott, Amgen, Asociacion Nacional Empresarial De La Industria Farmacéutica, Astellas, Biogen Idec, Bruker, Celgene, Covance, Da Volterra, Ellegaard, EFPIA Office, Esteve, Grünenthal, Intervet International, Lundbeck, Marti, Menarini, Merck Sharp & Dohme Corp, Merial, Novavax, Pfizer , Piramal, PsychoGenics, Rentschler, Takeda, Teva, UCB, as well as Associated Partners Simons Foundation and JDRF.

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 for 2018

The chart below includes both in-kind and financial contributions at the level of the action during 2018. 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 calendar year 2018.

In 2018, 43 different companies and organisations contributed to IMI2 projects.



Organisations included under 'Other' are: Amgen, Asociacion Nacional Empresarial de la Industria Farmacéutica, Astellas, AstraZeneca, Biogen Idec, Boehringer Ingelheim, Bruker BioSpin, Celgene, Covance, Da Volterra, Ellegaard Göttingen Minipigs, EFPIA Office, Esteve, Grünenthal, Lundbeck, Marti, Servier, Menarini, Merck Sharp & Dohme Corp, Merial Novavax, Piramal, PsychoGenics, Rentschler, Sanofi Pasteur, Takeda, Teva and UCB , as well as the following Associated Partners: JDRF International and The Leona M. and Harry B. Helmsley Charitable Trust.

IMI2 EFPIA and Associated Partner reported contributions by cost category

EFPIA companies' and Associated Partners' contributions can be broken down into in-kind and financial contributions.

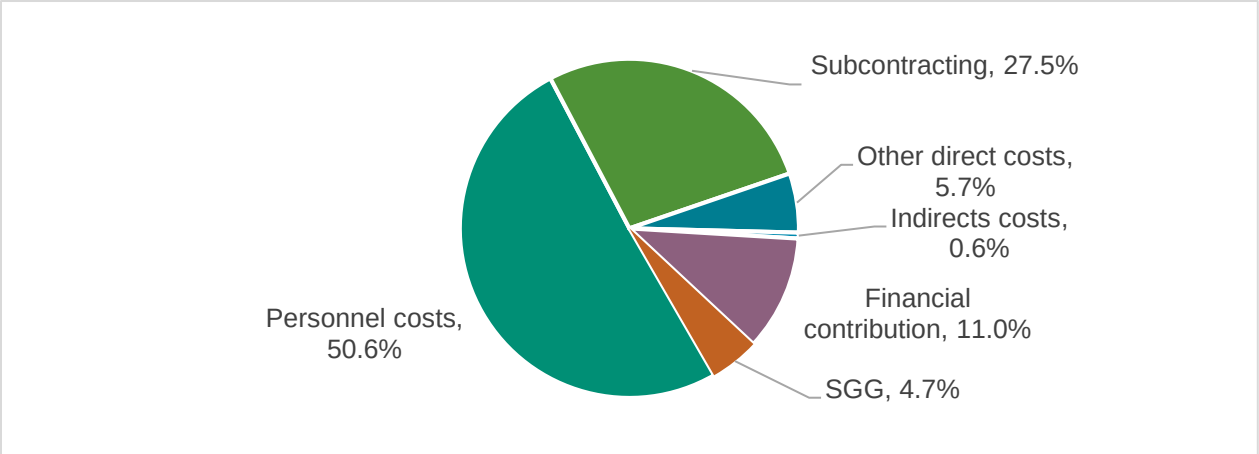
In-kind contributions incurred in projects may include the following cost categories:

- 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.
- Indirect costs: Overheads.

EFPIA companies can also make a financial contribution (FC), i.e. 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 beneficiaries receiving funding to cover project costs, such as hiring researchers during the lifetime of the IMI project or buying consumables or equipment.

In addition to costs incurred on projects, in-kind contributions also include costs (contributions) related to Strategic Governance Group (SGGs).

The graph below shows the breakdown of reported EFPIA / Associated Partner contributions.



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 19 EFPIA companies, covering a total of EUR 615.1 million of accepted contributions to IMI1 projects or 97 % of all EFPIA contributions.

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

Company	IKC validated as of 31/12/2018 (EUR million)
Total finalised audits	615.1
Total all EFPIA companies	633.3
Audit coverage	**97 %**

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 4 438 058, corresponding to 0.72 % of the total audited amounts.

Validated IKC (EUR)	IKC of audited companies (EUR)	Cover-age	Negative adjustments (EUR)	Positive adjustments (EUR)	Total absolute adjustments (EUR)	% of absolute adjust-ments
633 341 618	615 149 636	97 %	-2 237 926	2 200 131	4 438 058	0.72 %

A further three audits were launched at the end of 2018, to be finalised in 2019.

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).

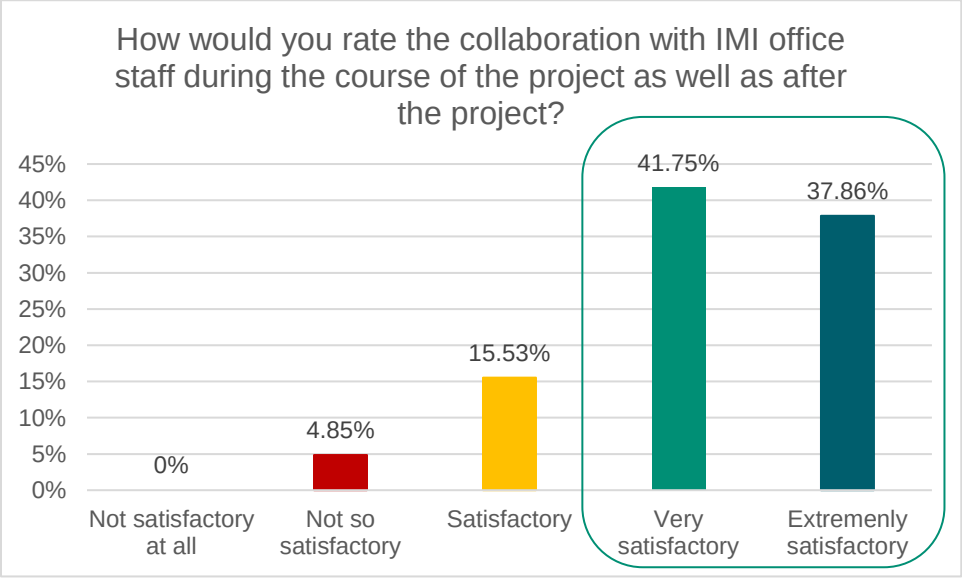
All reported costs must be accompanied each year by a certificate from an independent external auditor, confirming that the costs are in line with the requirements of the IMI2 Regulation. The certification must be based on standard terms of reference provided by IMI2. IMI analyses the audit reports and adjusts the amounts where necessary. EFPIA and Associated Partner contributions are only validated for inclusion in IMI's accounts after these checks and adjustments[12]. 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.

[12] 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

Over the lifetime of a project, project coordinators and leaders are often in close contact with a wide range of IMI staff. As part of a performance evaluation survey, the IMI Programme Office asked project coordinators and project leaders of IMI1 and IMI2 projects to rate the level of collaboration with IMI staff.

Over 90 % of the respondents rated the level of collaboration with IMI 4.13 on a 5-point scale, meaning that the collaboration with IMI office staff is perceived positively. Almost 80 % of IMI project coordinators and leaders believe that the relation with IMI staff was very satisfactory or extremely satisfactory.

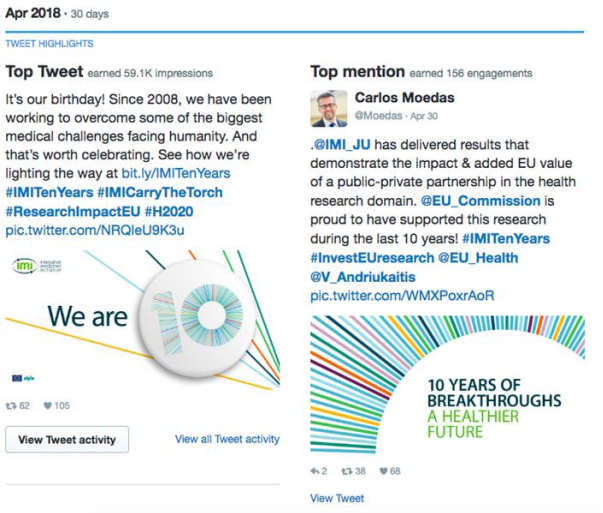


2.1 Communication activities

IMI 10 Years Anniversary Campaign

April 30th 2018 marked 10 years since the first IMI Call for proposals. Reaching this milestone provided the opportunity to step back and reflect on 10 years of activity and to celebrate the work of all the researchers, patients, SMEs and regulators who are collaborating in more than 100 projects in a new, open innovation ecosystem.

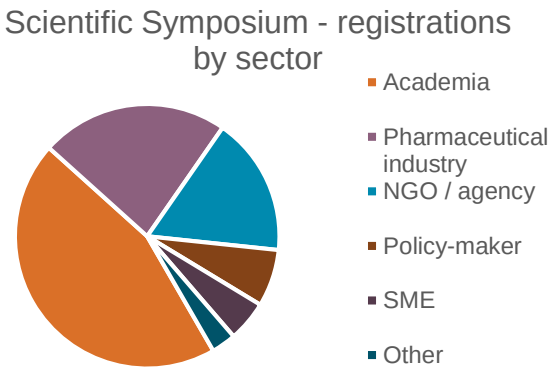
To mark the occasion, and to tell the story of IMI's achievements, IMI ran a communication campaign over several months under the general theme of 'IMI - carrying the torch of medical innovation'. It comprised several events, a series of videos, web, press and social media activities.



The content of the campaign was prominently featured on IMI's main social media channel, Twitter, via the hashtags #IMITenYears and #IMICarryTheTorch. Four content pillars were established to ensure variability in terms of the types of posts tweeted: brand awareness, event promotion, stakeholder quotes and project successes.

In order to reach out directly to IMI's main stakeholders, the Programme Office also organised two high-level events. The first, 'The Innovative Medicines Initiative: celebrating 10 years of medical innovations', held on 27 June, was co-organised with EFPIA and the European Commission. Over 400 people from the research and policy worlds participated and learnt first-hand from over 30 researchers and other stakeholders about IMI project results and their impacts. During the plenary session, speakers highlighted the way IMI has brought about what the European Commissioner for Research, Science and Innovation, Carlos Moedas, described as 'radical collaboration'.

The second 10 years anniversary event, the Scientific Symposium on 22-23 October, was attended by 269 participants, almost half of whom came from academia.



The goal of the IMI Scientific Symposium was to bring together young researchers from our projects to share with the wider scientific community their high-quality research, and to provide a space for projects to learn from one another.

A Programme Committee comprising top experts selected 72 posters and 28 oral presentations, all of which can be downloaded on the event web page. The best presenters of the presentations and posters, as judged by the Programme Committee and the audience, received prizes at the end of the event. Prizes were also awarded to the best IMI project communication products.

The Programme Office rounded off the campaign with a series of six videos featuring a range of stakeholders talking about their involvement in IMI, which, together with the rest of the activities developed in the in the framework of the 10 Years campaign, are hosted on a campaign landing page on the IMI website.

Campaign Indicators

IMI's 10th Anniversary elicited a positive response from the European health research community, and the social content helped to dramatically increase the visibility of both the IMI brand and the 10 Years

celebration. IMI invested in a series of promoted Tweets and additional paid activity in five Member States to amplify the messages, and to increase the audience and awareness of IMI and its activities. As the results below show, this resulted in over 4 million impressions, which reflects the considerable reach of the content throughout the milestone year.

Top-line results: organic and promoted tweets

- 455 tweets
- 4.2 million impressions
- 2 041 mentions
- 39 943 profile visits
- 1 073 new followers

Results by country

Location	Impressions	Link clicks	Video views	CTR *	VTR *
Spain	994 749	4 382	303 033	0.44 %	30.46 %
Poland	453 168	1 796	150 216	0.40 %	33.15 %
France	440 746	2 620	103 695	0.59 %	23.53 %
Czech Republic	221 016	915	100 313	0.41 %	45.39 %
Belgium	218 015	820	65 929	0.38 %	30.24 %
Germany	83 641	686	20 727	0.82 %	24.78 %

** CTR = click through rate; VTR = view through rate.*

The paid activity in November and December, in the form of website and Twitter cards, performed exceptionally well, achieving 2.4 million impressions and over 11 000 link clicks. The click through rate (CTR) was much higher than other months as there was a clear call to action. The view through rate (VTR) was also very strong at nearly 31 %. Not only are these results reflective of a successful campaign, but also of a highly efficient one, with a low cost per click (CPC) of EUR 0.68.

The main campaign landing webpage results were as follows:

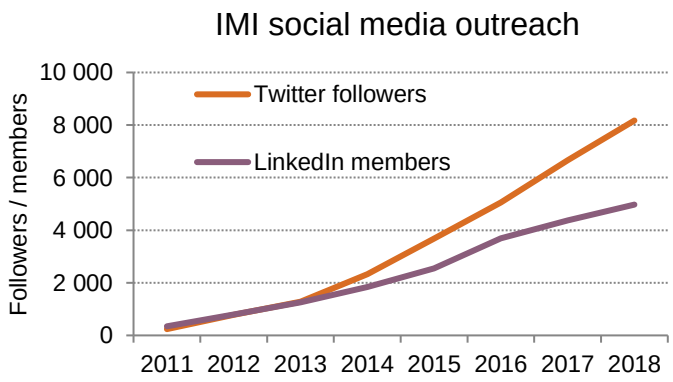
- 10 424 page views
- 9 458 unique page views

There was a noticeable spike in page views in December, which could be attributed to the paid campaign driving an increase in clicks from Twitter. Page views were also increased in the months of April, May, October and November, in line with strong organic and paid performance.

In more general terms, the IMI website attracted the attention of a considerable number of stakeholders and experienced a significant increase of number of sessions (231 736), page views (a total of 592 029) and visitors (a total of 171 045). The average number of visitors per month reached 14 254 (compared to 12 217 in 2017, and 11 546 in 2016).

As the graph shows, IMI's two social media channels, Twitter and LinkedIn, continue to show a steady growth curve.

The number of IMI twitter followers reached the figure of 8 172 at the end of 2018, while the number of LinkedIn group members reach 4 974.



The campaign videos were posted on both the campaign web page and YouTube and promoted heavily via Twitter and LinkedIn as well as other channels such as the newsletter. By the end of 2018, the videos had been viewed over 3 800 times between them on YouTube alone.

In a survey conducted after the Scientific Symposium, participants were asked to evaluate if the event goals had been achieved. Some 41 % totally agreed and 46 % tended to agree with the statement 'the IMI 10th Anniversary Scientific Symposium provided me with new networking opportunities'. Moreover, asked if 'the IMI 10th Anniversary Scientific Symposium provided a space for IMI projects to learn from one another', 67 % answered that they totally agreed and 31 % tended to agree.

In addition, participants were asked if the IMI 10th Anniversary Scientific Symposium had improved their understanding of what IMI is doing and an impressive 98 % gave a positive response (65 % totally agreed and 33 % tended to agree). When asked what difference, if any, the Scientific Symposium had made to their feelings about IMI, 57 % felt more positive, 32 % felt slightly more positive, and 9 % felt the event had made no difference.

As to the impact of the event, when participants were asked whether they had shared the information learnt at the event with other people, an overwhelming majority - 87 % - answered affirmatively.

Website

Besides the 10 Years campaign landing page, IMI created this year a completely new section under the title resources for projects. The aim of this new link in the navigation menu is to provide projects with the tools to fulfil their legal obligations and to guide them through issues such as project communications, project dissemination, open access and data management and how to engage with regulators. An additional web page has been added to this section compiling all project reporting documents.

Press

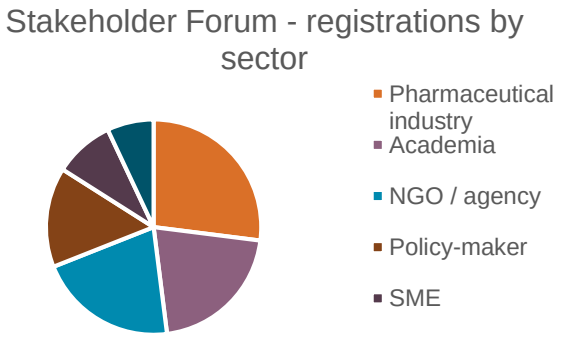
During 2018, IMI was mentioned in 4 048 articles worldwide; IMI was mentioned in the title or opening lines of some 7 % of these articles. The tonality of the media coverage was predominantly neutral (90 %), with the remaining 10 % of articles registering a positive tone. A selection of the most significant articles can be found in Annex 11. Highlights for IMI include an opinion piece by Executive Director, Pierre Meulien, in the Financial Times ('EU's Innovative Medicines Initiative brings collaborative power to development of drugs') and a Euronews documentary on our Ebola+ projects.

Newsletter

Due to the new data protection rules, IMI asked all newsletter recipients to re-subscribe in the summer. The fact that at the end of 2018, IMI had maintained 2 398 newsletter subscribers proves the relevance and quality of this communication channel.

Stakeholder Forum

The IMI Stakeholder Forum 2018 took place on 24 October (immediately after the Scientific Symposium). This year the event looked at IMI through the lens of cross-sector collaboration, and discussed the added value of technology convergence to address complex health challenges. The event brought in 32 speakers from diverse sectors, but key themes throughout the day were data and the involvement of patients in research.



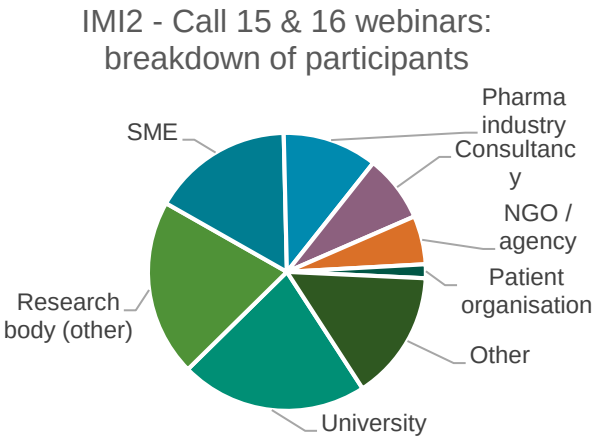
The event was attended by 272 participants (plus 120 live web streaming connections). As the graph shows, participants came from a range of sectors.

Whereas, as discussed above, the majority of Scientific Symposium participants came from academia, the breakdown of participants for the Stakeholder Forum was more balanced, with public administrations, non-governmental organisations and SMEs accounting for 65 % of participants between them. The percentage of industry participants remained stable for both events.

Asked through a survey if the Stakeholder Forum had made a difference, if any, to participants' feelings about IMI, the response was largely positive; 45 % of those who responded to the survey said that the event had made them more positive and 36 % slightly more positive.

Call outreach activities

IMI launched three Calls for proposals in 2018 (IMI2 – Call 14 on 15/03/2018, and IMI2 – Calls 15 and 16 on 18/07/2018). 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 ran 17 webinars covering the Call topics, IMI's rules and procedures, and opportunities for SMEs in the Call. In total, these webinars attracted 1 443 registrations. The graph below shows the breakdown of registrations for the Call 15-16 webinars by organisation type.



IMI has always published draft Call topic texts (with a disclaimer) when the formal consultation on the Call topics starts, around two months ahead of the Call launch. This allows applicants additional time to start building consortia and preparing proposals. However, feedback from the Scientific Committee and States Representatives Group among others suggested that applicants would benefit from even earlier information on Call topics under development. With this in mind, in December 2018, IMI started promoting Call topics that are in an early stage of development (i.e. that will not be ready for launch for several months).

Close-out meetings 2018

Once a project's final report has been submitted, IMI convenes a close-out meeting. This event provides an opportunity for the consortium to present to the IMI office how the project has reached its objectives, to highlight tangible results, put the achievements of the project into context, and discuss its potential impact and legacy management.

Following the meeting, the IMI communication team prepares a factsheet to communicate on the project's achievements and impacts. The factsheet is published on the IMI website and promoted through other IMI channels including the newsletter and social media. Depending on the project outputs, other communication materials may be produced, e.g. stories on specific findings, stories focused on specific partners, participant testimonials, etc.

- ADAPT-SMART: summary of project achievements.| interview with project coordinators
- COMPACT: summary of project achievements | interview with project coordinators
- DDMORE: summary of project achievements | interview with project coordinators
- EBISC: text under development
- STEMBANCC: text under development
- ETOX: summary of project achievements | interview with project coordinators
- GETREAL: summary of project achievements | interview with project coordinators

- K4DD: summary of project achievements | interview with project coordinators
- OPENPHACTS: summary of project achievements | interview with project coordinators
- PREDICT TB: summary of project achievements | interview with project coordinators
- WEB RADR: summary of project achievements | success story article | interview with project coordinators

Target audiences

Researchers

BIO International Convention, US, 4-7 June: IMI organised a session entitled 'Will public-private partnerships take the leap into open science?' under the BIO education programme, which featured high-level speakers from Europe and the US and received positive feedback. In addition, IMI Executive Director spoke at a session on vaccines and antimicrobial resistance and wrote an article on this subject for the convention magazine. Finally, IMI was an active partner on the European Commission's stand at the BIO exhibition.

ESOF 2018, France, 11 July: IMI participated with a session on 'My health, my data? A role-playing game surrounding the (re)-use of health data'. This session followed the PlayDecide format, a role-playing game to tackle controversial issues. Participants took on the roles of stakeholders involved in medical research with the goal of gaining new insights and perspectives on data sharing, and identifying potential actions relating to the use of patient data. The innovative format triggered lively discussions on this hot topic. To complement IMI's participation at ESOF, the IMI Executive Director spoke at a session organised by Science Business on 'sharing patient outcomes for better healthcare'. In addition, IMI was present at the European Commission stand in the exhibition.

SMEs

BIO-Europe, Denmark, 5-7 November: IMI teamed up with the European Commission to take part in BIO-Europe 2018. In addition to a session on funding opportunities for SMEs, which attracted 110 participants, IMI and the Commission had a stand at the exhibition.

European Parliament

19 June	Soledad Cabezón Ruiz (S&D ES) hosted a breakfast debate on 'Big data in health – IMI's HARMONY project'. The event featured a discussion with health and big data experts, policymakers, and researchers. Through the example of the IMI project HARMONY – which aims to improve the care of patients with haematologic cancer – the debate touched on the challenges and opportunities of using big data and eHealth services in healthcare systems.
9 October	The European Parliament Interest Group on Allergy and Asthma organised an event on 'Barriers to research in chronic NCDs- the example of allergy and asthma'. IMI presented 'IMI – an opportunity to implement research for patients and with patients'. The event was hosted by MEPs Nessa Childers (S&D, IE), Anna Záborská (EPP, SK), and David Borrelli (ALDE, IT).
21 November	The European Parliament Interest Group on Brain Mind and Pain organised a workshop on 'The Future of Healthcare in Europe What next for brain, mind & pain?' IMI highlighted the evidence-based approach taken by its projects and how this can feed EU policy in this field. The event was co-chaired by MEPs Marian Harkin, Jeroen Lenaers and Daciana Sârbu.
27 November	IMI project EBOVAC1 was one of only 20 projects chosen to showcase the best of European research and innovation at the high level conference 'EU Research and Innovation in our daily life"' co-hosted by the European Parliament and the European Commission. The fact that social media on the EC-EP high-level conference was extensively coordinated among the entire R&I family and with the European

Parliament helped generate a huge impact. The hashtag used for the conference, #ResearchImpactEU, gathered 55 million impressions between 17 October and 3 December.

In addition to the events listed above, IMI staff members and multipliers spoke at a large number of events both in Europe and elsewhere.

- 27-29 February: Workshop 'Agency for Medical Research and Development (AMED) - IMI to accelerate Japan's innovations - Focus on AMR' | Tokyo, Japan.
- 7 March: Workshop 'Developing synergies between Joint Undertakings and ESIF for optimising RIS3 implementation' | European Commission (DG JRC, DG REGIO), Brussels, Belgium.
- 8 March: Workshop 'Impact of health research for society', Scientific Panel for Health (SPH) | Brussels, Belgium.
- 14 March: 'A Debate on Solutions, Regional Cooperation and EU-Funding' | Representation of Lower Saxony to the EU, Brussels, Belgium.
- 21 March: Working group roundtable meeting on 'Smart investment for better outcomes - Health (dis)investment' | Friends of Europe, Brussels, Belgium.
- 5 April: Workshop 'A Day @ BIOASTER, public-private partnerships: united against antimicrobial resistance' | Bioaster, Lyon, France.
- 17 April: Annual event 'Co-shaping the future of European research and innovation with young scientists' | SwissCore, Brussels, Belgium.
- 19 April: 'DIA Europe', | Basel, Switzerland
- 2 May: 'Life at what cost? Hard choices in healthcare' | co-organised by Celgene and EFPIA, Brussels, Belgium.
- 16 May: World Precision Medicine Congress 'Making science personal. Bringing together big pharma, big data and healthcare providers' | London, UK.
- 24 May: Workshop 'Shaping the Future of Epilepsy Research' | European Commission (DG RTD), Brussels, Belgium.
- 4 June: '3rd Innovation Sessions - Healthcare Systems and Future Therapies' | European Economic and Social Committee (EESC), Brussels, Belgium.
- 1-7 July: '18th World Congress of Basic and Clinical Pharmacology' | Kyoto, Japan.
- 9-11 September: 'International summit on population genomics' | Illumina, Hampshire, UK.
- 18-19 September: Workshop 'The healthcare value chain: data and cooperation for efficiency gains. Personalised medicine and health systems research' | European Commission (DG RTD), Brussels, Belgium.
- 24-25 September: 'Biotech atelier' | Sofia, Bulgaria.
- 27 September: 'Big Bata for Better Health: Hype or Hope?' | Politico, Brussels, Belgium.
- 1-3 October: 'Aditec meeting 2018' | Aditec, Siena, Italy.
- 9 October: 'World Arthritis Day Conference 2018 - Bringing chronic diseases to the forefront of health innovation: from the lab to individualised health care' | EULAR, Brussels, Belgium.
- 9 October: Workshop 'Personalised Medicine: boosting health research at regional level' | European Committee of the Regions, Brussels, Belgium.
- 10 October: High-level roundtable 'Fostering Global Health Innovation: The critical role of the EU' | European Parliament, Brussels, Belgium.
- 15 October: 'The Corbel Medical Infrastructure-Users Forum' | Paris, France.
- 16 October: 'The Future is Calling – Flagship Research for Europe' | The Helmholtz Association, Brussels, Belgium.
- 16 October: Conference 'Innovation: is Europe falling behind?' | Centre for European Reform (CER), Brussels, Belgium.
- 18 October: Grand Challenges Annual Meeting | Berlin, Germany.
- 18 October: 'MyNewGut final conference' | European Food Information Council (EUFIC), Brussels, Belgium.
- 26-27 October:Workshop 'A global strategy for medicines research and integrated healthcare into 2030' | University of Lisbon, co-organised by EUFEPS and the Portuguese SPCF, Lisbon, Portugal.
- 29 October: 'Towards Transatlantic co-operation in pain research' | European Commission (DG RTD), Brussels, Belgium.
- 7 November: 'Innovative Medicines Initiative – 10 years & beyond' | Spanish Centre for the Development of Industrial Technology (CDTI), Madrid, Spain.
- 19-20 November: 'COST Connect: The future of European brain research', COST, Brussels

- 21 November: ‘Enhanced engagement through public-private partnerships: Sustaining therapeutic innovation to address patient needs’ | European Brain Council, Brussels, Belgium.
- 22 November: ‘Moonshots of the 2020s, Increasing Healthy Life Years - How to make the most of the missions of Horizon Europe?’ | Permanent Representation of Finland to the European Union, Brussels, Belgium.

2.2 Legal and financial framework

IMI2 JU Annotated Model Grant Agreement

In March 2018, the first version of the IMI2 JU Annotated Model Grant Agreement (AGA), based upon the Horizon 2020 AGA version 4.1, was adopted and published. This document was then updated in October 2018, to reflect the latest modifications that were introduced in version 5 of the H2020 AGA.

IMI2 JU guidelines for reporting in kind and financial contributions by Members other than the Union and Associated Partners

IMI2 JU is a public-private-partnership (PPP) where EFPIA, its constituent or affiliated entities, and Associated Partners contribute to the JU by supporting the costs they incur in participating in JU funded indirect actions. This guiding document, adopted in March 2018, provides a framework for the annual valuation and reporting of these organisations' activities.

IMI financial circuits

Following the verification of the local accounting system, IMI updated the internal procedures and ex-ante checklist for IMI2 JU transactions which are performed outside the H2020 common IT tools. In particular, in December 2018 (ED Decision 55/2018) a new manual was adopted in order to provide a detailed description of the financial circuits established at IMI2 JU for the implementation of its budget. In line with the IMI specific Financial Rules[13], and the Financial Regulation applicable to the general budget of the Union, the manual offers practical guidance to JU staff members involved in financial transactions and describes their main responsibilities. It also reflects the current financial circuits of, and the control strategy applied to, financial transactions by IMI2 JU. This manual contributes to the implementation of principle n°10 of the Internal Control Framework, i.e. 'the IMI2 JU selects and develops control activities that contribute to the mitigation of risks to the achievement of objectives to acceptable levels'.

[13] IMI Financial Rules will be revised in 2019 according to Article 71 of the new Regulation 2018/1046 of 18 July 2018 on the financial rules applicable to the general budget of the Union and the Commission Delegated Regulation on the framework financial regulation for the bodies set up under the TFEU, under the Euratom Treaty and referred in Article 70 of Regulation 2018/1046 currently in preparation.

2.3 Budgetary and financial management

2.3.1 2018 budget approval

The total IMI budget for 2018 was EUR 485 595 766 in commitment appropriations (CA) and EUR 235 963 022 in payment appropriations (PA). The budget execution of the commitment appropriations and the payment appropriations reached 99.73 % and 86.25 % 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 2018 budget on 15 December 2017.

The Governing Board approved the first budget amendment on 12 June 2018 in order to include the carry over amounts (EUR 209 698 405 Commitment appropriations and EUR 56 133 212 payment appropriations) from the previous year.

The Governing Board approved the second budget amendment on 13 July 2018 in order to include additional carry over amounts (EUR 25 669 commitment and EUR 25 669 payment appropriations) from the previous year, corresponding specifically to IMI1 amounts recovered from beneficiaries in 2017 and carried over to the 2018 budget.

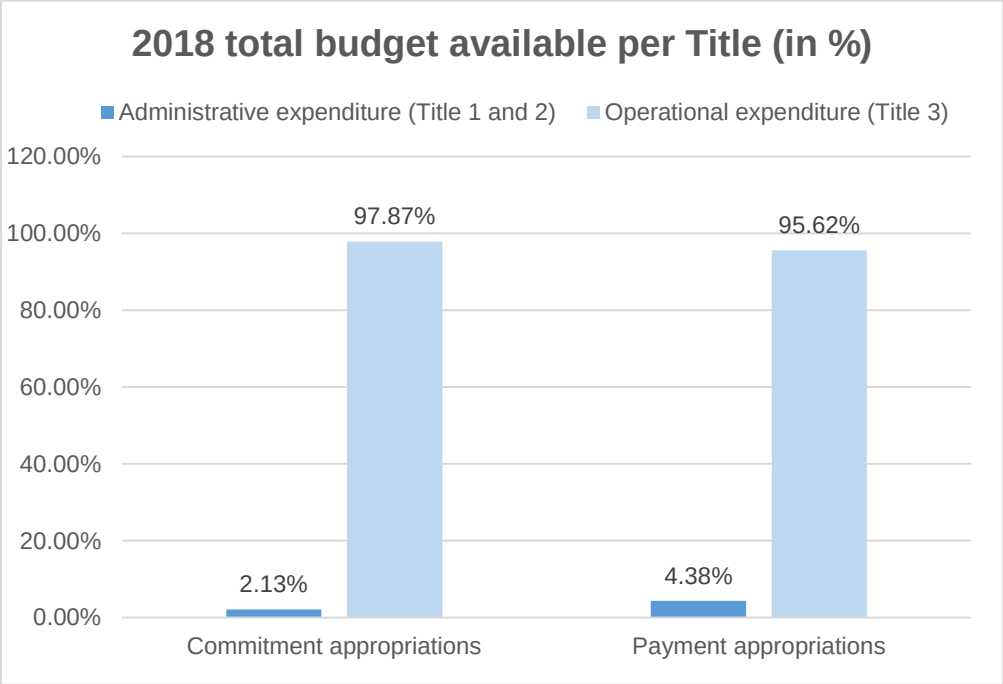
The Governing Board approved the third budget amendment on 5 December 2018 in order to reduce the operational payment appropriations by EUR 36 332 261, following the reduction of the European Union's contribution to operational costs (EUR 34 978 261) and the adjustment and carry over to next year the Associated Partner contribution (BMGF) to operational costs (EUR 1 354 000).

Budget 2018 in EUR

Budget 2018 in EUR										
	Approved budget		Carry over: Amending budget no 1 and 2		Amending budget no 3		Assigned revenue		Final budget	
	CA	PA	CA	PA	CA	PA	CA	PA	CA	PA
Revenue										
EC contribution to administrative and operational cost	270 487 957	208 398 667	209 724 074	56 158 881		-34 978 261			480 212 031	229 579 287
EFPIA contribution to administrative costs	5 156 500	5 156 500							5 156 500	5 156 500
EFPIA constituent entities and affiliated entities contribution to operational costs		1 000 000							-	1 000 000
***Associated Partners contribution to operational costs**		1 354 000				-1 354 000			-	-
Assigned revenue*							227 235	227 235	227 235	227 235
Total revenue	**275 644 457**	**215 909 167**	**209 724 074**	**56 158 881**		**-36 332 261**	**227 235**	**227 235**	**485 595 766**	**235 963 022**
Expenditure										
Title 1	6 015 000	6 015 000		73 830			772	772	6 015 772	6 089 600
Title 2	4 298 000	4 298 000		1 375 697			21 588	21 588	4 319 588	5 695 285
Title 3	265 331 457	205 596 167	209 724 074	54 709 354		-36 332 261	204 875	204 875	475 260 406	224 178 135
Total expenditure	**275 644 457**	**215 909 167**	**209 724 074**	**56 158 881**		**-36 332 261**	**227 235**	**227 235**	**485 595 766**	**235 963 022**

* The assigned revenue shows the amounts recovered during the year from suppliers and projects.

The graph below shows the total 2018 budget available per Title in %.



2.3.2 Budget transfers

One budget transfer between Title 1 and 2 was made during 2018 for an amount of EUR 40,000. Budget transfers between chapters were authorised in 2018, which led to the following changes:

Chapter		Budget approved (EUR)	Budget transfer (EUR)	Budget after transfers (EUR)
11	Staff in active employment	5 425 000	-226 648	5 198 352
13	Missions and duty travels	190 000	-70 000	120 000
14	Socio-medical structure	360 000	236 648	59 6648
17	Representation	20 000	20 000	40 000
20	Investments in immovable property rental of buildings	729 000	-43 185	685 815
22	Movable property	153 000	-89 152	63 848
23	Current administrative expenditure	123 000	25 800	148 800
24	Postage and telecommunications	68 000	-2 000	66 000
25	Expenditure on formal meetings	158 000	-23 000	135 000
26	Expenditure in connection with operational activities	300 000	-102 673	197 327
27	External communication information and publicity	625 000	60 000	685 000
28	Studies, consultancy and audits	730 000	-40 790	689 210
29	Expert contracts and meetings	700 000	255 000	955 000

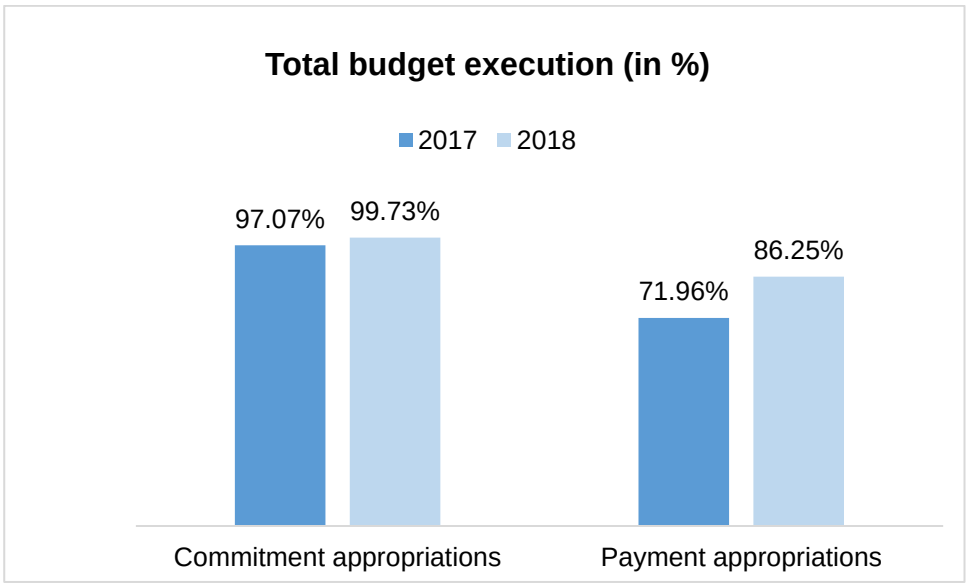
Overall, the budget transfers made in 2018 increased the approved budget for Title 2 by EUR 40 000 and decreased the approved budget for Title 1 by the same amount. The budget transfers made in 2018 had no impact on the approved budget for Title 3.

2.3.3 Budget execution

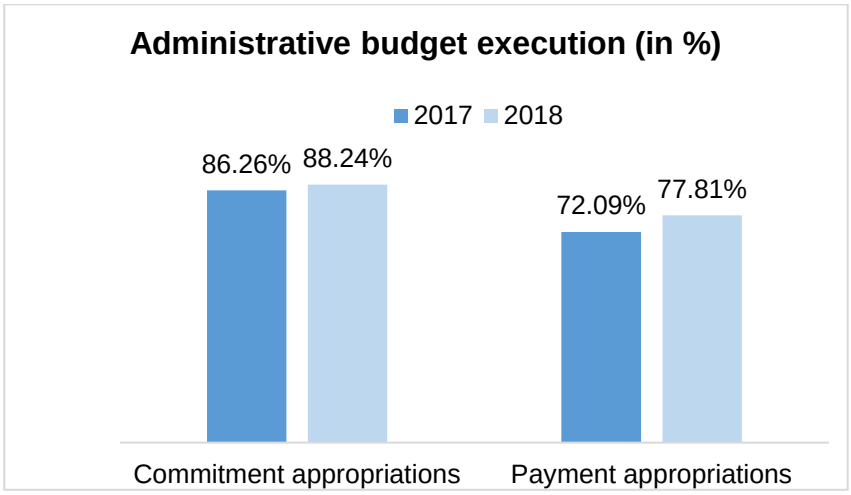
The table below shows the execution of the 2018 budget per Title in absolute amounts.

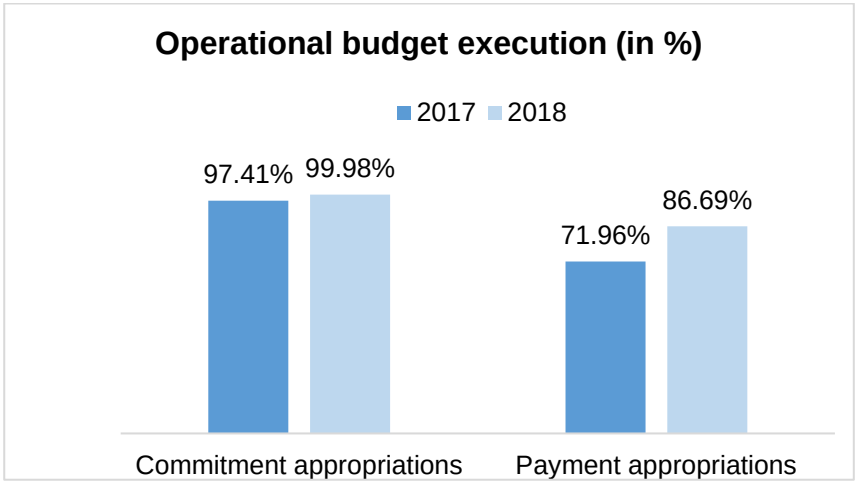
Title	2018 final budget execution per title in EUR					
	Commitment appropriations	Execution	%	Payment appropriations	Execution	%
Title 1	5 975 772	5 340 588	89.37%	6 049 602	5 315 336	87.86%
Title 2	4 359 588	3 779 405	86.69%	5 735 285	3 854 961	67.21%
Subtotal administrative expenditure	*10 335 360*	*9 119 993*	*88.24%*	*11 784 887*	*9 170 298*	*77.81%*
Title 3	475 260 406	475 159 723	99.98%	224 178 135	194 348 336	86.69%
Total (Title1, 2 and 3)	**485 595 766**	**484 279 716**	**99.73%**	**235 963 022**	**203 518 634**	**86.25%**

The graph below shows the 2018 total budget execution compared with 2017.



The graphs below show the 2018 budget execution for administrative costs (staff and infrastructure) and operational activities (project-related) compared with 2017.





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

Regarding administrative costs, the budget execution of the commitment and payment appropriations increased to 88.24 % and 77.81 % respectively.

The EC part of unused appropriations for administrative costs will be made available for operational activities in the 2019 budget – see section 2.3.4 for details.

In 2018, the time to pay (TTP) for administrative costs was 17 days on average and the number of payments made on time increased from 88.9 % in 2017 to 90.92 % in 2018. The following table shows the number and amount of all administrative transactions (including experts).

No. all administrative transactions made in 2018			
	No.	**Amount (EUR)**	**% payments**
Total no. payments	1 234	4 602 149.91	100 %
No. payments on time (within 30 days)	1122	4 019 725.80	90.92 %
No. late payments	112	582 424.11	9.08 %

The following table shows the number and amount of all payments made to experts only (evaluations and reviews). In 2018, the TTP for payments made to experts only was 13 days on average and the number of payments made on time improved again (from 92% in 2017 to 98% in 2018) due to the full use of the H2020 tools, such as COMPASS, EMPP (expert management participant portal) and EMI (Expert Management Internal).

	No payments	%
Total experts' payments	400	
Total on time payments	392	98 %
Total late payments	8	2 %
Total amount paid (EUR)	1 077 646.87	

The table below shows the summary of commitments outstanding at the end of 2018.

	EUR
Commitments carried from previous year	572 328 370
De-commitments (-)	(318 024)
Payments made during 2018 related to commitments carried forward (-)	(138 858 397)
Commitments made during 2018	484 279 716
Payments made during 2018 related to commitments made during 2018 (-)	(64 660 237)
Total commitments outstanding at the end of 2018	**852 771 428**

2.3.4 Overview of the carry over appropriations to 2019

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 2019 budget the unused commitment and payment appropriations from 2018.

Administrative expenditure: Payment appropriations of EUR 1 113 630, corresponding to the amount of commitments carried forward from the 2018 to the 2019 budget.

Operational expenditure: Unused commitment and payment appropriations to be carried over to 2019 budget of EUR 133 115* corresponding to commitment appropriations, and EUR 29 829 799* corresponding to payment appropriations.

	Commitment appropriation (EUR)	Payment appropriation (EUR)
Unused appropriations (operational and administrative)	* 133 115	* 30 943 429

* estimated; subject to Governing Board approval

2.4 Procurement and contracts

The majority of the IMI's contractual commitments in 2018 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 2018 outside existing FWCs with a value exceeding EUR 15 000.

Subject	Procedure	Contractor	Value (EUR)	Signature date
Bibliometric services	Negotiated	Clarivate Analytics	81 686	09/02/2018
Communication services	Open	The Leith Agency	229 326	05/03/2018
Venue and catering services	Negotiated	Crowne Plaza	120 480	08/03/2018
BIO Europe 2018 registration	Direct	EBD GmbH	33 000	11/06/2018

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 2018 were focused mainly on finalising the transition to eGrants, the migration of the common JU IT infrastructure to a new data centre, ICT procurement, enhancements of in-house developed applications, and user support.

Successful closure of eGrants transition project

In 2018, the IMI migration team, supported by Common Support Centre (CSC) of DG RTD successfully transferred to eGrants (Compass/SyGMa) all IMI2 projects from Call 1 to Call 8.

As a last step of implementing IMI2 JU's requirements, the CORDA team updated the Common Research Data warehouse and made available in-kind contributions and IMI-specific legal entity types. Having completed the project, a working group was formed to follow the implementation of IMI processes in the new tools and assist with the debugging with two main tasks:

1. to check that the project data had been transferred correctly;
2. to ensure that workflows match our practices and that templates and messages generated by the tools are accurate and tailored to IMI.

Migration of common (JUs) and private (IMI) IT infrastructure (IaaS) to a new data centre

Due to the expiry of the current framework contract, the common (six JUs) and private (IMI) IT infrastructures were migrated to a new cloud infrastructure provider in Q4 2018, ensuring long-term (at least 5 years) contractual stability and a higher level of security.

In Q1 2018, the migration of all users and devices to Windows 10 and MS Office 2016 was completed, 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

To enhance IMI's reporting system and to provide reliable data for analysis to different IMI stakeholders, management and staff, the first release of the IMI data warehouse (DW) – single repository, combing IMI1 (SOFIA) and IMI2 (CORDA) data, was deployed. The DW provides dynamic signed project data to the corporate website (via a dedicated web service) and to the SOFIA tool, so that EFPIA companies and Associated Partners can report their annual costs. In 2019, IMI will continue with further developments in order to improve data quality, IMI1 and IMI2 data integration, the loading of external reference data and a completely new reporting environment based on QlikSense.

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

- SOFIA (Submission of Information Application):
  - dataflow from DW to enable annual reporting of costs by EFPIA companies and Associated partners;
  - fixing data quality issues;
  - new report for amendment monitoring;
  - improved password handling process and policy aligned to the knowledge management platform (KMP /cloud);
  - improvements in the XML export of IMI2 data for integration with CORDA.

- Cloud applications:
  - new generic version of vacancies platform deployed to all JUs;
  - improvements and new features in all existing applications: vacancy (ref. documents), eMA, ISA, DORA and SRG;
  - preparation for DORA and ISA phase-out (planned for 2019) by creating consulting (read-only) security roles.

ICT procurement

Together with the five other JUs located in the White Atrium, IMI participated in a common call for tenders to renew the ICT operations and support services contract (led by FCH). The scope and technical requirements were tailored to the new infrastructure, an increased number of users and a more services-oriented approach as the majority of hardware is now purchased or leased via EC framework contracts.

In the new framework contract (awarded to Realdolmen), the JUs put in place enhanced mechanisms to closely monitor and improve the quality of the service provided.

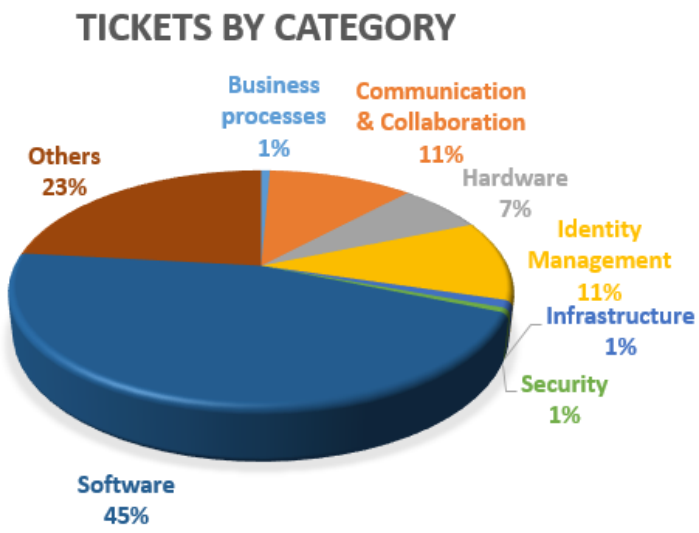
During 2018, IMI joined or activated several more EC framework contracts for various ICT services. Particularly important were those related to telecommunications, which achieved significant cost-savings:

1. for landline services, a framework contract with a new provider was implemented in 2018;
2. IMI deployed Webex as a new web conferencing tool.

Servicedesk support

In 2018 a total of 1 176 requests for support were sent to the IMI IT Helpdesk (helpdesk@imi.europa.eu) - a single point of contact and incident management system.

The following figure depicts the various categories related to the tickets



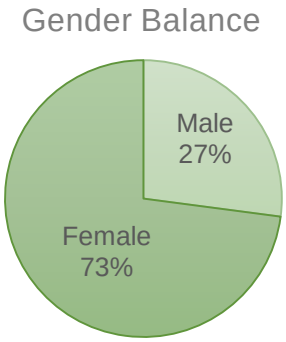
2.6 Human resources

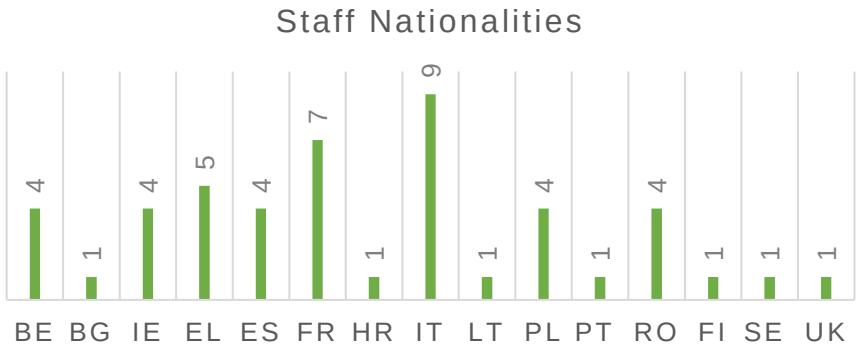
Staff and recruitment

The staff establishment plan (SEP) allows for a total of 56 staff members: 39 temporary agents, 15 contract agents and 2 seconded national experts. On 31/12/2018, there were 48 positions occupied (37 out of 39 temporary agents, 10 out of 15 contract agents and 1 out of 2 seconded national experts (SNEs)). A further four staff members (1 temporary agent and 3 contract agents) were appointed in 2018 and will take up their duties Q1 2019. The table below provides a summary of the staff planning:

	Positions planned in the SEP	Filled on 01.01.2018	Resignations / end of service in 2018	Recruitment / appointment in 2018	Filled on 31.12.2018
Temporary Agents	39	36	4	5	37
Contract Agents	15	13	6	3	10
SNEs	2	0	NA	1	1
Total	**56**	**49**	**10**	**9**	**48**

The two graphs below show the gender and geographical balance (15 EU nationalities were represented in IMI) within IMI2 JU on 31/12/2018.





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 Exercise

The reclassification exercise is a valuable tool to recognise and promote the performance of highly qualified staff members. The reclassification exercise for both temporary and contract staff took place successfully in 2018, in line with the staff regulations. As a result, seven staff members (five temporary agents and two contract agents) were reclassified to the immediate higher grade.

Staff regulations and implementing rules

During 2018, IMI continued working on the implementing rules in line with the Staff Regulations and the EC Human Resources and Security Directorate General (DG HR) guidelines.

2.7 Data protection

In 2018, IMI2 JU placed a great deal of emphasis on transitioning to the newly reformed European data protection regime. Before the entry into effect of the General Data Protection Regulation, the Joint Undertaking explained to IMI project coordinators (as well as EFPIA and the European Commission) the implications of the regulation for their activities in the context of IMI projects.

IMI operates under Regulation (EU) 2018/1725 of the European Parliament and of the Council of 23 October 2018 on the protection of natural persons with regard to the processing of personal data by the Union institutions, bodies, offices and agencies and on the free movement of such data. The JU strove to achieve compliance with this regulation by updating its tools, documents and procedures, by systematically and actively participating in dedicated inter-institutional training activities, and by developing appropriate training and communication material for staff.

2.8 Access to documents

IMI2 JU registered two applications for access to documents in 2018, pursuant to Regulation (EC) No 1049/2001. Both requests resulted in the partial disclosure of the documents sought.

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 2018, the Governing Board held seven meetings. The list of decisions taken by the Governing Board in 2018 can be found on a dedicated page of the IMI website.

The role of Chair of the Governing Board in 2018 was assumed as follows:

Dates	Chairperson
1 January - 28 February 2018	Jack Metthey (European Commission)
1 March – 15 April 2018	Signe Ratso (European Commission)
16 April – 6 July 2018	Wolfgang Burtscher (European Commission)
7 July – 31 December 2018	Jean-Christophe Tellier (EFPIA)

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 2018.

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 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.

As the mandates of the previous SRG Chair and Vice-Chair were due to end on 3 February 2018, IMI launched the election process in 2017, allowing the election to take place during the SRG's January 2018 meeting. The position of Chair is now held by Gunnar Sandberg (Sweden) and the position of Vice-Chair by Marta Gómez Quintanilla (Spain) for a period of two years until 3 February 2020.

In 2018, the SRG met in January, May and September in Brussels (Belgium). At the meetings, the IMI Programme Office provided detailed updates on IMI activities, with a specific focus on potential synergies with other EU policies and programmes (such as the EU health policy with DG SANTE, and the public-private partnership for Electronic Components and Systems with the ECSEL JU. Some SRG members also 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 2018, the SRG was consulted on the Call topics and documents and on the Annual Work Plan (including successive amendments), and was involved in the nomination process of new SC members and ad hoc members as well as for experts for scientific workshops organised by IMI.

In 2018, the IMI Programme Office organised a second annual joint meeting with the Scientific Committee and the SRG (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 Committee chaired by Beatriz Silva-Lima ended its mandate in September 2018. They met three times in 2018 and held three conference calls in between meetings to make progress on actions.

A new Scientific Committee, composed of 11 members and 2 additional experts, was appointed by the Governing Board based on suggestions made by the SRG. They met for the first time in November 2018. Isabelle Bekeredjian-Ding and Dolores Cahill were elected as Chair and Vice-Chair respectively. The members have expertise in a broad range of medical fields, including cancer, microbiology, neurology, metabolic disorders, digital technologies, research methodology and biostatistics, translational research, patient's vision and health economics. The biographies of all current members are published on the Scientific Committee page of the IMI website.

As part of their role, the members provided in 2018 advice on the proposed IMI scientific priorities for 2019 that are part of the Annual Work Plan, as well as on the proposed topics that were included in IMI2 - Calls 14 to 16 (launched in 2018) and Call 17 (launched in 2019). In 2018, the Committee provided also recommendations to the IMI Governing Board on matters important to the IMI objectives, particularly on digital innovation and data integration in the discovery of novel medicines' and the sustainability of outputs or deliverables from IMI-funded research programmes beyond the duration of the funding. The two recommendations are available on the Scientific Committee page of the IMI website. The Committee has been also working on elaborating high-level recommendations on what makes topics suitable for a public-private partnership funding model as well as on lessons learned from the IMI2 programme.

At each meeting, members representing the Scientific Committee in the different Strategic Governing Groups reported to the Committee on the work of the group. In addition, members reported on the IMI project reviews carried out in 2018 (see section 1.4.2), as well as on close-out meetings on IMI projects that have ended. Finally, representatives of the Committee participated in the Programme Committee of the IMI 10th Anniversary Scientific Symposium as well as in a consultation workshop organised by IMI on disease interception.

Synergies between the SRG and Scientific Committee

In 2018, synergies between the two advisory bodies, the Scientific Committee and the States Representatives Group, were further strengthened, for example by sharing more information with one another, such as the agendas and minutes of their meetings. A second IMI2 JU SRG - SC joint meeting was organised on 20 September 2018 to continue taking full benefit of these two advisory bodies on topics of mutual interest. This meeting provided an opportunity to obtain input on the IMI plan to bring its patient engagement strategy to the next level; share views on how to engage with general practitioners on topics of relevance; and discuss lessons learned from the IMI2 programme.

3.5 Stakeholder Forum

The Stakeholder Forum was held in Brussels, Belgium on 24 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)

Cross-SGG coordination

Two cross-SGG meetings were held in April and October. In addition, the October meeting was the first joint cross-SGG and EFPIA Partners in Research meeting. It brought a valuable perspective from different types of companies (e.g. contract research organisations, diagnostics, connected technologies, biomedical engineering, etc.). In 2018, a continuous effort was made to optimise the use of, and benefit from, the fully

operational SGG IT platform, which gathers in one place all the rules, templates, timelines, guidelines on IMI and SGG processes. In addition, an effort was made to share and facilitate access to the SGGs' meeting agendas, publishable minutes and attendance lists across SGGs and IMI advisory bodies, especially the SRG. In 2018, the EC representation in some SGGs was reinforced and enlarged by adding new members. Presently the EC participation in the SGGs encompasses DG RTD, DG CNECT and DG SANTE.

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 2019, and developed one topic that was launched in IMI2 – Call 15.

SGG Translational Safety

The SGG Translational Safety met twice in 2018. Discussions focused on the strategy to prioritise and implement new Call topics to be launched in future IMI Calls. The SGG developed one Call topic that was launched in IMI2 –Call 15.

SGG Oncology

The SGG Oncology held three face-to face-meetings in 2018 and discussed several topics of interest that are currently under development. The SGG Oncology provided input to the IMI Governing Board regarding the scientific priorities for 2019.

SGG Immunology

The immunology SGG held two face-to-face meetings in 2018. In total, the SGG contributed four topics to calls launched. Two topics were included in IMI2 - Call 14 and two topics were included in IMI2 - Call 15.

SGG Digital Health and Patient Centric Evidence Generation

The SGG Digital Health and Patient Centric Evidence Generation builds on the achievements of the former SGG on data and knowledge management. The new SGG met four times during 2018: two face-to-face meetings and two teleconferences. The SGG provided input to the IMI Governing Board regarding the scientific priorities for 2019, and developed four topics that were launched in IMI2 - Calls 14 and 15.

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 2019.

SGG Infections control

The SGG Infections Control met four times in plenary session during the year, twice during face-to-face meetings and twice via teleconference. The SGG Infections Control was very active in developing nine topics with a budget of almost EUR 300 million and which were published through IMI2 – Calls 15 and 16. The topics represent the first building blocks of a promising new AMR Accelerator Programme.

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.

IMI has continued to develop Associated Partner methodologies. This includes the refinement of Associated Partner application documentation and the finalisation of a dedicated standard operating procedure for internal management of applications. The IMI website was continually updated as new Associated Partners or new participations of existing Partners were approved and now shows a total of 21 Associated Partners, many of whom are participating in multiple topics. As of the end of 2018, the following organisations had become IMI Associated Partners. As detailed in section 1.7, at the end of 2018 the total Associated Partner commitment to IMI projects stood at EUR 75.7 million.

- Accelerate Diagnostics will contribute to IMI2 - Call 13, topic 3 (The value of diagnostics to combat antimicrobial resistance by optimising antibiotic use).
- Autism Speaks contributes to the AIMS-2-TRIALS project on autism. They are also involved in the IMI1 project EU-AIMS.
- Autistica contributes to the AIMS-2-TRIALS project on autism.
- BD Switzerland Sarl will contribute to 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 and will contribute to IMI2 - Call 15, topic 8 (Accelerator programme Pillar B: Tuberculosis drug development network to accelerate and validate scientific discoveries and advance the R&D pipeline of new and innovative agents to address the global tuberculosis epidemic).
- Bio-rad Laboratories will contribute to IMI2 - Call 13, topic 3 (The value of diagnostics to combat antimicrobial resistance by optimising antibiotic use).
- Cepheid Europe contributes to the VHFMoDRAD project on diagnostics for Ebola and related diseases.
- CHDI Foundation will contribute to IMI2 - Call 15, topic 6 (Digital endpoints in neurodegenerative and immune-mediated diseases).
- Children's Tumor Foundation will contribute under IMI2 - Call 15, topic 1 (Integrated research platforms enabling patient-centric drug development).
- International Diabetes Federation contributes to the Hypo-RESOLVE project on diabetes.
- JDRF contributes to the diabetes projects INNODIA, BEAT-DKD and Hypo-RESOLVE. JDRF will also contribute to IMI2 - Call 14, topic 4 (Centre for excellence – remote decentralised clinical trials) and IMI2 - Call 15, topic 4 (Emerging translational safety technologies and tools for interrogating human immuno-biology).
- Leona M. and Harry B. Helmsley Charitable Trust contributes to the diabetes projects INNODIA and Hypo-RESOLVE.
- Medicines for Malaria Venture (MMV) will contribute to IMI2 - Call 13, topic 7 (European Screening Centre: unique library for attractive biology (ESCulab)).
- Parkinson's UK will contribute to IMI2 - Call 13, topic 4 (Mitochondrial Dysfunction in Neurodegeneration); IMI2 - Call 13, topic 5 (Support and coordination action for the projects in the neurodegeneration area of the Innovative Medicines Initiative); and IMI2 - Call 15, topic 6 (Digital endpoints in neurodegenerative and immune-mediated diseases).
- Simons Foundation Autism Research Initiative (SFARI) contributes to the AIMS-2-TRIALS project on autism.
- Software AG will contribute to 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)).
- SpringWorks Therapeutics will contribute to IMI2 - Call 15, topic 1 (Integrated research platforms enabling patient-centric drug development).
- T1D Exchange (formerly Unitio) contributes to the Hypo-RESOLVE project on diabetes.
- TB Alliance will contribute to IMI2 - Call 15, topic 1 (Integrated research platforms enabling patient-centric drug development) and IMI2 - Call 15, topic 8 (Accelerator programme Pillar B: Tuberculosis drug development network to accelerate and validate scientific discoveries and advance the R&D pipeline of new and innovative agents to address the global tuberculosis epidemic).
- University of Dundee will contribute to IMI2 - Call 15, topic 8 (Accelerator programme Pillar B: Tuberculosis drug development network to accelerate and validate scientific discoveries and advance the R&D pipeline of new and innovative agents to address the global tuberculosis epidemic)
- Wellcome Trust will contribute to IMI2 - Call 13, topic 3 (The value of diagnostics to combat antimicrobial resistance by optimising antibiotic use).

4 Internal control framework

This section explains how IMI delivered the achievements described in the previous sections. It reports in particular the control results and other relevant information that support management's assurance on the achievement of the financial management and internal control objectives. It includes additional information to support the conclusion that the available evidence is accurate and complete.

4.1 Financial procedures

In accordance with the EU financial regulation, IMI adopted specific financial rules and operating procedures[14]. These documents outline the financial principles and processes applied and describe the responsibilities of the financial actors as well as the internal control framework applied in order to:

- ensure 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.

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 2018, IMI continued the implementation of its programme in accordance with the H2020 rules and applying the EC operational tools, 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).

Overview of Control system for budget implementation - 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.

[14] See above Section 2.2 "Legal and financial framework".

	Ex-ante controls	Ex-post controls
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 tables below present the balance between the actions implemented under the IMI1/FP7 and IMI2/H2020 programmes in terms of project portfolio and operational expenditure on 31/12/2018.

IMI1 (FP7) projects portfolio on 31/12/2018

				Pre-financing payments	Interim & final payments[15]	Total paid
Total projects funded	**59**	Running on 01/01/2018	**27**	0	58 886 630	58,886,630
		Ended[16] during 2018	**(11)**			
Total IMI1 projects running on 31/12/2018			**16**	**0**	**58 886 630**	**58 886 630**

IMI2 (H2020) projects portfolio on 31/12/2018

				Pre-financing payments	Interim & final payments[17]	Total paid
Total projects funded	**60**	Running on 01/01/2018	**37**	91 916 675	45 545 031	**135 461 706**
		Ended during 2018[18]	**(3)**			
		Signed in 2018	**20**			
Total IMI2 running on 31/12/2018			**54**	91 916 675	45 545 031	**135 461 706**

[15] 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).

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

[17] 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).

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

IMI1 and IMI2 full project portfolio on 31/12/2018

				Pre-financing payments	Interim & final payments[19]	Total paid
Projects	119	Total running projects	70	91 916 675	102 431 661	194 348 336
		Total ended projects[20]	49	/	/	/

Control system for budget implementation - Overview of ex ante control results

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

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

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	Target	Results 2018		Result 2017	Result 2016
% of annual coverage of Call topics identified in AWP 2018	100 %	Topics planned in AWP 2018: 19 Topics launched in 2018: 19 ▪ Call 14: 4 topics ▪ Call 15: 8 topics ▪ Call 16: 7 topics	100 %	100 %	93 %
No. redress procedures on the result of the evaluation and selection procedure	0	1 (IMI2-Call 13)		0	0

[19] 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).

[20] Of which 43 IMI1 projects and 6 IMI2 projects.

II - Grant Agreement preparation phase (GAP)

Grant Agreement preparation starts after the evaluation, upon approval of the results by the Governing Board, with the GAP invitation letter — no later than 5 months after the Call deadline (time-to-inform / TTI). In this phase, the Grant Agreement (GA) is prepared and signed. The IMI Programme Office checks administrative data submitted – including the budget, legal and financial status of each participant, gives consortia the opportunity to correct shortcomings identified by the independent experts in their evaluation, and ensures that the description of the action (DoA) matches the proposal. The result of the checks performed is documented in the grant preparation report. The pre-financing is transferred to the consortia as soon as the Grant Agreement is signed to enable the timely start of project activities.

In 2018, IMI2 JU achieved a general improvement in the efficiency of the granting process as reflected by the following three performance indicators:

- **Time to Inform (TTI)** represents the time needed by IMI2 JU to manage the evaluation and selection phase from the Call deadline to informing the participants. In 2018, the average TTI was reduced to 75 days against a legal target of 153 days, and 6 days fewer than in 2017.
- **Time to Grant (TTG)** represents the maximum eight months between the Call deadline and grant signature. In 2018, the average TTG decreased by 38 days and is maintained at 232 days, against the target of 245 days.
- **Time to Pay (TTP)** represents the outcome of the process for the payment of pre-financing to newly signed Grant Agreements, enabling the projects to kick-start their activities. In 2018, pre-financing payments took 9 days on average, against a target of 30 days. That is a further improvement in comparison to 2017's result.

This overall improvement on all three operational efficiency indicators is due to a couple of factors: the full implementation of the H2020 IT management tools, appointment of IMI grant coordinator, enhanced management supervision and regular monitoring.

Indicators	Target	Results 2016	Results 2017	Result 2018
Total average Time to Inform (TTI)	**153 days**	76 days	81 days	**75 days**
Total average Time to Grant (TTG)	**245 days**	232 days	270 days	**232 days**
Total average Time to Pay (TTP) for pre-financing	**30 days**	12 days	11 days	**9 days**

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 IMI vade mecum on monitoring, reporting and payment, which is aligned with the horizontal guidance by the Common Support Centre of the EC. 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).

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[21].

Ex-ante controls provide the Authorising Officer with the assurance that costs claimed are accurate and in compliance with the applicable legal and contractual provisions. A complementary 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.

a) Volume of operational transactions

The total number of operational transactions performed during the year is one of the main indicators used by IMI to assess the efficiency of the Programme Office and its use of human resources to handle the workload related to project management. The verification process of each transaction is particularly complex due to the nature of the projects implemented by IMI, as well as the amounts at stake per project (average 22.5 million with projects having a budget higher than 140 million) and the high number of participants per project (average 21).

Another element to take into consideration while assessing the control workload is the percentage of final payments handled during the year (21, an increase of 33 % compared to 2017). The payment of the final balance concludes the project life cycle and therefore needs a more in depth and extensive analysis and assurance elements in comparison to interim payments.

The table below provides a cumulative overview of pre-financing payments, interim, and final transactions made by IMI (or recognised against pre-financing payments[22]) from 2012 to 2018. It shows that in 2018, the total volume of financial transactions related to IMI projects has increased by 10 % and will continue to increase in the coming years as new projects are gradually added to the IMI portfolio until the end of 2020.

Number of operational transactions

	2012	2013	2014	2015	2016	2017	2018
Pre-financing payments	12	14	18	16	16	16	**20**
Interim and final payments [23]	26	33	32	30	59	66	**70[24]**
Total	38	47	50	46	75	82	**90**

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

Due to the modalities of the reporting mechanism and diverging timelines, the number of payments made during the year, cannot correspond to number of reports received. That because the reports received during

[21] More information can be found in Section 1.4.2 above.

[22] 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.

[23] Including the clearings of pre-financing.

[24] Of which, 37 on IMI1 projects and 33 on IMI2 projects.

the last quarter are processed within the legal deadline of 90 days and naturally some payments are carried over into the following year.

Cost claims received with project reports against payments made

	2016	2017	2018
Cost claims received with project reports during the year	70	53	**80**
Cost claims received with project report not validated within the year (to be paid the following year)	15	7	**17**
Cost claims paid or cleared against pre-financing	59	65	**70**[25]

b) Value of operational transactions

The breakdown of the costs accepted and paid in 2018 by IMI based on the operational transactions described above is presented in the table below.

In total, 90 financial transactions were processed for the total value of EUR 254 855 345. EUR 194 348 336 was actually paid to beneficiaries as pre-financing or interim/final payments while EUR 60 507 009 are the result of full and partial clearing made against pre-financing paid at the beginning of the project.

		No of transactions		Value of payments	Value of clearings[26]	Value of all transactions
IMI1	Pre-financing payments	0		0		0
(FP7)	Interim payments	**13**	**37**	58 886 630	53 571 140	112 457 770
	Final payments	**18**				
	Full Clearing	**6**				
IMI2	Pre-financing payments	**20**	**53**	91 916 675		91 916 675
(H2020)	Interim payments	**30**		43 545 031	6 935 869	50 480 900
	Final payments	**3**				
	Full Clearing	**0**				
TOTAL		**90**		**194 348 336**	**60 507 009**	**254 855 345**
Budget				**223 973 260**		
			Budget execution %	**87 %**		

[25] Of which 63 (32 for IMI1 and 31 for IMI2) received in 2018 and 7 received in previous years and paid in 2018.

[26] Which includes both full and partial clearing.

In 2018, the number of financial transactions related to operational costs increase by 9.7 % (from 82 in 2017 to 90 in 2018); the value of all transactions processed by IMI increased by 28% (EUR 199 097 701 in 2017); the value of actual payments (excluding clearings) increased by 38.5% (EUR 140 251 318 in 2017)

- The improvements in the project management workflow and the coordinated effort made by the staff resulted in a considerable increase of the annual budget execution rate, which reached 87 % in 2018. This demonstrates that cautious planning and enhanced monitoring of payment appropriation absorption yielded a positive result.

c) Costs rejected following ex-ante controls

In order to monitor and measure the efficiency of the ex-ante controls, another key indicator is the percentage of declared costs considered ineligible (i.e. rejected) by IMI services.

In 2018, the financial impact of the systematic ex-ante controls performed on the cost claims before proceeding to the payment increased to 1.40 % of reported costs compared to 1.26 % in 2017 and 0.77 % in 2016.

Total reported costs	IMI1	118 542 133	169 306 327
	IMI2	50 764 194	
Of which covered by CFS[27]			80 848 345
Accepted costs	IMI1	112 457 769	162 938 669
	IMI2	50 480 900	
Suspended costs [28]	IMI1	3 967 052	3 967 052
	IMI2	0	
Rejection	**IMI1**	**2 117 312**	**2 383 119**
	IMI2	**265 807**	
Rejection (in %)			**1.40 %**

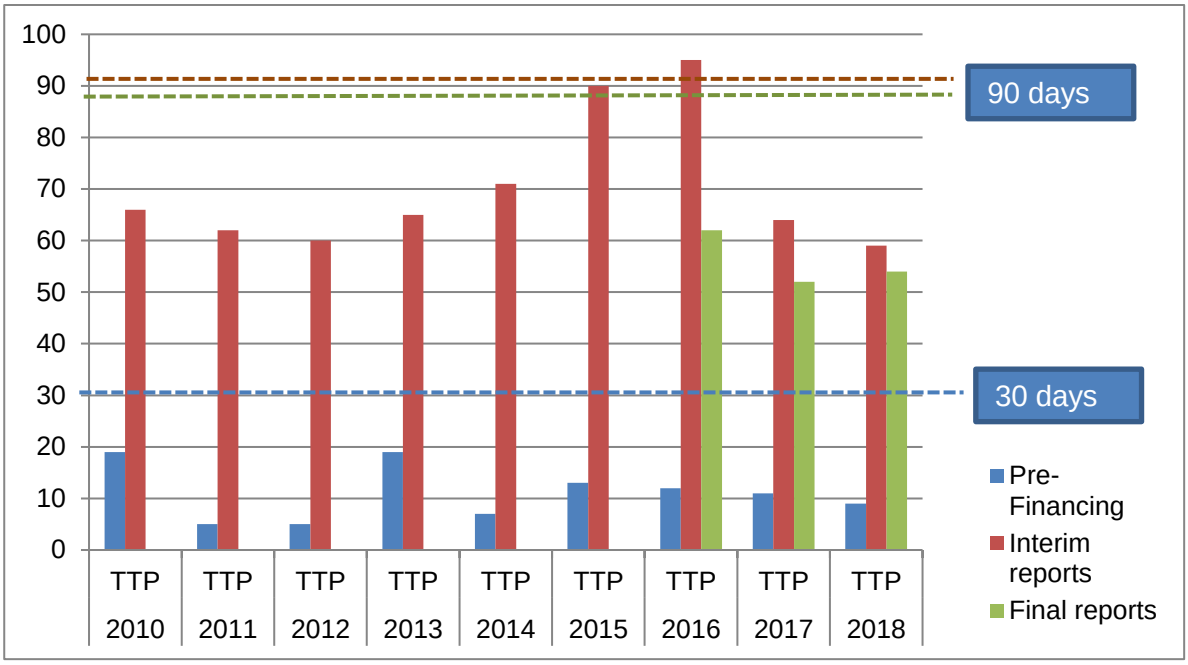
d) Time to Pay (TTP)

Figures of 2018 show a further improvement in TTP for pre-financing payments (from 11 to 9 days) as well as for interim payments. The IMI office managed to further bring down the average time to pay for interim payments from 64 to 59 days (8 % improvement). The time taken for final payments was on average for 54 days well below the target of 90 days.

The following chart represents the average time to process payments against the deadlines set by the Financial Regulation.

[27] For IMI2/H2020 actions a certificate on financial statements (CFS) must be submitted only at the end of the project.

[28] These costs are still under assessment. A decision to reject or accept them has not been taken yet.



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 human resource allocation, 17 FTEs (scientific, financial and other support officers) are involved in the ex-ante control of the grant management life cycle (i.e. from grant preparation until the payment of reported costs and project balance. This represents about 58 % of the FTEs allocated to the management of the operational programme and around 35 % of the staff currently employed.

While IMI administrative costs in 2018 represent 4.5 % of the total IMI payments, the costs for ex-ante controls can be estimated at EUR 2 565 000/year of which: EUR 730 000 for controls related to evaluation, selection and grant preparation phase; EUR 1 835 000 for controls related to grant management and reporting (including the costs of externalised interim reviews).

The estimated cost for ex-ante controls would then represent 1.26 % of the IMI operational expenditure as described in the first table below, and can be quantified as EUR 30 535 per Grant Agreement, which corresponds to 0.01 % of the total operational expenditure.

IMI budget 2018 (Payments in EUR)		% in total budget	Total estimated costs of ex-ante control	Cost of ex-ante control as % of annual expenditure
Administrative expenditure	9 170 298	4,5 %	2 565 000	27.97 %
Operational expenditure	194 348 336	95,5 %		1.32 %
Total	**203 518 634**	**100 %**	***/***	**1.26 %**

Benefits of ex-ante controls (in EUR)	**1 867 761**
Total cost of ex-ante controls (in EUR)	**2 565 000**
Average cost (in EUR) of ex-ante control for one running Grant Agreement (Total costs / no. 84 projects running in 2018, including projects that concluded their activities in 2018)	**30 535**

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[29]	Other costs related to controls	Total
		(Costs are indicated in EUR)		
Call management, selection and evaluation phase	2.0	268 000	25 000*	
Grant award	3.5	437 000	/	
Grant management	13.5	1 585 000	250 000*	
Total cost of ex-ante controls		**2 290 000**	**275 000**	**2 565 000**
Ex-post control	1.5	169 000	262 000	
Total	**20.5**	**2 459 000**	**537 000**	**2 996 000**
Cost-effectiveness ratio	Cost of controls / Total expenditure 2018 (Administrative and operational)			**1.47 %**
	Cost of controls / Operational expenditure 2018			**1.47 %**
	Cost of controls / Total validated cost 2018 (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.

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.

[29] 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.).

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 2018, the majority were still under FP7 Grant Agreements (EUR 58 886 630 paid) compared to EUR 45 545 031 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	237	34.6 %
Projects	59	54	91.5 %
Contributions accepted by IMI (EUR, cumulative)	**476 901 148.63**[30]	**85 233 728.83**	**17.87 %**

The following table gives an overview of the status of individual audit assignments as of 31 December 2018.

	Total audits	Audits finalised[31]	Audits ongoing
Representative	240	223	17
Risk-Based	15	14	1
Total	**255**	**237**	**18**

In 2018, 23 audits were finalised in total. One sample of representative audits was drawn in June 2018.

Representative and residual error rates as of 31 December 2018

At this point, the **cumulative Representative Error Rate** (RepER) resulting from all representative audits finalised by 31 December 2018 is 1.80 % in terms of IMI contribution.

[30] Figure as of the cut-off date of 14 June 2018, corresponding to the last audit sample from which finalised audits were included in the current AAR.

[31] 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.

The **cumulative Residual Error Rate** (ResER: error remaining in the population after corrections and recoveries) is 0.87 % in terms of IMI contribution. The residual error rate is thus below the 2 % materiality threshold established in Annex 10 of this report.

Implementation of audit results

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 2018.

Number of cases of unduly paid amounts identified in audits	Number of cases implemented	Percentage of cases implemented	Amount implemented (EUR)
166	162	96 %	1 661 716.45

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	237
Pre-information letters / letters of conclusion sent	231
Of which affected by systematic errors[32]	47
Extrapolation feedback received from beneficiary	44
Of which implemented	40

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[33]. 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

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

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

reports on the error rates drawn from these programme level controls. Extension of findings across the programme also provides an additional element of assurance.

However, as the IMI2 Regulation[34] 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 2018

At this stage of the programme lifecycle, cost claims totalling 9 billion euro of requested funding had been received by the services by the end of 2018. The first Horizon 2020 audits were launched in the middle of 2016 and further audits were launched in 2017 and 2018. Two Common Representative Samples (CRS), Common Risk Samples and Additional Samples[35] have been selected. In total, by December 2018, 2383 participations had been selected for audit, covering all the services signing grants in Horizon 2020.

In total, the audit of 1155 participations has been finalised by 31/12/2018 (763 in 2018). This includes 164 out of 303 participations selected in the first 2 CRS. The error rate at 31/12/2018 is:

Overall Detected Error Rate based on 1155 participations: 1.62 %

The Detected Error Rate[36] based on 164 out of 303 participations selected in the first and second CRS is 2.43%. However, if we take into account the draft audit reports, then the expected representative error rate for the full sample will be around 3.32%.

Residual Error Rate for the Research and Innovation Family: 2.22 %, expected to rise to around 2.45 % when taking into account the draft audit reports.

Ex-post controls specific to IMI's population in 2018

By 31 December 2018, IMI has launched four individual representative samples. Audits were finalised from the three first of these samples. A total of 12 representative audits sampled by IMI were finalised, as well as one further audit selected in the first programme level Common Representative Sample, which is also considered for IMI's representative error rate. In addition, three risk-based audits were finalised by the end of 2018, of which two were selected by CAS at the programme level risk-based sampling and one by IMI.

The total IMI contribution in the finalised audits is EUR 4 825 738 including both representative and risk-based audits. This represents 16.5 % of the total population of contributions claims paid out, EUR30 533 589[37].

Representative and residual error rates specific to IMI's population as of 31 December 2018

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

- **Cumulative representative error rate** (RepER) resulting from the 13 finalised audits considered representative is 0.76 % in terms of IMI contribution.
- **Cumulative Residual Error Rate** (ResER: error remaining in the population after corrections and recoveries) is 0.67 % in terms of IMI contribution.

Comments on the control results

As last year, the error rates set out above must still be treated with care. The two first CRS are not yet complete, and so the error rate is not yet fully representative of the expenditure that it covered. In addition, the

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

[35] This sampling accommodates special needs of certain stakeholders with regard to audit coverage and selection method. In addition, top ups, which are participations of selected beneficiaries which are added to the selected participations, are included in the total participations selected.

[36] This error rate is not named at this stage common representative error rate as the audits of the first CRS are not yet all finalised.

[37] The figure corresponds to the population considered for the samples from which audits have been finalized as of 31 December 2018.

first CRS was taken at an early stage of the programme in order to provide an early indication of the error rate, and to help assess 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 rate, must be considered over time. In particular, the cleaning effect of audits over time will tend to increase the difference between the representative/detected error rate and the residual error rate, with the latter finishing at a lower rate.

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 rates both at programme level and for IMI's specific population remains below the 2 % materiality level. Additional evidence to support this conclusion will arrive as the programme progresses. 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 2018.

Number of cases of unduly paid amounts identified in audits	Number of cases implemented	Percentage of cases implemented	Amount implemented (EUR)
5	4	80 %	361 587

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

4.4 Audit of the European Court of Auditors

Audit on IMI annual accounts 2017

On 12 November 2018, the European Court of Auditors (ECA) published its report on IMI's annual accounts for the financial year 2017. 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 2017 budget* – the auditors noted that the low implementation rate for payment appropriations (72 %) was mainly due to a reduction or postponement of clinical trials within some large and complex projects of the antimicrobial resistance and Ebola programmes and to delays in concluding grant agreements for calls under Horizon 2020.
  The auditors also indicated that the unused payment appropriations from previous years amounted to EUR 78.7 million, reflecting that during the last years, there were weaknesses when planning and monitoring the need for new payment appropriations.
- *Internal control framework* – the auditors noted that at the end of 2017, the Commission's Common Support Centre (CSC) had not finished specific developments in the Horizon 2020 grant management and monitoring tools to serve the Joint Undertaking's reporting and processing needs for in-kind contributions.

IMI acted upon ECA's comments and took immediate measures to mitigate the risks as described below.

Implementation of the budget

In order to break the cycle of over budgeting, the following corrective measures have been implemented: (see also section 1.6 of the report)

- In preparation of the 'Fiche Financière' for 2019 in December 2017/January 2018, the claim for fresh credits (C1) was significantly reduced up front (to EUR 185 million) in order to integrate in the total budget envelope the carryover estimates between 2018 and 2019.
- The Commission services reduced 2018 payment appropriations by EUR 35 million (Bourlange procedure) following the IMI2 Governing Board's adoption of the required amendment to the AWP 2018.

The corrective measures put in place have already yielded results, as demonstrated by the positive trend of rising implementation rate of payment appropriations (2016: 69.6 % in payment appropriations, 2017: 72 % in payment appropriations, 2018: 87%).

Common H2020 IT tools

As further specified in section 4.5 of this report, following the internal audit on cooperation with the CSC, IMI is implementing the IAS recommendation to 'further investigate the possibility of implementing the EFPIA in-kind contribution reporting requirements within the common H2020 IT tools'. IMI is collaborating with the CSC in analysing the possible options of migrating industry in-kind contribution reporting into the H2020 tools. In June 2018 IMI tabled detailed technical specifications needed to address the reporting obligations by industry partners as laid down in the Council Regulation (see also part 4.5). At the end of the year, further discussions were still ongoing.

Audit on IMI annual accounts 2018

In October 2018, a team from the ECA performed a fieldwork visit to IMI within the scope of the statement of assurance for the financial year 2018. The auditors examined a sample of FP7 transactions, administrative expenditure, revenue recovery, recruitments; and analysed procedures in place for one procurement and two Calls for proposals. They reported 'no findings' at this stage.

In accordance with the IMI2 Financial Rules, IMI's 2018 annual accounts are audited by the external audit company (Ernst&Young), who were contracted under an EC DG Budget framework contract for a period of two financial years. The preparatory work started in November 2018.

The Court of Auditors will draw the final audit opinion on the 2018 accounts, revenue and transactions on the basis of the work by independent external auditors as well the audit work performed by the ECA dedicated team. They will report on it in autumn 2019.

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 IAS issued the final audit report on the 'Coordination with the Common Support Centre and implementation of CSC tools and services in the IMI2 JU' on 9 March 2018.

The audit objective was to assess the adequacy of the design and the efficiency and effectiveness of the IMI2 JU governance, risk management and internal control processes for the coordination with the CSC and the implementation of the CSC tools and services.

The audit covered the following elements:

- the sub-processes most significantly dependent on the CSC, with a direct impact on the IMI2 JU operations (implementation of the H2020 Calls, grant management, project implementation and monitoring, dissemination of programme and project data) and on the IMI2 JU internal control system (ex-ante controls for interim and final payments, ex-post audits);
- the governance of relations with the different levels of the CSC.

The IAS observed a number of good practices, specifically:

- the active participation of the IMI2 JU representatives in meetings with the Common Audit Service;
- the quick sharing of information within IMI2 JU, allowing all staff to be aware of developments in their respective areas;
- bilateral meetings with the director of the CSC, which enabled the JU to share its feedback on the implementation of the CSC tools and services;
- joint letters of the Directors of the JUs addressed to the Director of the CSC, which enabled the JUs to collectively voice their concerns about the confidentiality of project data and the arrangements for ex-post audits.

The IAS concluded that IMI2 JU has implemented adequate governance, risk management and internal controls processes that effectively and efficiently support its coordination activities with the CSC and the implementation of the CSC tools and services.

The audit did not result in the identification of any critical or very important issues. However, the IAS considered that there was some room for improvement and issued three 'important' recommendations in the areas of:

- transition to the common H2020 it tools;
- access to confidential project information and participation in the DiEPP (Dissemination and Exploitation Practitioners Platform) group;
- arrangements for ex-post audits.

IMI prepared an action plan that was approved by the IAS on 4 May 2018. All three recommendations were translated into five actions. Four actions (addressing two recommendations) were implemented by the end of 2018. Their implementation and closure is confirmed by the IAS letter of 11 January 2019 (Ares(2019)158428). One action related to the migration of EFPIA IKC reporting into the H2020 tools and possible solutions is planned for implementation in the course of 2019. IMI is collaborating closely with the common IT services.

4.6 Risk management and conflict of interest

Risk management at IMI is 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)[38] 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 the course of 2018 the Programme Office systematically monitored the evolution of the risks identified at operational and corporate level through the annual risk assessment exercise[39]. The regular follow up ensures that risk management is a dynamic and proactive process in view of evolving corporate priorities. A working group established by the Executive Director reviews, discusses and updates the residual risks and corresponding mitigating actions.

The risks identified during the assessment exercise are reported in two risk registers:

- the Strategic Risk Register (SRR) brings together the most critical risks at corporate level;
- the Operating Risk Register is an operational tool to be implemented at department level.

Both registers:

a) list the risks identified and assess them in terms of impact and likelihood;

b) describe the mitigating actions proposed to reduce either the probability of the risk materialising, or the severity of the exposure if the risk does occur;

c) assign responsibility to a specific team or individual.

The key risk management activities in 2018 focused on the following areas:

1. Streamlining the process for defining Call topics

Programme Office actions:

- implemented extensive preparatory consultations with the Members;
- developed a fixed plan of Call development stages shared in advance with all stakeholders;
- assisted the SGGs in ensuring coordination in certain strategic areas and making the development of new topics more transparent and effective;
- enhanced collaboration between IMI Scientific Officers and Call topic writers through targeted briefings and training courses.

2. Maintaining scientific attractiveness for the scientific community, patients and industry (especially SMEs)

Programme Office actions:

- improving the transparency of participation process through info days, local workshops and webinars, revision of the rules of procedure, and the new corporate website;
- recruitment of a Seconded National Expert to promote the involvement of, and facilitate patients' participation in, IMI projects;
- implementing the action plan for increasing SME participation.

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

[39] RAE Report 2017/2018 of 5 December 2017 (IMI2/INT/201702160)

3. Improving budget execution to ensure efficient management of the grant award process and optimal budget implementation for ongoing projects

Programme Office actions:

- reinforced its monitoring activities in liaison with all project coordinators in order to reassess the project needs and their work plan in a timely fashion;
- thoroughly reviewed the overall need for payment appropriations in 2018 as the basis for a revised forecast;
- enhanced interactions between science and finance operations;
- ensured closer monitoring of high-risk projects.

4. Maintaining the balance – at the end of the programme – between the EU financial contribution and the in-kind contribution provided by industry and Associated Partners

Programme Office actions:

- monitoring projects' financial management through the periodic reports received from coordinators and performing ex-post control of costs incurred in indirect actions by industry according to a risk-based plan;
- performing a regular assessment of the level of in-kind contributions (committed and reported) and presenting this to the Governing Board at each meeting.

5. Promoting a positive external perception of IMI

Programme Office actions:

- continued to implement an ambitious communication strategy to demonstrate, in a spirit of openness and transparency, the results achieved by the partnership;
- identified and sponsored projects and actions that highlight IMI's successes;
- maintained transparent relationships with key decision-makers to ensure they have an informed view of how IMI works.

Concerning risks related to the performance of the Programme Office and operations, particular attention has been given to the organisational structure and human resource management, especially as regards project related activities, the efficiency of which is dependent upon a sound interaction between science and finance. This is considered crucial by the management in order to ensure that the structure and resources of the JU continue to meet evolving organisational objectives and needs.

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)[40]. As part of the common antifraud strategy, IMI has also appointed an antifraud correspondent to support internal activities and to coordinate relations with the European Commission, other agencies and OLAF[41].

This strategy is implemented at JU level and in coordination with DG RTD and other research agencies through a multiannual action plan coordinated by the Fraud and Irregularity in Research (FAIR) Committee. During 2018, in particular, IMI's activities within the FAIR Committee were focused on assessing the outcome of the implementation of the action plan 2015/2018 and setting up a new operational plan for the next three years.

At JU level, IMI continued to implement its action plan to address the specificities of its 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 risks linked with conflict of interest, delegation of authority, and segregation of duties.

As regards suspected fraud cases, in 2018 there were no instances of suspicion of irregularities in IMI projects. IMI did not receive any OLAF enquiries or requests for information.

[40] 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.

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

4.8 Compliance and effectiveness of internal control

The internal control framework (ICF) implemented by IMI is intended as a process applicable at all levels of management and designed to provide reasonable assurance that: i) operations are effective, efficient and aligned with the strategy; ii) financial reporting is reliable; and iii) the JU complies with the applicable laws and regulations.

The IMI internal control framework is based on 17 control principles. It is aligned with the Commission control framework[42] and was adopted by the Governing Board in December 2017[43]. All the principles of the new control model are embedded across IMI's organisational structure and rely on a combination of ex-ante and ex-post controls, segregation of duties, documented processes and procedures, control of deviations, and promotion of ethical behaviour.

Within this context, the Executive Director steers and supervises the risk and internal control management 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 during 2018 included:

- coordination, supervision and monitoring of the implementation of the revised internal control framework;
- assessment of the JU's compliance with the internal control principles and preparation of the annual self-assessment of the effectiveness of the internal control system, complemented by intermediate reports where needed;
- implementation of the annual risk assessment exercise in order to manage and mitigate the risks that might threaten the achievement of the JU's objectives.

In 2018, IMI's internal control action plan focused on the implementation of the new principles of the internal control framework. To that end, the Executive Director revised and progressively developed the structure of the internal control environment, taking into account the structure and size of IMI and the nature of the tasks entrusted to it. A new operational guidance for the implementation and measurement of the effectiveness of the control system was adopted[44].

Management assessment of the effectiveness of the internal control system

The 2018 measurement and self-assessment of the effectiveness of the internal control framework was mainly based on the criteria set out in the new implementation guidance, namely:

- a set of pre-defined indicators complemented by targets and baselines;
- interviews with the staff to assess their degree of awareness and understanding of internal control principles and procedures;
- implementation of the operating procedures developed or revised in 2018;
- an objective examination of reports and assessments 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's overview on progress made on the implementation of the corresponding action plans.

[42] Adopted by the European Commission on 19 April 2017. 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.

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

[44] IMI2/INT/2018-07079 of 18/12/2018.

In order to assure that all aspects of IMI operations and control were covered by the assessment, the 17 control principles were analysed both individually and as part of the corresponding control component[45]. An assessment table covering all the functions of the JU (financial management, governance, administration and horizontal support, procurement and contracts, HR, IT, communication) was created to check compliance as well as the effectiveness and consistency of the internal control framework.

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

The IMI Programme Office keeps a register of all exceptions and non-compliance events potentially leading to weaknesses; reports are entered into the register through a dedicated procedure and using pre-defined templates. A central register is reviewed regularly by the Internal Control Coordinator (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 cases reported in 2018 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 impacts 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 of the most frequent issues.

Reliability of financial reporting and accounting

DG Budget carried out its annual evaluation of the local financial systems set up in IMI as provided in Article 49 (e) of the Financial Rules of IMI and as announced by the Accounting Officer on 14 June 2018. In addition to the assessment and conclusions issued on 8 December 2017, in 2018, the DG Budget team reviewed the information on changes in the local systems and/or in the control environment; evaluated internal control deficiencies identified by audits and supervisory controls; and verified a sample of transactions for the operations authorised by IMI during the 2017 financial year.

The evaluation did not identify any weaknesses in the internal control systems which would have a material impact on the accuracy, completeness and timeliness of the information required to draft the annual accounts and produce reliable reporting. On the basis of the evidence available, DG BUDG concluded on 13 December 2018 that the internal control systems were working as intended. The accounting systems implemented in IMI JU are therefore validated.

Moreover, IMI completed the implementation of the action plan (approved by the Accounting Officer on 5 February 2018). The state of play was assessed by DG BUDG resulting in the closure of all five recommendations (BUDG note Ares(2019)478593 of 28 January 2019).

Assessment of the functioning of the internal control system

In conclusion, the results of the 2018 internal control assessment confirm that the IMI control system is compliant with the revised internal control framework, is working to an acceptable level of effectiveness, and allows sufficient control of risks and achievement of control objectives. In this context, in 2018, the IMI internal control system was strengthened by fully implementing the action plans addressing ECA and IAS audit recommendations as well as IMI's Accounting Officer's observations. The assessment process and methodology were supported with the new implementation guidance.

[45] The new ICF consists of 5 internal control components: "Control environment", Risk assessment", "Control activities", "Information and Communication" and "Monitoring activities".

5 Management 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[46];
  - 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 European Court of Auditors;
- External verifications and investigations:
  - reports by the EC accounting officer;
  - reports by the Ombudsman;
  - reports by the European Data protection Supervisor;
  - conclusions by the Anti-fraud Office;
- 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 2018, 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 % for both operational programmes. The control strategy foresees the implementation of further controls during subsequent years designed to detect and correct these errors.

The results of grant management operational indicators (time to grant, time to sign, time to inform) are well within the legal targets demonstrating maturity of control systems and supporting the declaration of assurance.

[46] 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 Statement of the manager in charge of risk management and internal control

For the Manager in charge of risk management and internal control:

I declare that in accordance with the IMI2 JU Governing Board decision No 2017-28 on Revision of IMI2JU internal control framework, I have reported my advice and recommendations on the overall state of internal control in the IMI2 JU to the Executive Director.

I hereby certify that the information provided in Chapter 4 of the present Annual Activity Report and in its annexes is, to the best of my knowledge, accurate and complete.

Brussels, 28 February 2019

Francesco Ronfini, Internal Control and Risk Manager

For the Manager taking responsibility for the completeness and reliability of management reporting on results and on the achievement of objectives:

I hereby certify that the information provided in Chapters 1 and 2 of the present Annual Activity Report and in its annexes is, to the best of my knowledge, accurate and complete.

Brussels, 28 February 2019

Hugh Laverty, Head of Scientific Operations

7 Declaration of assurance

I, the undersigned,

Executive Director of the Innovative Medicines Initiative 2 Joint Undertaking

In my capacity as authorising officer

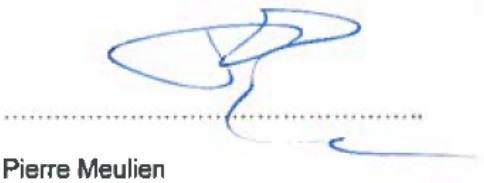
Declare that the information contained in this report gives a true and fair view[47].

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 2019



Pierre Meulien

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 Horizon 2020 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

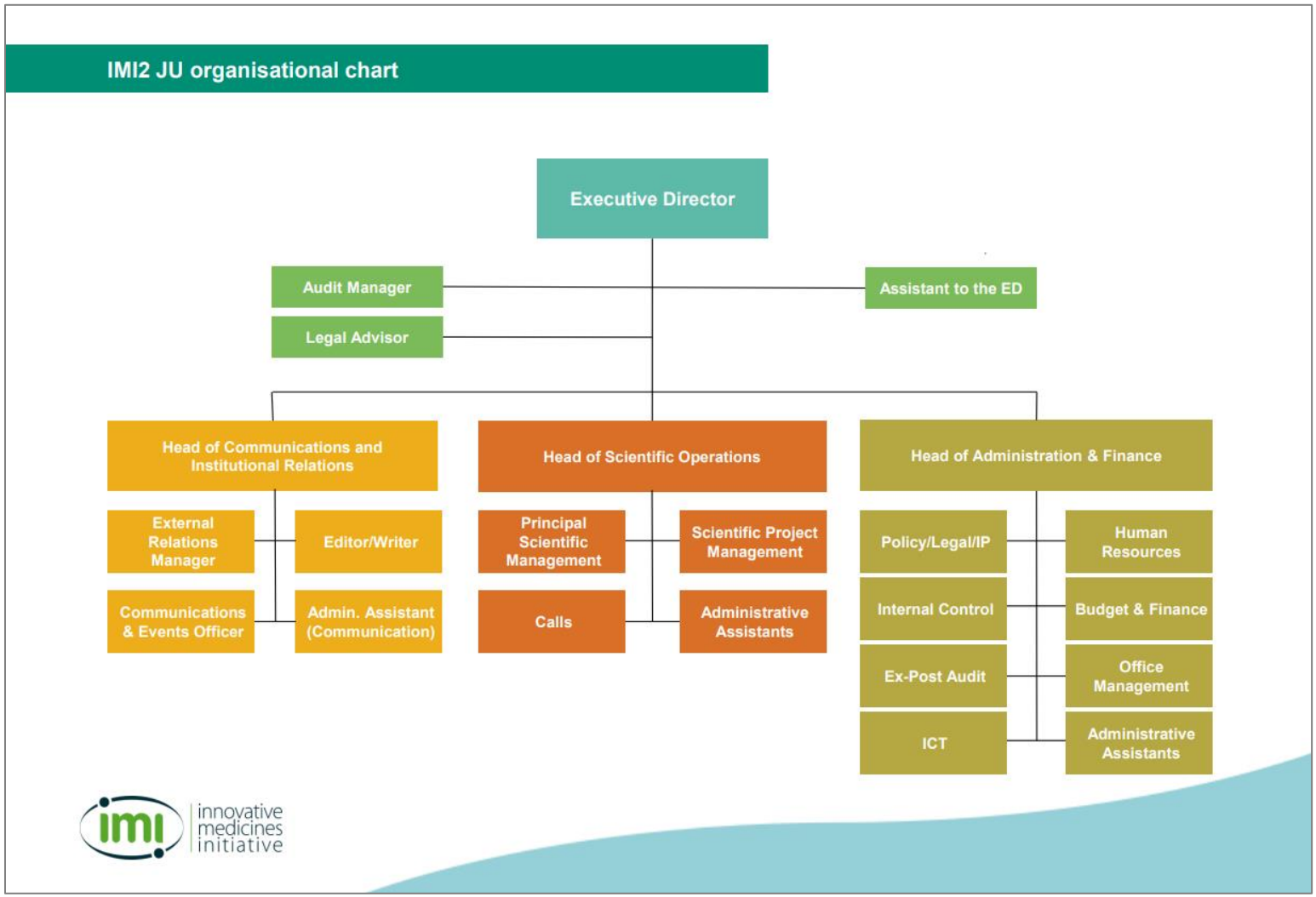
Annex 11 – Media highlights

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

Temporary agents

Grade	Year 2017			Year 2018												
	Establishment plan 2017			Evolution in posts						Organisational evolution			Establishment plan 2018			Posts filled on 31/12/18
				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	TA
AD16																
AD15																
AD14		1	1											1	1	1
AD13																
AD12		2	2											2	2	1
AD11		2	2											2	2	2
AD10																
AD9		3	3											5	5	3
AD8		7	7											7	7	6
AD7		6	6											4	4	6
AD6														2	2	2
AD5		12	12											10	10	10
Total AD		**33**	**33**											**33**	**33**	**31**
AST11																
AST10																
AST9																
AST8		1	1											1	1	1

AST7																
AST6																
AST5																
AST4														2	2	2
AST3		4	4											2	2	2
AST2																
AST1		1	1											1	1	1
Total AST		**6**	**6**											**6**	**6**	**6**
SC6																
SC5																
SC4																
SC3																
SC2																
SC1																
Total SC																
Overall total		**39**	**39**											**39**	**39**	**37**

Notes

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

Contract agents

Grade	2017	2018	Posts filled on 31/12/18
CA FG IV	2	2	1
CA FG III	12	12	8
CA FG II	1	1	1
CA FG I	0	0	0
Total CA	**15**	**15**	**10**

Notes:

- CA = contract agent
- FG = function group

Seconded national experts (SNEs)

SNEs	2017	2018	Posts filled on 31/12/18
Total	**0**	**2**	**1**

Annex 3 – Project outputs

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

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.

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.

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.

Biomarkers for the efficacy and safety of vaccine candidates: Vaccines are one of the most effective public health measures out, saving some two to three million lives worldwide every year. During vaccine development, biomarkers are an essential tool to help researchers identify vaccine candidates that will be both safe and effective. Ultimately, these biomarkers will advance the development of new vaccines and contribute to greater public confidence in vaccines.

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.

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.

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.

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.

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.

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.

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 IMI website includes a catalogue of accessible results, including a brief description of each resource and a link for more information. The list, which is not exhaustive, can be found in the 'projects and results' section of the IMI website.

IMI1 project outputs

New tools/resources for drug discovery & preclinical drug development

Project title	Description of result
COMPACT drug delivery	Development of a wide repertoire of drug delivery systems, fully characterised and tested. Two patents have been filed: one for brain delivery and another for the nano-carrier system for lung delivery.
ELF drug discovery	Keapstone Therapeutics, a start-up formed on the back of the results obtained through the European Lead Factory has received additional EUR 1.1 million in funding from Parkinson's UK to make the next steps in clinical candidate selection and first-in-human studies.
ELF drug discovery	During 2018, the European Lead Factory hit another milestone with the announcement that the public part of its compound library now contains over 200 000 novel compounds. To generate this library, design ideas were crowdsourced from scientists in academia and industry alike. All ideas were screened by experts and the most promising were turned into physical compounds by the project's team of chemists. Coupled with the 300 000 compounds provided by the pharma partners, this means a library of 5000 000 is available for public screens. The project's compound collection and state-of-the-art screening centre have allowed researchers across Europe to successfully start drug discovery projects in a range of disease areas.
ELF drug discovery	An ELF programme aimed at identifying small molecules for the treatment of Alzheimer's Disease has culminated in the most potent compound yet identified by the ELF team at Newhouse, Scotland with the most active compound. The complete package of data generated for this programme includes a series of compounds which establish the progressive nature of the structure-activity relationships, detailed biochemical studies to demonstrate the mechanism of action supported by biophysical data from two independent methods, cellular activity, physicochemical and DMPK

Project title	Description of result
	profiling of the best compounds. Thus, excellent starting points for a novel treatment for this terrible disease have been identified
ENABLE antimicrobial resistance	One of the lead molecules - the aminoglycoside apramycin – has been selected as clinical candidate for the treatment of critical systemic bacterial infections caused by Gram-negative pathogens. These include carbapenem-resistant Enterobacteriaceae and Acinetobacter baumannii – both listed as Priority 1 on the WHO priority pathogens list. The clinical potential of apramycin was discovered by researchers at the University of Zurich who set up a spin-out company, Juvabis, to develop it further. Juvabis joined ENABLE in 2016. Thanks to the collaboration with ENABLE, the Juvabis team has now been able to demonstrate the safety and efficacy of apramycin in animal models.
EU-AIMS autism spectrum disorders	Performed a multisite preclinical study and identified the factors to be controlled in a standardised protocol to obtain reproducible results for the behavioural evaluation and drug testing in a genetic rat model of Autism Spectrum Disorder (ASD).
EU-AIMS autism spectrum disorders	Discovered four potential targets for autism: increased brain serotonin, modulation of glutamate/gamma-Aminobutyric acid (GABA) balance, GABA-A and cannabinoid receptors.
iABC antimicrobial resistance	Carried out Murepavadin (POL7080) susceptibility testing (conventional and biofilm) against *P. aeruginosa* strains from cystic fibrosis patients; the results support the decision to proceed to pre-clinical inhalation toxicology studies
K4DD drug development	The K4DD project launched a web-based toolbox that provides methods for computing drug binding kinetics has been established (http://kbbox.h-its.org). This toolbox provides also a guide for potential users, examples and tutorials.
K4DD drug development	Developed an infrared sensor that rapidly reveals how a drug binds to its target and how long that effect lasts. The tool, which could aid in the development of more effective drugs with fewer side effects, is described in a paper in Angewandte Chemie. Current methods to assess the nature of these structural changes need weeks or even months to deliver results. The new technique delivers results in just minutes. In the sensor, the target protein is bound to the surface of a crystal, which is rinsed with solutions containing a drug that should attach to the protein. An infrared light is shone through the crystal; any changes to the protein structure caused by the drug are detected by a sensor. The team tested their device on medicines designed to affect the heat shock protein HSP90, which is implicated in a number of diseases including cancer. The device delivered the same results as conventional tests and provided new information on the activity of 11 additional HSP90 inhibitors. The authors of the paper conclude: 'Particularly when scaled up in an automated screening platform, our method could be used to identify new drug candidates in the early drug-discovery process.'
Onco Track cancer	Identified a new way of tackling colon cancer; the findings are published in the journal Cell Reports. Research has shown that cancer stem cells play a key role in driving the growth of colon cancer tumours. They are also thought to be behind relapses, when cancer returns following treatment. In this study, researchers found that cancer stem cell survival is controlled by a specific feature of the 'Hedgehog' signalling pathway, which allows cells to respond to external signals and inhibits stem cell differentiation. Targeting the Hedgehog pathway in a similar way has delivered promising results in early-stage research on pancreatic and breast cancer cells.
TRANS-LOCATION antimicrobial resistance	The outer membrane proteome distribution of *P. aeruginosa* and *A. baumannii* in different *in vitro* and *in vivo* conditions was characterised. The results can assist in the future design of drugs with potentially better penetration properties into bacteria.
TRANS-LOCATION antimicrobial resistance	First crystal structure of the outer membrane protein MlaA solved that has led to a model to describe how MlaA, which plays a critical role in the maintenance of the asymmetry of the bacterial outer membrane, functions. This functional model further clarifies how MlaA could play a role in Gram-negative drug discovery, as disruption of

Project title	Description of result
	this system would be expected to reduce or remove one of the barriers to drug penetration.
TRANS-LOCATION antimicrobial resistance	A protocol was developed to quantify the permeation of charged compounds through porins in a quantitative manner.
TRANS-LOCATION antimicrobial resistance	A mass spectrometry-based protocol to measure compound uptake into whole cells was designed and cross-validated against a fluorescence-based method. This new assay could be used to guide future efforts to discover Gram-negative antibiotics by providing quantitative data on penetration into bacteria.
TRANS-LOCATION antimicrobial resistance	A scoring function based on structural and physical properties to describe penetration through porins of Enterobacteriaceae. This scoring function correlated with in vitro permeation assays and in vivo antibacterial activity and also offered a physical mechanism and explanation for the observed permeability trends which opens the way to the screening of virtual libraries for identifying molecules with optimal permeation
ULTRA-DD drug development	The project has generated 4 593 protein expression constructs to date. This has enabled the delivery of 701 purified soluble proteins and 194 integral membrane proteins samples for various analyses (e.g. assays and screening). In addition, 104 antigens were generated within ULTRA-DD, which to date has led to the production of 33 high quality antibodies.
ULTRA-DD drug development	Chemical screening efforts were mainly directed at epigenetic targets including the YEATS domain epigenetic reader protein family (MLLT1, YEATS2, MLLT3, YEATS4) as well as the Kme reader SPIN1. In total, *in vitro* screening has been performed on 22 targets and approximately 120 000 data points have been generated.
ULTRA-DD drug development	The project has created a widely accessible atlas of drug target prioritisations for 30 immune disease traits, including the identification of ~75 highly rated and under-explored genes. The research teams are now processing them for potential inclusion as novel immune targets with strong genetic support.
ULTRA-DD drug development	20 novel and follow-up 3D-structures of soluble ULTRA-DD targets were solved. In addition, one team completed and deposited fragment screens on 10 targets (PHIP, BAZ2B, ATAD2, FALZ, SP100, BRD1, JMJD2D, NUDT22, JARID1B, JMJD1B) and a further six screens (NUDT4, NUDT7, NUDT21, DCP2, PARP14A and MACROD1) have been completed and are ready for deposition in the PDB (www.rcsb.org). In addition, the structure of the integral membrane protein ABC transporter, ABCB8, with ADP was solved and deposited, and additional Cryo-EM structures were solved in cooperation with EFPIA partners, providing access to instrumentation and advice. Another partner successfully analysed 10 protein complexes during the year (23 in total since start of the project). In addition, the same team identified a high-resolution interaction map of activated TNF-alpha receptor complexes using a ligand binding approach.
ULTRA-DD drug development	Novel target-disease associations have been discovered using patient-derived cell assays: (1) screening with the chemical probe SGC-CBP30 reveals that the bromodomain targets CREBBP/EP300 are important regulators of myofibroblast phenotype and function, pertinent to disease activity in fibrosis; (2) novel but distinct roles for bromodomains BRPF1 and BRPF2 in regulating Th17 biology in Ankylosing spondylitis cells have been identified; (3) follow-up work is ongoing to validate the potential role of specific methyl transferases in B-cell responses (myositis and lupus).

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

Project title	Description of result
ABIRISK drug safety	By comparing anti-drug antibody (ADA) positive and negative patients, the project was able to identify 4 predictive markers of an immunosignature (frequency of B-, T- and monocytes subsets and their phenotypic signature in peripheral blood mononuclear cells) that could predict ADA development. The markers were validated in independent disease cohorts and in a longitudinal cohort.
ABIRISK drug safety	All data generated within the project is compiled in a data repository. Using a web-based tool, which allows the interactive exploration of this data, it is possible to get a comprehensive analysis of the T cell response of 4 antibodies and human IFN Beta, which can be used for predictive analysis of ADA development.
AETIONOMY Alzheimer's disease & Parkinson's disease	Integrated genotype information, neuro-imaging as well as clinical data (including neuro-psychological measures) from ~900 normal and mild cognitively impaired (MCI) individuals and developed a highly accurate machine learning model to predict the time until Alzheimer's disease is diagnosed.
CANCER-ID cancer	Developed a streamlined procedure for studying certain alterations in cancer cells found circulating in the blood stream. The method could prove useful in helping clinicians to better identify which treatments will work in which patients, and to monitor disease progression. The study focused on the analysis of copy number alterations (CNAs) in the tumour cells. Different CNA profiles have been linked to increased response or resistance to different types of drugs. In PLoS ONE, the CANCER-ID team describes a robust yet simple, one-step method to detect the number of CNAs in single cells. According to authors, the new technique, dubbed Ampli1, provides comparable or superior performance at lower cost than current methods.
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	Demonstrated that in obese subjects with type 2 diabetes, while Gamma-glutamyltranspeptidase (GGT) activity is generally associated with impaired glucose metabolism, the b-GGT fraction specifically and independently tracks with insulin resistance.
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	Demonstrated using primary care electronic medical record data from two European countries that non-alcoholic fatty liver disease (NAFLD) does not improve beyond traditional cardiovascular risk factors the prediction of incident cardiovascular events in at risk individuals.
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	Identified type 2 diabetes as a significant risk factor associated with disease progression in patients with a diagnosis of non-alcoholic fatty liver disease (NAFLD) / non-alcoholic steato hepatitis (NASH).
EMIF knowledge management, Alzheimer's disease,	Identified the circulating chemokine (C-C motif) ligand 18 (CCL18), and mannose as potential biomarkers for metabolic complications of obesity.

Project title	Description of result
metabolic syndromes	
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	Identified glycine as a causal biomarker for coronary disease through measurement of metabolomics in EPIC-Norfolk and Fenland cohort studies.
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	Demonstration of a seven plasma protein marker set predictive of Alzheimer's disease pathology (from gold-standard markers) suitable for use in clinical trials to reduce screen failure, useful in both Apolipoprotein E APOE –ve and +ve individuals This panel of proteins is the product of over a decade of research. It is biologically relevant, it is measurable using practical immunocapture arrays, and could significantly reduce the cost incurred to clinical trials through screen failure due to absence of amyloid pathology.
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	Studied the 'obesity paradox' (which suggests it is possible to be overweight or even obese yet not have an increased risk of heart disease). Found that in fact the risk of heart and blood vessel problems such as heart attacks, strokes, and high blood pressure, rises as body mass index (BMI) increases beyond 22-23 kg/m^2. People with a BMI of 22-23 kg/m^2 had the lowest risk of heart disease. The risk rises by 13% for every 5.2 kg/m^2 increase in BMI in women and 4.3 kg/m^2 in men. The risk also rises with an increase in waist circumference. The study was published in the European Heart Journal.
EU-AIMS autism spectrum disorders	Developed a positron emission tomography (PET) protocol for quantification of metabotropic glutamate (mGluR5) receptors in ASD subjects and examined twin pairs discordant for Autism spectrum Disorder (ASD) as well as controls. Also developed a methodology for comparisons of GABA and glutamate measured with PET and magnetic resonance spectroscopy (MRS).
EU-AIMS autism spectrum disorders	Collected follow-up data on the high-risk infant cohort with over 80 % of the cohort followed to age 2 and replicated the earlier observation linking reduced temporal lobe specialisation to later autism.
EU-AIMS autism spectrum disorders	Completed an initial case series study of ten infants with a known genetic disorder linked to autism (neurofibromatosis type 1), essential to translational insights.
EU-AIMS autism spectrum disorders	Demonstrated that excitation–inhibition (E-I) flux can be 'shifted' with a pharmacologic challenge in autism patients, but that responsivity is significantly different from controls. In addition, the initial evidence suggests that abnormalities in functional connectivity can be 'normalised' by targeting E–I, even in adults.
EU-AIMS autism spectrum disorders	Discovered three biomarkers useful to determine target engagement.
Quic-Concept cancer	Validation in several cohorts of patients and murine datasets the concept of radiomics. Radiomic analysis exploits sophisticated image analysis tools to generate image-based signatures for precision diagnosis and treatment.

Improved protocols for clinical trial design and processes

Project title	Description of result
CANCER ID	Benchmarking of liquid biopsy technologies allowed selection of best suited technologies/protocols for CANCER-ID clinical validation phase.
COMBACTE-NET antimicrobial resistance	A white paper, published in the journal Clinical Infectious Diseases paper provides recommendations for improving the design and analysis of clinical trials for antibacterials against multidrug-resistant organisms. The COMBACTE-NET team assessed a number of ways of improving clinical trial design and analysis, and scored each one on its alignment with regulatory frameworks; its technical feasibility; ease of data interpretation; ease of practical implementation; and the strength of the evidence base for the recommendation. The authors note that not all recommendations will be applicable to all trials, and some score better than others on the different criteria. Nevertheless, they note that 'they are all relevant to the debate supporting change'.
EPAD Alzheimer's disease	Published Open Access the study protocol of the European Prevention of Alzheimer's Dementia Longitudinal Cohort Study (EPAD LCS). https://bmjopen.bmj.com/content/8/12/bmjopen-2017-021017
EU-AIMS autism	Demonstrated that is possible to collect eye-tracking-based putative biomarkers with high degrees of precision across multiple European sites despite varied lab set-ups, critical to clinical utility.
SPRINTT geriatrics	Publication of the main demographic and clinical characteristics of older adults with physical frailty and sarcopaenia (PF&S) who were found to be eligible for participating in the SPRINTT trial. (The 'Sarcopenia and Physical fRailty IN older people: multi-componenT Treatment strategies' (SPRINTT) randomised controlled trial: Case finding, screening and characteristics of eligible participants. Marzetti et al., Exp Gerontol. 2018 Sep 24; 113:48-57. PMID: 30261246
SPRINTT geriatrics	Contribution of data from the SPRINTT trial to the regulatory science debates on the operationalisation of physical frailty & sarcopaenia discussed at: meetings held in 2018: International Conference on Frailty and Sarcopenia Research (ICFSR); and the Sarcopenia Consensus conferences by the Foundation of the National Institute of Health.

Biomarkers for the efficacy and safety of vaccine candidates

Project title	Description of result
BioVacSafe vaccines	Creation of a digital archive of 2 000 clinical samples and linked laboratory data following immunisation in vaccine trials to be uploaded in the public domain. This can be a resource for future safety biomarker benchmarking and research beyond the lifetime of the project.
FLUCOP vaccines	Creation and characterisation of a PBMC (peripheral blood mononuclear cells) biobank, which consists of more than 1 900 vials collected from 62 blood samples. All the samples were characterised by determining their immunogenicity profile against four or five influenza strains. This should help to better evaluate influenza vaccine immunogenicity.
FLUCOP vaccines	Thanks to the project, there was a successful cloning of a soluble and active neuraminidase – source of antigen that can be used in ELLA and in ELISA for serum titration.
ZAPI infectious diseases	With this project, there was an optimisation of the SpyT/SpyC vaccine platform with regard to optimal conjugation efficiency, purification of conjugation products, and quantification of conjugated antigens. Based on these analyses, final conjugation protocols have been developed and are currently used for vaccine preparation.

Project title	Description of result
ZAPI infectious diseases	The RVFV (Rift Valley fever virus) peptide GnTE3 was identified in this project as a promising vaccine candidate using a newly established mouse infection model.
ZAPI infectious diseases	A RVFV sheep infection model was successfully established and is currently being used for evaluation of RVFV candidate vaccines.
ZAPI infectious diseases	One industrial partner has defined a panel of QC (quality control) methods for the future ZAPI vaccine candidates.

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

Project title	Description of result
EU-AIMS autism spectrum disorders	Applied novel analysis approaches, such as normative modelling, to the data of the Longitudinal European Autism Project (LEAP) study for subtyping individuals with autism into biologically more homogeneous 'biotypes'.
EU-AIMS autism spectrum disorders	Developed and applied new techniques such as genetic-based machine-learning algorithms to both behavioural and neuroimaging data to move beyond group-based effects to individual-level prediction in autism.
DIRECT diabetes	DIRECT project has identified that people with altered ARRB1 and GLP-1R genes show improved response to the GLP-1 receptor agonist (GLP-1RA) injectable anti-diabetic drugs, such as: Exenatide (Byetta, Bydureon) and Liraglutide (Victoza, Saxenda). Those medications not only improve blood sugar control but also help with weight reduction, lower blood pressure and improve blood fat levels. This discovery was made based on a study of glycaemic response in 4,563 patients with Type 2 Diabetes who were treated with a GLP-1RA drug. Around 5% of the population has been found to have one or more copies of the altered ARRB1 gene. They show a much better response to GLP-1RA drug treatment, whereas in the rest of the population with a normal or altered GLP-1R genetic code only a slightly better response to GLP-1RA treatment is observed (as measured by HbA1c levels - an indicator of long-term blood glucose control). The difference is equivalent to receiving an extra 0.6mg of Liraglutide or 10µg of Exenetide. This study sheds important light by identifying distinct subgroups of diabetic patients that respond well to GLP-1RAbased medicines, so implying doctors in the future may need to check your genes before prescribing these drugs. Thus, this is a step towards personalised medicine in type 2 diabetes.
DIRECT diabetes	It has been suspected for a while that Type 2 Diabetes represents in fact a mixture of patient subpopulations, within which the disease develops and progresses differently. The DIRECT project has identified 5 distinct subpopulations of diabetic patients based on the main underlying disease drivers: insulin production (beta-cell function), insulin resistance, obesity and unhealthy levels of one or more kinds of fat in your blood (LDL, HDL and triglycerides); this is called "dyslipidaemia". The different combinations of these underlying problems lead to disease of varying severity. Two groups of patients who showed issues with only one of the above-mentioned mechanisms: patients who are overweight but otherwise metabolically healthy, as well as patients who have a generally healthy lifestyle, but suffer from poor beta-cell function. Their condition generally does not get worse over time (at least within the 36 months duration of the DIRECT study), and majority of these patients do not require glucose-lowering drugs to manage their symptoms. On the other hand, patients who have problems in all of the areas mentioned above tend to get worse more quickly than in patients with only a single affected disease mechanism. After 36 months of study

Project title	Description of result
	over 70% of these patients required glucose-lowering drugs. One of the important findings of the study was that the fastest progressing subjects had abnormal lipid profiles (i.e. unusual levels of different fats in their blood) compared to otherwise similar overweight and insulin resistant individuals whose blood sugar levels remained more stable over time. This observation is being investigated further to see if it can help doctors identify at an early stage, which patients may benefit from more prompt drug treatment to prevent rapid progression of the disease.

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

Project title	Description of result
AETIONOMY Alzheimer's disease & Parkinson's disease	Completed recruitment of a cohort of 421 patients and controls as part of the AETIONOMY study working to identify biomarkers for a mechanism-based taxonomy of neurodegenerative diseases: 280 Parkinson's disease (PD) patients, 39 subjects at risk for PD, 2 prodromal Alzheimer's disease (AD) subjects, 5 subjects at risk for AD, and 95 healthy control subjects.
CANCER-ID cancer	Collaboration between sites in Groningen, Twente, Graz, Berlin, and industry partners Menarini, Boehringer, Eli Lilly and Bayer allowed non-small-cell lung cancer (NSCLC) immune checkpoint inhibitor (ICI) study analysing clinical utility of CTCs and ctDNA. Similarly, the ongoing ICI/chemotherapy studies in Oslo will be supported by UKE, Menarini, Thermo Fisher and Bayer. These studies aim at assessing the clinical utility of CTC and ctDNA as a non-invasive biomarker of response/resistance to different treatments used as standard of care in lung cancer.
COMBACTE-CARE antimicrobial resistance	Completion of the recruitment of the EURECA study, with a total of 2 266 patients enrolled in this prospective observational study on cohorts of patients with serious carbapenem-resistant Gram-negative bacterial infections. Cases of infections caused by bacteria known as carbapenem-resistant enterobacteriaceae (CRE) are on the rise, and are most common in healthcare settings. They are extremely hard to treat (very often the only treatment options are combinations of old, toxic antibiotics) and can be fatal.
COMBACTE-CARE antimicrobial resistance	Finalisation of the report of the REJUVENATE study, the first interventional clinical trial (Phase 2a) to be conducted entirely within the collaborative framework. The trial confirmed safety and dose, provided PK/PD data of ATM-AVI in a population of hospitalised adults with complicated intra-abdominal infection (cIAI). Basic results can be found at https://eudract.ema.europa.eu/ (2015-002726-39) and https://ClinicalTrials.gov (NCT02655419).2015-002726-392015-002726-39. With these results, the phase 3 trial (REVISIT) has been initiated in collaboration with BARDA (protocol, sites selected).
COMBACTE-MAGNET antimicrobial resistance	Publication on risk factors and prognosis of *P. aeruginosa* cUTIs in a scenario of increasing multidrug resistance (MDR). These data were generated from the RESCUING study, a multinational, retrospective, observational study at 20 hospitals in south and south-eastern Europe, Turkey, and Israel. https://www.combacte.com/uploads/2018/12/f_idr-185753-risk-factors-and-prognosis-of-complicated-urinary-tract-infe-121718_47049.pdf
COMBACTE-MAGNET antimicrobial resistance	Progress with the recruitment of patients to the EVADE study (>30 % randomised), including recruitment from sites in the US further to the collaboration established with Antibacterial Resistance Leadership Group (ARLG). EVADE is a Phase II, randomised, 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.

Project title	Description of result
COMBACTE-NET antimicrobial resistance	Strengthening of CLIN-NET network that includes more than 900 hospitals & 2 900 hospital contacts across 42 European countries. As of June 2018: ▪ 116 hospitals in 18 European countries actively recruiting in clinical studies ▪ Over 10,000 patients enrolled in clinical studies ▪ 800 investigators from 28 countries had so far GCP trainings. Of those, 389 joined face-to-face meetings, and 411 followed the e-learning GCP course. ▪ Consolidation of LAB-Net network (>750 labs) and development activities focusing on implementing the LAB-Net Quality Assurance Program including External Quality Assessment panel development & GCP training for laboratories.
COMBACTE-NET antimicrobial resistance	Completion of the enrolment in ASPIRE-ICU (2 000th subject enrolled in this prospective, observational, multi-centre, epidemiologic cohort study aiming at advanced understanding of *Staphylococcus aureus* and *Pseudomonas aeruginosa* infections in Europe. Enrolment reached 50 % (out of 5 000 subjects) in ASPIRE-SSI, a prospective, observational, multi-centre cohort study performed with adult surgical patients as subjects. All sites (35) are actively recruiting.
COMBACTE-NET antimicrobial resistance	Database lock for the SAATELLITE study, allowing work to start on the analysis of the results. 213 patients were randomised into the SAATELLITE study, which aimed to study the safety, characteristics and efficacy of suvratoxumab (MEDI4893) in patients at high risk of developing ventilator-associated pneumonia in an intensive care unit. The long-term follow up of the last randomised patients continues. (https://clinicaltrials.gov/ct2/show/NCT02296320); https://www.imi.europa.eu/sites/default/files/events/2018/ScientificSymposium/26-%20Ana%20Catalina.pdf
COMBACTE-NET antimicrobial resistance	Completion of the ANTICIPATE study with database lock in March 2018. Final analysis ongoing. Poster of preliminary results presented. https://www.combacte.com/posters/incidence-antibiotic-associated-diarrhea-clostridium-difficile-infection-europe/. ANTICIPATE is an observational study conducted with 1 007 patients aged over 50 receiving broad-spectrum antibiotics in hospital recruited in 34 European clinical centres aiming to identify the risk factors for these infections, establishing for whom the prevention of this pathology will prove the most beneficial. This study supports the Phase III study with DAV132, Da Volterra's promising new therapeutic agent for the prevention of *Clostridium difficile* infections in high-risk patients.
DIRECT diabetes	Collected intensively phenotyped prospective diabetes/metabolism cohorts at unprecedented scale. DIRECT recruited over 3 000 people at 6 centres across Europe who had either been recently diagnosed with diabetes or were considered to be at high risk of developing the disease. The cohort have been physiologically characterised cohorts, including imaging, diet and activity data. Furthermore many levels of –omic data have been collected, including GWAS, RNA Seq, miRNA, proteomic, metabolomics and metagenomics. Phenotyping is repeated at two follow-up visits at 18 and 36 months (diabetes cohort) and 18 and 48 months (pre-diabetes cohort) to track the disease progression.
EPAD Alzheimer's disease	The Longitudinal Cohort Study has screened 1 314 research participants and enrolled 1 145 from 20 sites in Europe. The individuals (either at risk of Alzheimer's disease or in the very early stage of disease) will be deeply phenotyped as a 'trial ready' cohorts for future clinical trials.
EU-AIMS autism spectrum disorders	The Longitudinal European Autism Study (LEAP) aims to identify risk factors that contribute to differences in brain development, difficulties in social behaviour and other core symptoms of autism spectrum disorders (ASD). It has collected a total of 749 participants including 422 individuals with ASD, 34 with intellectual disability (ID) and 293 with typical development (TD). In addition to these participants, LEAP collected phenotypic information on 1 004 relatives (mostly parents of individuals with ASD). LEAP collected blood for 77 % of the participants (N=323 ASD, 23 ID and 230 TD) and

Project title	Description of result
	74 % of the relatives (N=742). DNA was isolated for 519 participants (N=291 ASD, 17 ID and 211 TD) and 589 relatives. The blood DNA was used for the genotyping of 700 000 SNPs of 491 participants (N=266 ASD, 16 ID and 202 TD) and 562 relatives.
EU-AIMS autism spectrum disorders	The synaptic (SynaG) cohort was designed to better understand the genotype-phenotype relationship in carriers of deleterious mutations in synaptic genes associated with ASD. It includes 156 individuals, including 44 individuals with ASD, mostly with Phelan McDermid syndrome, 9 with typical development (TD), and 103 relatives. Blood collected for 95 individuals including 27 individuals with ASD, 1 TD and 67 relatives.
EU-AIMS autism spectrum disorders	190 genotyped individuals added to the dataset on cognitive, structural and neurofunctional phenotypes (N~1 500) of carriers of copy number variations (CNV), some other large or genic CNV, no CNV, or a point mutation in a gene of interest to autism or related neurodevelopmental disorders. This study will clarify the contribution of CNVs to the differences among individuals with ASD.
iABC antimicrobial resistance	EU bronchiectasis registry has to date recruited over 14 265 patients in 33 countries, providing an invaluable resource for academic and clinicians. There are 27 502 unique records with nearly 80 % eligible for year 1 follow up recording and greater than 60 % eligible for year 2 follow up.
Quic-Concept cancer	The project such has established a network of universities and hospitals equipped to measure and analyse validated imaging biomarkers in a standardised way
SPRINTT geriatrics	Completion of the recruitment for the SPRINTT trial, a phase III, single-blind, multi-centre randomised clinical trial: Out of the 1 566 eligible participants, 1 519 older persons were randomised into either the healthy aging lifestyle education (HALE) group or the MCI group (i.e., physical activity, nutritional counselling/dietary intervention, and ICT intervention) in 10 European countries. (ClinicalTrials.gov identifier: NCT02582138)
StemBANCC stem cells	There was the final recruitment of 496 subjects with defined diseases, drug responses and healthy volunteers of the 500 planned for the StemBANCC cohort – from those subjects the induced pluripotent stem cells will be generated in order to modelling the disease for research purposes.

Big data solutions to leverage knowledge / implementation of data standards

Project title	Description of result
ADVANCE vaccines	The AIRR (ADVANCE International Research Readiness) survey allows essential metadata to be collected from databases. The metadata collected allows an initial assessment of the suitability of databases to participate in benefit risk studies. This assessment will be helpful to decide if a given database is suitable to be considered for further feasibility analysis and/or fingerprinting.
AETIONOMY Alzheimer's disease & Parkinson's disease	Using patient data from the Alzheimer's disease NeuroImaging Initiative (ADNI) developed the first version of the Virtual Dementia Cohort (VDC), a platform for *in-silico* testing and validation of candidate mechanisms. The VDC overcomes legal and ethical limitations and allow access to a cohort with enriched data and of sufficient statistical power.
AETIONOMY Alzheimer's disease & Parkinson's disease	Integrated genotype information, neuro-imaging as well as clinical data (including neuro-psychological measures) from ~900 normal and mild cognitively impaired (MCI) individuals and developed a highly accurate machine learning model to predict the time until Alzheimer's disease is diagnosed. (https://www.nature.com/articles/s41598-018-29433-3#Sec13)

Project title	Description of result
EHR4CR knowledge management	The InSite platform, a spin-off from the EHR4CR platform was awarded the Clinical Informatics News European Innovation Award 2018. The platform, managed by Custodix NV, speeds up clinical trial design and greatly facilitates patient recruitment. https://www.insiteplatform.com
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	The EMIF Code of Practice was finalised through pilot testing and liaison with other relevant initiatives, to define the code of conduct regarding the protection of privacy and rules for equitable data sharing in the context of EMIF. It is available at: https://link.springer.com/article/10.1007/s11023-018-9467-4
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	Private remote research environment (EMIF-AD tranSMART) with subject-level clinical data from 14 cohorts on 3 423 subjects, including high-dimensional omics and imaging data of ~1 000 subjects of the EMIF Multi-modal Biomarkers Discovery (EMIF-MBD) study. This is a unique harmonised and integrated dataset of Alzheimer's disease patient data available in order to support Alzheimer's disease research in the EU.
EPAD / AETIONOMY Alzheimer's disease & Parkinson's disease	Developed and published the Study Viewer, an interactive information portal for the EPAD and AETIONOMY studies allowing longitudinal modelling of disease progression based on data from ADNI (Alzheimer's disease) and PPMI cohorts.
iPiE environmental issues	Released an online tool that summarises the properties, environmental toxicity and characteristics of active pharmaceutical ingredients (APIs). Dubbed, iPiE Sum ('iPiE Summary Database Search'), the tool is designed to allow public and regulatory bodies to obtain a high-level overview of what studies were collected during the iPiE project and what eco-toxicity data and studies are available.
K4DD drug discover	In collaboration with EBI, the K4DD consortium exported the data items collected during the K4DD project and transferred them to EBI for inclusion in the ChEMBL database. This way, sustainability and open access to the data beyond the project's lifetime is guaranteed.
WEB-RADR pharmaco-vigilance	At the end of the original WEB-RADR project, the consortium updated the app code to a more generic format to allow the functionality to be taken up more easily by other users. The consortium also gained funding to promote this aspect and started work to roll out the app for side-effect monitoring in developing countries, in pharmaceutical companies and also to allow the patient reports to feed automatically into their health records.

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

Project title	Description of result
AETIONOMY Alzheimer's disease & Parkinson's disease	3 webinars were hold explaining how Bayesian modelling of clinical data can improve the understanding of features, mechanisms and stratification of patient subgroups

Project title	Description of result
AETIONOMY Alzheimer's disease & Parkinson's disease	Developed online tutorials (https://data.aetionomy.scai.fraunhofer.de/bioinformaticians-and-students) on how to apply innovative bioinformatics techniques to identify and validate new disease mechanisms.
COMBACTE-MAGNET antimicrobial resistance	Patient and public involvement (PPI) toolkits developed and published to help primarily principal investigators, research teams, and pharmaceutical companies to involve the public in medicines development research, in particular antimicrobials. https://www.combacte.com/publications/patient-public-involvement-toolkit-practical-guide
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	Tutorials on the use of the EMIF platform have been developed and are available on YouTube: https://www.youtube.com/channel/UCSpN7hTQe4lzyRgRzc7gFuw
EU-AIMS autism spectrum disorders	Produced a video that explains to families what study participation involves, created a Facebook page for families SynaG: www.facebook.com/euaimssynag | Facebook LEAP: www.facebook.com/euaims, and created a puppet movie ('Pip and the Brain Explorers') which shows families and young children what a magnetic resonance imaging (MRI) scan involves
GetReal relative effectiveness	Second edition and 3rd edition of the online introductory course 'Real-World Evidence in Medicine Development'.
iABC antimicrobial resistance	Certification of the sites in multiple breath washout (MBW) testing to measure lung clearance index (LCI). 20/27 sites in the iBEST study have completed training (MBW training was a blended training programme: 1 day face-to-face session, use of an e-learning tool and mentoring support thereafter). (https://clinicaltrials.gov/ct2/show/NCT02712983)
K4DD drug discovery	Developed a guide for users, examples and tutorials for the project's web based toolbox that provides methods for computing drug binding kinetics Further tutorials will be added as the results from K4DD are published.
StemBANCC stem cells	Training of many consortium partners (and external participants) through 7 workshops including 5 iPS cell culture practical workshops and a cortical neuron workshop.

Impact on regulatory framework

Project title	Description of result
ADVANCE vaccines	A working group of the European Network of Centres uses the ADVANCE Code of Conduct for Pharmacoepidemiology and Pharmacovigilance (ENCePP) as a reference document for the revision of the ENCePP Code of Conduct in vaccine benefit-risk studies.
ADVANCE vaccines	Published a blueprint of a framework to rapidly provide scientific evidence of the benefits and risks of vaccines that are on the market. The document is the culmination of the project's work and is designed to help health professionals, regulatory agencies, public health institutions, vaccine manufacturers and the general public make more informed decisions on the benefits and risks of vaccines. The blueprint has two parts.

Project title	Description of result
	Firstly, there is a comprehensive manual for the future use of the framework. This sets out the steps needed to use the framework, the tools that can be used, and how to disseminate results. The second part of the blueprint addresses the future sustainability of the network through four different scenarios. The blueprint was written by ECDC (European Centre for Disease Prevention and Control) based on the outputs from almost all work packages of ADVANCE. It underwent a comprehensive consultation process with representatives of the main stakeholders interested in the assessment of benefits and risks of vaccines, including the ECDC Advisory Forum. It has also gone through a public consultation on ECDC website.
ADVANCE vaccines	Developed a web application with an interactive dashboard designed to make it easier to monitor the benefits and risks of vaccines in near real time. The tool is described in a paper in the journal Drug Safety. Once implemented, it would allow users to rapidly determine whether further regulatory or public health actions may be needed. Feedback from stakeholders (including public health institutes, regulatory authorities, and pharmaceutical companies) revealed broad support for the dashboard, with users appreciating the interactive interface and the ability to visualise individual components. The stakeholders were however less in favour of the composite benefit-risk measures offered. The ADVANCE team concludes that 'the proposed methodology is promising' and they are now testing the dashboard with real-world data.
CANCER-ID cancer	FDA nominated a public-private partnership representative for CANCER-ID in 2018 and an Innovation Task Force meeting at EMA took place in autumn 2018. As a result, it will be evaluated further by CANCER-ID whether data are sufficient to undergo the formal EMA qualification advice process for ctDNA standard material in technology benchmarking studies.
DRIVE-AB antimicrobial resistance	Data generated by the project's systematic review of the impact of AMR formed part of the evidence base that experts used to formulate the WHO's global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics (also called the Priority Pathogens List – PPL). This list ranks the resistant organisms for which new antibiotics are most urgently needed.
DRIVE-AB antimicrobial resistance	The project's contributions helped to create the G20 AMR R&D Hub: a new, international R&D collaboration hub in the field of antimicrobial research and product development aimed at maximising the impact of existing and new initiatives in antimicrobial basic and clinical research as well as product development. This Hub is mainly composed of members like the G20 and non-G20 countries as well as non-governmental donor organisations investing in R&D on AMR and observers like the representatives of relevant intergovernmental organisations, such as WHO, FAO, OIE, UNEP and the Organisation for Economic Co-operation and Development (OECD).
DRIVE-AB antimicrobial resistance	The project's team worked actively with the French government as a part of the European Joint Action on AMR and healthcare-associated infections to include assistance with implementation of innovation incentives.
PROactive chronic obstructive pulmonary disease	Final qualification opinion issued on the two patient reported outcome (PRO) instruments to capture physical activity (PA) data in patients with chronic obstructive pulmonary disease (COPD) in clinical trial settings. ▪ D-PPAC (for daily data collection with a recall period of 1 day) and ▪ C-PPAC (recall period of 7 days, intended to collect PA data during specified clinical study visits) The tools can now be used in clinical trials to understand how medicines will improve or not physical activity.

Implementation of project results inside industry

Project title	Description of result
ABIRISK drug safety	The monoclonal antibodies generated from the patients of ABIRISK's prospective cohorts were 'scaled-up' by Sanofi to be exploited as human anti-drug antibody positive controls (PCs) by the National Institute for Biological Standards and Control (NIBSC). After they have gained World Health Organization (WHO) endorsement, these PCs will be made available to laboratories worldwide, under the custody of NIBSC: 2 PCs each for infliximab, adalimumab and anti-IFNb (Rebif), 3 PCs for Natalizumab and 1 for rituximab.
CANCER-ID cancer	Industry partners started implementing technologies and respective protocols evaluated in the course of CANCER-ID for internal research in the field of liquid biopsy (e.g. ddPCR). In addition, particularly ctDNA analysis receives growing interest as selection and PD biomarker in industry sponsored studies.
ELF drug discovery	Servier and Swedish spin-out ScandiCure entered into an agreement on the further development of the compounds that were identified through a screen run by the European Lead Factory. Scandicure had identified inhibitors of a novel biological target for non-alcoholic steatohepatitis (NASH), type-2 diabetes and potentially other metabolic diseases but lacked the screening facilities to identify chemical matter against these targets. By accessing the ELF facilities and screening library, a number of compounds that interact with the target were identified. Under the new agreement, Servier will carry on the research started by ScandiCure, advancing the novel compounds through preclinical development. Further information: https://www.europeanleadfactory.eu/node/269
EU-AIMS autism spectrum disorders	Developed a human pluripotent stem cell (hPSC) culture system and showed it is a valid and relevant model system for modelling ASD in drug discovery programmes and transferred to EFPIA partners.
OrBiTo drug delivery	Development of guidance tools to be used by industry: - Decision tree for biorelevant *in vitro* dissolution testing. This can be used for the selection of appropriate *in vitro* dissolution method testing strategies to provide improved predictions of *in vivo* performance of oral formulations. This guidance can also be used to select the optimal dissolution methodology to determine the impact of process changes made during scale-up or post-approval on the clinical performance of oral drug products. - Decision tree for active pharmaceutical ingredient (API) characterisation. This can been used to guide work needed to select compounds that have optimal properties for product development, enable more accurate dose predictions to be made for first time in human studies, provide a basis for product design strategies, and improve the quality of input parameters for advanced *in silico* models of drug absorption.
Quic-Concept cancer	The project contributed to the international consensus imaging biomarker roadmap in oncology drug development that equips European imaging companies to develop and validate their imaging biomarkers in the most effective and efficient way. http://dx.doi.org/10.1038/nrclinonc.2016.162

Accessibility of resources/outputs beyond consortium

Project title	Description of result
ABIRISK drug safety	The project has developed a predictive tool (for time-to-event outcome = time to first anti-drug antibody (ADA)) implemented in an R package called iBST (improper bagging survival tree) and is freely available on the CRAN repository. The procedure GPLTR (generalized partially linear tree-based regression model for binary outcome) has also been implemented in an R package is freely available on the CRAN repository. iBST: https://cran.r-project.org/web/packages/iBST/index.html GPLTR: https://cran.r-project.org/web/packages/GPLTR/index.html
ABIRISK drug safety	The database generated by the project is hosted by ELIXIR in Luxembourg (https://portal.etriks.org/portal/) with restricted access to ABIRISK members for 2 years after the end of the project and then open to the scientific community.
ADVANCE vaccines	The ADVANCE web catalogue will act as the infrastructure and access portal for the metadata profiles created using the AIRR survey responses. The web catalogue is a useful resource for researchers conducting benefit-risk studies to find suitable databases for their studies.
CANCER ID cancer	UKE establishes the European Liquid Biopsy Society (ELBS) that is planned to maintain and extend the CANCER-ID public-private network. This includes support for ring studies, protocol and data base access and a platform for partnering for clinical studies utilising liquid biopsies.
COMBACTE-MAGNET antimicrobial resistance	Launch of the EPI-NET website (https://epi-net.eu/), a freely accessible online platform that brings together epidemiology data from 32 European countries on the priority list of pathogens released by the World health Organisation in 2017. The platform allows users to explore and visualise data on antibiotic resistant infections in humans and animals across Europe and includes data on outbreaks and emerging cases of resistance to newly-developed antibiotics. Data is displayed via colour-schemed maps that allow users to easily track things like the setting, resistance rates, sample sizes and data sources. If users register, they can also select and download data.
COMPACT drug delivery	Generation of a new *in vivo* model (transgenic mice) to be used for the analysis of biodistribution of nano-carrier systems. This tool is already accessible to researchers through a commercial company.
DRIVE-AB antimicrobial resistance	The project has developed a conceptual framework of responsible antibiotic use. Four clinical case studies in different socioeconomic and care settings were used to illustrate this framework and its quality indicators and quantitative metrics. The cases include: ▪ urinary tract infection in the community in a high income country in the EU; ▪ complicated bacteraemia in the hospital in a high income country in the EU; ▪ severe nosocomial infection in upper-middle income countries of Europe; ▪ the gonorrhoea resistance problem in community care settings in developing countries. Altogether these cases highlight the need for new drugs (oral drugs, with better pharmacokinetic properties), better worldwide access to expensive newly developed antibiotics as well as the need for newly developed drugs that need careful positioning (guidelines for diagnostics, use and surveillance).
DRIVE-AB antimicrobial resistance	Publication of the report on research-based suggestions for driving antibiotic development while ensuring access and sustainable use - http://drive-ab.eu/wp-content/uploads/2018/01/CHHJ5467-Drive-AB-Main-Report-180319-WEB.pdf and the report on quality indicators and quantity metrics of antibiotic use - http://drive-ab.eu/wp-content/uploads/2014/09/WP1A_Final-QMs-QIs_final.pdf .
EBiSC stem cells	The EBiSC hiPSC (human induced pluripotent stem cells) catalogue is composed of up to 795 lines covering 35 diseases, including gene-edited isogenic variants. For 70 of these lines, managed access whole genome sequencing data is available through the

Project title	Description of result
	EBiSC Data Access Committee with an allelic search functionality available thought the catalogue. All the described services are accessible worldwide for a fee.
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	The EMIF data catalogue (https://emif-catalogue.eu) was further developed in 2018 and currently serves 9 distinct research/clinical communities, engaging over 1 000 users from 40 countries. The catalogue now contains data from 416 databases including those of other IMI projects (ADVANCE, BigData@Heart, EPAD). It was accessed over 4 000 times in 2018. In addition, a cloud-based private remove research environment (PRRE) was developed and it is currently available for collaborative research, simplifying privacy/legal data issues. http://www.emif.eu/assets/e/m/emif-june-meeting-report.pdf
EMIF knowledge management, Alzheimer's disease, metabolic syndromes	EMIF-AD catalogue with metadata on 56 cohorts to allow search queries, used by 450 users worldwide https://emif-catalogue.eu/.
iPiE environmental issues	iPiE released an online tool that summarises the properties, environmental toxicity and characteristics of active pharmaceutical ingredients (APIs) was released in 2018. Dubbed, iPiE Sum ('iPiE Summary Database Search'), the tool is designed to allow public and regulatory bodies to obtain a high-level overview of what studies were collected during the iPiE project and what eco-toxicity data and studies are available. The tool is freely accessible at: https://www.ipiesum.eu/
K4DD drug discovery	The K4DD project launched a freely available web based toolbox that provides methods for computing drug binding kinetics has been established (http://kbbox.h-its.org). This toolbox provides also a guide for potential users, examples and tutorials. Further tutorials will be added as the results from K4DD are published.
K4DD drug discovery	In collaboration with EBI, the K4DD consortium exported the data items collected during the K4DD project and transferred them to EBI for inclusion in the ChEMBL database (release 24). This way, sustainability and open access to the data beyond the project's lifetime is guaranteed. https://www.ebi.ac.uk/chembl/
K4DD / eTOX / Open PHACTS	Some of the results of the eTOX, K4DD and OpenPHACTS projects have been sustained through an innovation driven start-up. This start-up, called Phenaris, is making the cutting edge technologies developed in these projects available to other researchers. They provide data, models, and decision support in all aspects of *in silico* toxicology. https://www.phenaris.com/
OrBiTo drug delivery	Development of a dissolution stress test device; this system is used to predict the intra-gastric disintegration and drug release behaviour of dosage forms. This tool is commercially available.
PreDiCT-TB tuberculosis	In addition to the 21 clinical trial datasets which are being hosted in the WHO-sponsored TB-PACTS platform (https://c-path.org/programs/tb-pacts/codr-database), the preclinical data gathered in the project have been transferred to the University of Luxembourg Elixir node (https://datacatalog.elixir-luxembourg.org). After an embargo period to allow the consortium to finalise their analyses, the data will be available under open access. In addition, model code and scripts are available at the DDMoRe repository (http://repository.ddmore.eu).

Project title	Description of result
Quic-Concept cancer	Project results lead to numerous publications, and the data is available for secondary research use subject to EORTC policies (for studies where EORTC was the legal sponsor). Data applicants are required to submit a research proposal that will be evaluated for scientific validity and feasibility. More information: https://www.eortc.org/data-sharing/
StemBANCC stem cells	The StemBANCC iPSC lines (induced Pluripotent Stem Cells) are available on the catalogue of EBiSC – a European biorepository developed by another IMI project – and Coriell – a US based one, for use by the international research community for fee.
StemBANCC stem cells	A variety of iPSC-based assay methodologies and techniques have been established. A large number of SOP protocols for cell-based assays with iPSC lines are available on www.stembancc.org and a book has been commissioned by Springer Nature Verlag to make these protocols publicly available.
ULTRA-DD drug development	All protein structures delivered to date have been deposited in the PDB (www.rcsb.org) for public access. In addition, more detailed structural descriptions, including material and methods, are available from the SGC website, and through publications.
ULTRA-DD drug development	Chemical probes generated within ULTRA-DD are made publicly available, mainly through the SGC website http://www.thesgc.org/chemical-probes and the ULTRA-DD website https://www.ultra-dd.org/probes. The four ULTRA-DD probes generated and approved in year 3 will soon or have already been communicated using these sources as the main channels. Probes are provided to collaborators from ULTRA-DD/SGC, whereas the community at large can acquire these probes through chemical vendor partnerships (e.g. Cayman and TOCRIS). More than 200 requests for ULTRA-DD probes were made during reporting period 3, from at least 20 organisations.
ULTRA-DD drug development	Four public dissemination data sets from the project's patient-derived cell assays have been completed following internal quality review. They have now published four assay data-sets pre-publication from the ULTRA-DD website and in various scientific presentations at conferences and symposia https://www.ultra-dd.org/tissue-platforms/cell-assay-datasets.

IMI2 project outputs

New tools/resources for drug discovery & preclinical drug development

Project title	Description of result
ADAPTED Alzheimer's disease	Three fully characterised sets of isogenic inducible pluripotent stem cell (iPSC) lines carrying one of the following apolipoprotein E (APOE) genotypes: APOE-Ɛ2/Ɛ2, APOE-Ɛ3/Ɛ3, APOE-Ɛ4/Ɛ4, APOE-Ɛ3/Ɛ4, and APOE-KO have been developed and fully quality controlled.
ADAPTED Alzheimer's disease	Developed 5 isogenic inducible pluripotent stem cell (iPSC) lines and 40 lines from 20 participants/patient-specific with triggering receptor expressed on myeloid cells 2 (TREM2) and sialic acid binding Ig-like lectin 3 (CD33) variants.
ADAPTED Alzheimer's disease	A biobank has been established including 1 179 patients' human plasma samples, 265 patients' paired cerebrospinal fluid/plasma/serum and white blood cells samples and 41 patients' fresh human blood samples. This resource is used to study the biology of the apolipoprotein E (APOE) risk factor for Alzheimer's disease and to identify relevant new pathways and targets for drug discovery.
eTRANSAFE drug safety	Developed and published an open, flexible framework supporting predictive modelling. It allows for the easy development of machine-learning models, for example QSAR-like models, starting from annotated collections of chemical compounds stored in standard formats (i.e. SDFiles). It also allows for the transfer of the new models into a production environment where they can be used by web services to predict the properties of new compounds. The software is freely available at https://github.com/phi-grib/flame.
IMPRIND neuro-degenerative disease	Assessed the effectiveness of different reagents to clean and disassemble potentially pathogenic assemblies adsorbed on non-disposable materials in laboratories, contributing to reducing potential health hazards associated to manipulating protein assemblies with prion-like properties.
IMPRIND neuro-degenerative disease	Determined the structures of tau filaments from patients with Alzheimer's disease and from Pick's disease (a neurodegenerative disorder characterised by frontotemporal dementia), and showed how tau can adopt distinct folds in the human brain in different diseases, an essential step for understanding how to target this protein specifically in different neurodegenerative diseases.
IMPRIND neuro-degenerative disease	Compared (among different laboratories working in parallel in industry and academia) Tau assembly seeds for their capacity to induce aggregation. The results allowed selection of the best method to purify Alzheimer's disease (AD) relevant seeds feasible for medium throughput screening purposes in drug discovery.
INNODIA diabetes	Identified the molecules that trigger the immune system in people with type 1 diabetes. In this study, the researchers analysed the molecules on the surface of the pancreatic beta cells and how the T lymphocytes respond to them. They found that in both healthy people and diabetes patients, T lymphocytes recognised these molecules when they encountered them in the blood. However, in diabetes patients, the immune cells also recognised them in the pancreas. The team will use this new-found knowledge to develop vaccines to prevent and treat type 1 diabetes. However, while conventional vaccines seek to boost the immune response, the aim here will be to neutralise it. The study was published in the journal Cell Metabolism.
INNODIA diabetes	Discovered and published new knowledge on how T1D develops and the role of CD8+ T-cells in type 1 diabetes. The publications 'Conventional and Neo-Antigenic Peptides Presented by β Cells Are Targeted by Circulating Naïve CD8+ T Cells in Type 1 Diabetic and Healthy Donors.' and 'Islet-reactive CD8+ T cell frequencies in the pancreas, but not in blood, distinguish type 1 diabetic patients from healthy donors.' were published in the top journals Cell Metabolism and Science Immunology.

Project title	Description of result
	These recent results help with understanding the transformation from benign autoimmunity to the development of T1D, which will allow to diagnose T1D earlier and to develop therapies to revert autoimmunity to this benign state. This work shows that all individuals are autoimmune, and that only a small percentage of them develop type 1 diabetes, which gives rise to the question 'why?'. It might be possible that non-diabetic individuals are capable of keeping autoimmune T lymphocytes under control while individuals who will develop diabetes were not capable of doing so, possibly because of inflammation of the pancreas. Another possibility is that the difference between T1D patients and healthy individuals is not just in their T lymphocytes, but also in the vulnerability of the beta cell to their attack. This suggests that the beta cell is not an innocent victim but may actively contribute to its own demise by making itself more visible via the exposure of the incriminated peptides, and thus more vulnerable to lymphocytes.
ITCC-P4 paediatrics, cancer	First ~50 patient derived xenograft models of high-risk paediatric solid tumours generated to be used for rational paediatric drug development.
ITCC-P4 paediatrics, cancer	First paediatric organoids generated from paediatric neuroblastoma patients (from primary and relapse neuroblastoma), that represent an important tool for drug testing *in vitro*.
PHAGO Alzheimer's disease	The R47H variant of the triggering receptor expressed on myeloid cells 2 (TREM2) significantly increases the risk for late onset Alzheimer's disease. Two independent Trem2 R47H knock-in mouse models were created and showed reduced Trem2 mRNA and protein production. Human models studied in parallel did not show these alterations. Thus currently described phenotypes of Trem2 R47H knock-in mice can therefore not be translated to humans and should not be used as models. This is an important negative result. https://molecularneurodegeneration.biomedcentral.com/articles/10.1186/s13024-018-0280-6
PHAGO Alzheimer's disease	Generated induced pluripotent stem cell-derived microglia-like cells (iPSC-MGLCs) from patients with Nasu-Hakola disease (NHD), an early-onset dementia caused by homozygous T66M or W50C missense mutations.
PHAGO Alzheimer's disease	Generated cellular triggering receptor expressed on myeloid cells 2 (TREM2) and sialic acid binding Ig-like lectin 3 (CD33) reporter systems and assays for screening, as well as tools for modifying expression of TREM2 in primary microglia.
PHAGO Alzheimer's disease	PHAGO has compared transcriptome profile of different protocols to obtain microglia from human induced pluripotent stem cells (iPSCs) and has agreed on a common minimum standard.
PRISM neurological disorders	A genome wide association study (GWAS) including 342 498 adult participants from the UK Biobank resulted in 584 genome-wide significant single nucleotide polymorphisms (SNPs) located in 20 genetic loci. Gene-based analysis showed that (embryonic lethal, abnormal vision, drosophila)-like 2 (Hu Antigen) BELAVL2, Aryl hydrocarbon receptor nuclear translocator-like protein 1 ARNTL and dopamine D2 receptor gene DRD2 are the top genes associated with social withdrawal and thus could be considered for drug discovery targeting this symptom in patients.
PRISM neurological disorders	Developed and published the 'visible burrow system', a behavioural paradigm to reliably assess sociability and social withdrawal in mice strains for preclinical drug discovery and development.
RESCEU respiratory disease	RSV (Respiratory syncytial virus) antibody assay developed.

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

Project title	Description of result
Beat-DKD diabetes	Completed the central study protocol and put in place the infrastructures for sample collection for a longitudinal 4-year observational study in 500 patients with early stage diabetic kidney disease (DKD), recruiting in 5 sites across Europe. All study centres are aligned in their tasks and the first patients have recently been recruited and scanned. Extensive characterisation is done at baseline and annual follow-ups to identify associations between imaging biomarkers and known biomarkers of disease progression and test whether imaging biomarkers at baseline improve predictions of functional decline.
INNODIA diabetes	Three new blockers of interferon-Alpha signalling, capable of preventing overexpression of HLA (human leukocyte antigen) class I, ER (endoplasmic reticulum) stress and beta-cell apoptosis have been identified and validated in human islets, providing pre-clinical evidence for future clinical trials. Those new blockers are potential candidates for early interventions to prevent T1D and the interferon-alpha signalling pathway is a target for future therapeutic strategy.
TransQST drug safety	A tool in the R-Shiny package to visualize and analyse toxicogenomic weighted correlation network analysis (WGCNA) module data has been developed. The tool is available to the broad scientific community (https://wgcna-lacdr-dds.nl) and dissemination activities are underway to raise awareness.
TRISTAN drug safety	Carried out a review that showed that drugs used to treat a wide range of conditions may carry a higher risk of side effects for the lungs than previously thought. The team notes that while the drugs studied work well for most patients, doctors should be more aware of the potential risks to their patients' respiratory systems. They also note that more research is needed in this area. The team arrived at their findings after analysing 156 papers with data on 6 200 patients taking 27 drugs to treat diseases like arthritis, cancer and heart disease. Their focus was on cases of drug-induced interstitial lung disease (DIILD). Interstitial lung disease occurs when lung tissue become scarred, making it hard for patients to breathe. The review showed that around 3-5 % of interstitial lung disease cases are caused by DIILD. The paper is published in the Journal of Clinical Medicine.

Improved protocols for clinical trial design and processes

Project title	Description of result
INNODIA diabetes	INNODIA has assembled a clinical network (described below), developed aligned protocols and trained all the personnel, so now they are ready for clinical trials to be plugged in both from within and outside of the consortium. The first INNODIA clinical trials will start in 2019: a paediatric trial (Thymoglobulin or ATG intervention in children) and an adult trial (Verapamil intervention). All data will be collected and analysed under one centralised system to avoid the need for multiple testing, gain efficiency by using a common control group, and simplify screening since trials are recruiting from the INNODIA population.
INNODIA diabetes	An eCRF (electronic case report form) capture system has being developed; over 250 participants have been registered by December 2017. Both eCRF data capture system as well as secure analysis cloud are being upgraded to be compliant with the EU General Data Protection Regulation (GDPR)
INNODIA diabetes	A specific handbook and a standardised checklist for the accreditation visits were developed. The accreditation process was presented to all partners. Between January and September 2017, 15 participating clinical trial centres of the network were visited and approved. All centres could be accredited as eligible clinical research centre for the INNODIA.

Project title	Description of result
PERISCOPE vaccines	Two novel clinical protocols have been developed: booster pertussis clinical study protocol (BERT) and controlled pertussis challenge in human volunteers.
PREFER patient involvement in R&D	Finalisation of the first phase of the project focusing on the elicitation of stakeholders' concerns and priorities, the identification of medical decision points across the medical product life cycle, the examination and prioritisation of patient preference methods and methodological research questions. Results of the systemic literature search and review performed to identify factors and situations influencing the value of patient preference studies, as well as applications throughout the medical product lifecycle to support decision-making published. https://www.sciencedirect.com/science/article/pii/S1359644618302447?via%3Dihub
PREFER patient involvement in R&D	Characterisation and appraisal of 33 preference exploration and elicitation methods. Out of these, the consortium identified 13 promising preference exploration and elicitation methods likely to meet decision makers' needs. https://www.imi.europa.eu/sites/default/files/events/2018/ScientificSymposium/68-%20Whichello%20chiara.pdf
PREFER patient involvement in R&D	Identification of the research questions which will be used to formulate the final methodological questions that will be tested in the empirical case studies and the simulation case studies. Linkage of the prioritised methodological questions to the clinical research questions that were proposed for the clinical case studies. Finalisation of the protocol for the case studies progressing in three disease areas: rheumatoid arthritis, neuromuscular disorders and lung cancer.
RESCEU respiratory disease	The consortium has developed SOPs (Standard Operations Protocols) for the handling of samples in the laboratory after collection, and some clinical SOPs.

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

Project title	Description of result
BEAT-DKD / RHAPSODY diabetes	Identified five subtypes of diabetes based on a study of over 13 000 newly-diagnosed diabetes patients. The groups have different risk levels for certain complications associated with diabetes. For example, patients in group 2 ('severe insulin-deficient diabetes') are at greatest risk of eye disease, while patients in group 3 ('severe insulin-resistant diabetes') had the highest incidence of kidney damage. The work is published in The Lancet Diabetes and Endocrinology.

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

Project title	Description of result
AMYPAD Alzheimer's disease	The AMYPAD diagnostic study has enrolled 90 patients from six centres in six European countries, and the AMYPAD prognostic study has scanned the first patient from the first centre. The studies will show the value of using amyloid positron emission tomography (PET) in the diagnosis of Alzheimer's patients and in for patient selection for clinical trials.
COMBACTE-CDI antimicrobial resistance	Sample collection complete. Over 3 000 samples from 120 sites in 12 countries have been processed. Initial analysis show that the diagnosed burden of *Clostridium difficile* infection varies markedly across Europe in both hospital and community settings.

Project title	Description of result
INNODIA diabetes	INNODIA is setting up a clinical network to facilitate clinical studies for type 1 diabetes by recruitment of people with newly diagnosed T1D and their unaffected family members. It comprises 40 centres in 12 countries (UK, Belgium, France, Italy, Germany, Denmark, Norway, Finland, Austria, Slovenia, Luxembourg, and Poland). So far 1 673 unaffected family members have been recruited, of which 110 are autoantibody positive, and 201 people with newly diagnosed T1D.
LITMUS liver disease	Establishment of European NAFLD Registry and LITMUS biobank - the largest international registry of 3 850 histologically characterised NAFLD patients.
MOPEAD Alzheimer's disease	In order to find better ways to detect as early as possible patients with Alzheimer's disease in the community four models of patient engagement (the 'RUNs') have been designed and have started patient enrolment. All four models of patient engagement in the community (the RUNs) have started enrolling patients. The numbers of patients recruited for RUNs 1 to 4 are 4, 75, 24 and 21 respectively.
PRISM neurological disorders	The clinical study on the biological underpinnings of social withdrawal in Alzheimer's disease and schizophrenia has enrolled 57 subjects out of 200. Participants are undergoing a range of tests, including brain scans, blood tests and questionnaires. They will use a smartphone app called BeHapp to measure people's sociability and social exploration in their daily lives.
RADAR-CNS neurological disorders	The RADAR-CNS project has recruited the first participants into its multiple sclerosis (MS) and major depressive disorder studies to complement the epilepsy study already started. The participants of each study will wear a Fitbit device for up to 24 hours a day. This will capture information about mobility, heart rate and sleep quality in order to provide a better picture of how patients experience their disease.
VSV EBOVAC Ebola and related diseases	Extension of the three clinical trials (Geneva, Lambaréné, Gabon) to include a M12 follow-up visit, the Phase I/II dose-finding randomized, single-centre, double-blind, placebo controlled safety and immunogenicity trial of the rVSV-ZEBOV vaccine against Ebola virus disease in healthy adults

Big data solutions to leverage knowledge / implementation of data standards

Project title	Description of result
DO->IT big data	Delivered a toolkit to support the other BD4BO projects in the identification, selection and measurement of patient outcomes. The BD4BO programme currently has projects focusing on Alzheimer's disease, blood cancers, prostate cancer, and heart disease. The new toolkit represents a practical guide which will help the projects to adopt a standardised approach when developing core outcome sets in their disease areas. The toolkit is available at http://bd4bo.eu/index.php/toolkit/ A training webinar on the toolkit is available at http://bd4bo.eu/index.php/portfolio/public-webinar-on-outcomes-standardisation/
INNODIA diabetes	There was the establishment of an entirely novel platform of bespoke 'omics assays for interrogation of INNODIA samples to enable analysis of complex multi-dimensional phenotypes, and including new analytical techniques for microRNA detection, whole blood flow cytometry, cytotoxic T cell analysis and lipidomics, as well as the study of immune cell function at single cell resolution.
RADAR-CNS neurological disorders	RADAR-Base, a research platform developed by IMI's RADAR-CNS was launched in early 2018 and went on to win the 'Best of Show' award in the data integration and management category at the Bio-IT World Conference & Expo in Boston, US in May. This open source platform allows RADAR-CNS study participants to share their health data (e.g. from sensors and questionnaires) with clinicians and researchers in a secure way, keeping identifiable data local while linking to other non-identifiable data centrally. The platform is also being used by other projects such as RADAR-AD and

Project title	Description of result
	BigData@Heart. More information on the platform is available at https://radar-base.org/.

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

Project title	Description of result
DO->IT big data	Developed a training webinar on the toolkit to support the other BD4BO projects in the identification, selection and measurement of patient outcomes. The webinar is available at http://bd4bo.eu/index.php/portfolio/public-webinar-on-outcomes-standardisation/
EBODAC Ebola and related diseases	Guidebook & online training on communication, community engagement & enabling technologies for a clinical trial during an outbreak https://www.vaccineconfidence.org/ebohandbook-introduction/
EBOVAC2 Ebola and related diseases	As part of the clustering activities and the dissemination, a workshop on methodology on vaccine clinical research was organised for a public of young African PIs in January 2018. 35 participants (MDs, investigators, biologists, MSc & PhD students) attended the training from 4 different countries (Mali, Burkina-Faso, Benin, Côte d'Ivoire) and 11 different institutions. This adds on to trainings provided in the previous years (e.g. sample processing).
MOPEAD Alzheimer's disease	Delivered a number of educational tools to raise awareness in the public of the need for a timely Alzheimer's disease diagnosis. These are infographics, animated infographics, leaflets and newsletters delivered through digital channels (website, Twitter, Facebook and LinkedIn)
PERISCOPE vaccines	Over a period of 17 months (July 2016- December 2017), seven EuroFlow-PERISCOPE Educational & Training Meetings have been organised. 49 people have participated in the EuroFlow training sessions up until December 2017.
RTCure rheumatoid arthritis	One of the partners organised a workshop to harmonise cytometric methods for use in RTCure.
VSV EBOVAC Ebola and related diseases	8 post-docs, 4PhDs, 7 students, 5 technicians were trained.

Impact on regulatory framework

Project title	Description of result
ADAPT-SMART MAPPs	The project released its main results and conclusions on enabling enable medicines adaptive pathways to patients (MAPPs), including engagement criteria, decision moments, and barriers, through a range of channels, most notably: ▪ An infographic at (https://www.infographic.adaptsmart.eu/) includes all relevant documents that reflects the key lessons and outcomes from ADAPT SMART that enable medicines adaptive pathways to patients (MAPPs) in Europe. The infographic won the highly commended prize at the IMI Scientific Symposium. ▪ Publication in Clinical Pharmacology & Therapeutics: 'Medicine Adaptive Pathways to Patients: why, when and how to engage' ▪ Publication 'Managed Entry Agreements for Pharmaceuticals in the Context of Adaptive Pathways in Europe' that presents the work of the consortium through interviews and a multi-stakeholder workshop https://www.frontiersin.org/articles/10.3389/fphar.2018.00280/full.

Project title	Description of result
	▪ Report on the legal constraints showing the current legal framework does not include any legal constraints in implementing MAPPs at both European and national level or prevent the implementation of an adaptive approach to medicines development.
DRIVE vaccines	Published a report on its pilot study on flu vaccine effectiveness during the 2017-2018 season. The learnings from the pilot are now being implemented in a larger scale multi-centre study during this winter's flu season. Until now, data on the effectiveness of different vaccines has been collected on a relatively small scale, meaning it has not been possible to evaluate, together, the effectiveness of the different brands and types of vaccines in use during a given flu season. DRIVE collects results of independent studies from several countries and analyses them together. The studies are conducted by the public partners only (without the involvement of the vaccine manufacturers), and reviewed by an independent scientific committee. The results of DRIVE will help all involved in vaccine development to improve the effectiveness of flu vaccines in the future.
EBOVAC2 Ebola and related diseases	Experience has been gained via EBOVAC2 in conducting clinical studies in sub-Saharan Africa. The lessons learned in EBOVAC2 have contributed to developing a clinical guideline that includes an optimized operating model with better oversights from the R&D company towards local clinical trial conduct.
ITCC-P4 paediatrics, cancer	International workshop organised aiming at reaching scientific consensus on preclinical evaluation that will facilitate and improve new anticancer drug development for children and adolescents (consensus to be published).
MACUSTAR eye disease	Initiation of the observational study aiming at generating data for the development and validation of appropriate clinical endpoints (functional, structural and patients reported outcomes measures) for future clinical trials and drug development in intermediate Age Related Macular Degeneration (iAMD). As of Dec 2018, all 20 clinical sites have been activated all over Europe and have already recruited 25 % of patients with different stages of AMD. Letter of support issued by the EMA on the proposed approach in the framework of an EMA, FDA, HTA (UK's NICE) parallel advice and the Agency issued a letter of support. https://www.ema.europa.eu/documents/other/letter-support-intermediate-age-related-macular-degeneration-amd-biomarker-novel-clinical-endpoint_en.pdf
RESCEU respiratory disease	An EMA ITF Briefing Meeting with RESCEU representatives took place on March 16th at the EMA headquarters in order to provide a useful and valid scientific support to EMA for all those matters related to the development of medicinal products intended for the treatment and prophylaxis of RSV infection.
RESCEU respiratory disease	Some RESCEU representatives met with the EMA Vaccine Working Party (VWP) on June 7th at the EMA in London, in order to provide support to highlight target groups for interventions, inform research investment prioritisation, inform the design of clinical trials (such as by aiding in the selection of appropriate outcomes and case/severity definitions), and produce "baseline" burden data that will help assess the impact of future interventions, including by sharing the results of the RSV burden estimates.

Implementation of project results inside industry

Project title	Description of result
VSV EBOVAC Ebola and related diseases	The detailed analyses of immune and molecular signatures of immune responses, elicited by rVSV-ZEBOV in humans, conducted within the project provide relevant information on VSV-ZEBOV Ebola vaccine immunogenicity and support its development by the industry partner.

Accessibility of resources/outputs beyond consortium

Project title	Description of result
ADAPTED Alzheimer's disease	Three fully characterised sets of isogenic inducible pluripotent stem cell (iPSC) lines carrying one of the following Apolipoprotein E (APOE) genotypes: APOE-Ɛ2/Ɛ2, APOE-Ɛ3/Ɛ3, APOE-Ɛ4/Ɛ4, APOE-Ɛ3/Ɛ4, and APOE-KO are available to the scientific community, distributed by the ECACC (https://www.phe-culturecollections.org.uk).
DO->IT	See 'Big data' section for link to toolkit
EBODAC Ebola and related diseases	Free access to online training tool on communication, community engagement & enabling technologies for a clinical trial during an outbreak on EBODAC website. Printed guidebook has been distributed at several events. https://www.vaccineconfidence.org/ebohandbook-introduction/
eTRANSAFE	See 'New tools' section for available modelling tool.
INNODIA	The INNODIA T1D clinical network is open for clinical trials conducted by entities outside of the consortium, as vehicle for intervention studies in T1D. Trial proposals from academic and industry are welcome.
PHAGO Alzheimer's disease	5 isogenic inducible pluripotent stem cell (iPSC) lines with Triggering Receptor Expressed On Myeloid Cells 2 (TREM2) and sialic acid binding Ig-like lectin 3 CD33 variants have been deposited in the EBiSC iPSC repository (https://cells.ebisc.org/) and made available to the public.
ROADMAP	The ROADMAP consortium have published a catalogue of relevant Alzheimer's Disease models which is publically available for download at: https://roadmap-alzheimer.org/wp-content/uploads/2018/09/116020_ROADMAP_D4.1_Catalogue-of-RWE-relevant-AD-models-and-simplistic-disease-stage-framework.pdf
TransQST	A tool in the R-Shiny package to visualize and analyse toxicogenomic weighted correlation network analysis (WGCNA) module data has been developed. The tool is available to the broad scientific community (https://wgcna-lacdr-dds.nl) and dissemination activities are underway to raise awareness.

Other

Project title	Description of result
EbolaMoDRAD Ebola and related diseases	A partner in the EbolaMoDRAD project, Coris Bioconcept developed a prototype rapid Ebola diagnostic based on laminar flow. This test can deliver a result in under 15 minutes and was partly validated during the project. Further studies are ongoing to complete the validation.
EBOMAN	The EBOMAN project covers the development of a manufacturing process for a vaccine candidate; its priority was the acceleration of the vaccine development and GMP manufacturing process. It has performed the development process usually lasting about 8 years within 2 years. This significant acceleration was not achieved by technological advances but by taking substantial risks, leveraging platform data for both components and performing multiple activities in parallel. All of this was possible thanks to the IMI public-private partnership.
FILODIAG Ebola and related diseases	The project delivered a very new and innovative test system, based on Laser PCR, for detecting ebolavirus. This test system is much faster than conventional real-time PCR methods and can be operated with dried reagents, stored at room temperature, making it possible to test for Ebola in non-conventional laboratory environments. This technology is now commercially available through GNA Biosolutions GmbH.

Project title	Description of result
	In addition, the experiences with the prototype instrument, with its Laser PCR amplification and fluorescence-based detection, laid the foundation for developing and launching an industrialized laboratory instrument, the Pharos V8, after this project.
INNODIA	INNODIA makes significant efforts to encourage involvement of people living with T1D and their families, prioritizing the needs of the main stakeholder. The very active Patient Advisory Committee (PAC) is an example of that. This group, consisting of eight people living with T1D (and parents), is very committed to keep INNODIA stakeholders as well as their families engaged in the project. In the last year, PAC members have visited four clinical centres to meet the staff as well as potential or current participants in INNODIA. During one of these visits in Helsinki, a new video was made with the help of a participant, who showed how to perform a dry blood spot, one of the procedures patients need to perform at home. Visits of the PAC are always followed with an increased recruitment rate in the centres, showing how motivating this is to project partners. For the younger participants, the PAC has created a cartoon hero: Delta, which now has an animation video in different languages as well as an interactive booklet that has won second place in the competition for the ‘Best communication product in IMI projects’.

Annex 4 - Publications from projects

Hot publications in 2018

Hot publications are those that received enough citations to place in the top 0.1% of papers in their research field.

- Falcon, Benjamin et al. (2018) Structures of filaments from Pick's disease reveal a novel tau protein fold, NATURE 561: 137
- Ahlqvist, Emma et al. (2018) Novel subgroups of adult-onset diabetes and their association with outcomes: a data-driven cluster analysis of six variables, LANCET DIABETES & ENDOCRINOLOGY 6: 361
- Rodriguez-Bano, Jesus et al. (2018) Treatment of Infections Caused by Extended-Spectrum-Beta-Lactamase-, AmpC-, and Carbapenemase-Producing Enterobacteriaceae, CLINICAL MICROBIOLOGY REVIEWS 31
- Zerbino, Daniel R. et al. (2018) Ensembl 2018, NUCLEIC ACIDS RESEARCH 46: D754
- Lewczuk, Piotr et al. (2018) Cerebrospinal fluid and blood biomarkers for neurodegenerative dementias: An update of the Consensus of the Task Force on Biological Markers in Psychiatry of the World Federation of Societies of Biological Psychiatry, WORLD JOURNAL OF BIOLOGICAL PSYCHIATRY 19: 244
- Lambin, Philippe et al. (2017) Radiomics: the bridge between medical imaging and personalized medicine, NATURE REVIEWS CLINICAL ONCOLOGY 14: 749
- Siravegna, Giulia et al. (2017) Integrating liquid biopsies into the management of cancer, NATURE REVIEWS CLINICAL ONCOLOGY 14: 531
- Frisoni, Giovanni B. et al. (2017) Strategic roadmap for an early diagnosis of Alzheimer's disease based on biomarkers, LANCET NEUROLOGY 16: 661
- Fitzpatrick, Anthony W. P. et al. (2017) Cryo-EM structures of tau filaments from Alzheimer's disease, NATURE 547: 185
- Visscher, Peter M. et al. (2017) 10 Years of GWAS Discovery: Biology, Function, and Translation, AMERICAN JOURNAL OF HUMAN GENETICS 101: 5
- O'Connor, James P. B. et al. (2017) Imaging biomarker roadmap for cancer studies, NATURE REVIEWS CLINICAL ONCOLOGY 14: 169
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2018 publications featured in in the top Journals

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- Berry-Kravis, Elizabeth M. et al. (2018) Drug development for neurodevelopmental disorders: lessons learned from fragile X syndrome, NATURE REVIEWS DRUG DISCOVERY 17: 280
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- Kasinath, Vignesh et al. (2018) Structures of human PRC2 with its cofactors AEBP2 and JARID2, SCIENCE 359: 940

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- Barault, Ludovic et al. (2018) Discovery of methylated circulating DNA biomarkers for comprehensive non-invasive monitoring of treatment response in metastatic colorectal cancer, GUT 67: 1995
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Annex 5 - Patents from IMI2 projects

Since the start of IMI2 programme, IMI projects have been patenting developed technologies. The statistics below encompass applications 5 patent applications and 1 patent awarded from the beginning of IMI2 until 31 December 2018.

FILODAG – 1 patent application

- Superparamagnetic particles

FILODIAG project objectives: The FILODIAG project aims to deliver an ultra-fast, accurate diagnostic instrument that will test for Ebola in under 15 minutes. Such a system could be used in both healthcare settings and at critical infrastructures like airports. Current tests for Ebola virus take a long time because samples must be heated and then cooled in each of the many processing cycles. This project will replace the heating/cooling steps with a technology based on laser-heated nanoparticles.

MOFINA – 2 patent applications

- Filovirus detector

MOFINA project objectives: 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.

EBOVAC 1 – 2 patent applications

- Methods and composition for enhancing immune response

EBOVAC 1 project objectives: Between them, the EBOVAC 1 and 2 projects are assessing, through clinical trials in Europe and Africa, the safety and tolerability of the ‘prime-boost’ Ebola vaccine regimen, in which patients are first given a dose to prime the immune system, and then a boost dose which is intended to enhance the immune response over time. As such it contributes to broader efforts to ensure that future outbreaks of Ebola can be tackled speedily.

PHAGO – 1 patent awarded in 2018

- TREM2 cleavage modulator

PHAGO project objectives: Clumps of proteins in the brain called amyloid plaques are a hallmark of Alzheimer’s disease, and very often specialised immune cells cluster around these plaques. Recent research has shown that two genes involved in the immune system, TREM2 and CD33, appear to be involved in this immune response to Alzheimer’s disease and could therefore be targets for drugs. However, their exact role in the disease is still poorly understood. The PHAGO project aims to develop tools and methods to study the workings of these genes. The project results will therefore pave the way for the development of novel drugs that could tackle Alzheimer’s disease via this route.

Annex 6 - Scoreboard of Horizon 2020 common KPIs

Table I[47] - 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 2018
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

[47] 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 2018
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)]	31 (12.35%)
	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	5 patent applications 1 patent awarded
	16	Number of prototypes testing activities and clinical trials[48]	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]	Since the start of IMI2 programme, cumulatively: - Prototypes: 10 - Testing Activities: 33 - Clinical Trials: 44

[48] 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 2018
	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]	27 (10.76%)
	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]	Since the start of IMI2 programme, cumulatively: -New Products: 13 -New Processes: 8 -New Methods: 10
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: 95 (100 % on time) No. information letters for Full Proposals: 24 (100 % on time) Average TTI: 75 days Statistics refer to letters sent out in 2018 (SPs for IMI2 – Calls 12, 13 and 14; FPs for IMI2 – Calls 8, 12 and 13). Letters for IMI2 – Call 15 SPs and IMI2 – Call 16 will be sent out in 2019.
	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		1 redress request. The review committee evaluated the complaint and found no grounds to re-evaluate the proposal.

	Correspondence to general Annex 1	Key Performance Indicator	Definition/Responding to question	Type of data required	Target at the end of H2020	Results in 2018
GRANTS	**NA**	Time to grant (TTG) measured (average) from call deadline to signature of grants	To minimise the duration of the granting process aiming at ensuring a prompt implementation of the Grant Agreements through a simple and transparent grant preparation process	Number and % of grants signed within target Average TTG in calendar days Maximum TTG in calendar days	TTG < 243 days (as % of GAs signed)	14 out of 20 (70 %) were signed within the target Average TTG: 232 days. Maximum TTG: 321 days
	NA	Time to sign (TTS) Grant Agreements from the date of informing successful applicants (information letters)		Number and % of grants signed within target Average TTS in calendar days Maximum TTS in calendar days	TTS 92 calendar days	0 out of 20 (0 %) was signed within the target.[49] Average TTS: 153.8 days Maximum TTS: 235 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: 90 days	Pre-financing: 9 days (100 % on time) Interim payments: 59 days (100 % on time) Final payments: 54 days (100 % on time)

[49] IMI can only sign a Grant Agreement once the consortium has signed its own consortium agreement. Given the size and complexity of IMI consortia, it is rarely possible for these multi-stakeholder, multi-disciplinary teams to conclude their own consortium agreement (covering issues such as intellectual property and governance) within 92 days. This in turn impacts on the time to sign the Grant Agreement.

	Correspondence to general Annex 1	Key Performance Indicator	Definition/Responding to question	Type of data required	Target at the end of H2020	Results in 2018
HR	**NA**	Vacancy rate (%)		% of post filled in, composition of the JU staff		Overall vacancy rate: 14.29 % TAs: 5.13 % CAs: 33.33 % SNEs: 50 %
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	99.73 % CA to total budget 86.25 % PA to total budget
	NA	Administrative Budget: Number and % of total of late payments	realistic yearly budget proposal, possibility to monitor and report on its execution in line with sound financial management principle	Number of delayed payments % of delayed payments (of the total)		1 234 payments of which 112 were late (9.08 %)

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[50] - 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 2018
2	Widening the participation	2.1 Total number of participations by EU-28 Member State	Nationality of H2020 applicants & beneficiaries (number of)	YES	Eligible proposals: Applications: 4 173 Applicants: 1 604 Beneficiaries: 1 179 Country — Participations (Participants) Austria 18 (11) Belgium 109 (45) Czech Republic 6 (6) Denmark 47 (17) Estonia 2 (1) Finland 23 (10) France 144 (68) Germany 186 (92) Greece 5 (4)

[50] 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 2018
					Hungary 6 (4) Ireland 8 (6) Italy 74 (48) Luxembourg 13 (5) Netherlands 135 (50) Poland 3 (2) Portugal 9 (9) Slovenia 4 (4) Spain 63 (37) Sweden 51 (18) United Kingdom 273 (92) **Total EU-28 1 179 (529)** (Cumulative figures as of 31/12/2018)
		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	Country % (EUR m) Austria 2.3 % (14.5) Belgium 4.1 % (25.9) Czech Republic 0.4 % (2.2) Denmark 1.8 % (11.3) Estonia 0.2 % (1.5) Finland 1.4 % (8.8) France 9.7 % (60.8) Germany 9.3 % (58.5) Greece 0.2 % (1.5)

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2018
					Hungary 0.3 % (1.6) Ireland 1.0 % (6.5) Italy 9.4 % (59.1) Luxembourg 0.5 % (3.2) Netherlands 15.7 % (98.5) Poland 0.2 % (0.9) Portugal 0.5 % (3.0) Slovenia 0.1 % (0.5) Spain 7.8 % (48.9) Sweden 3.3 % (21.0) UK 31.8 % (199.7) **Total EU-28 627.8** (Cumulative figures as of 31/12/2018)

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2018
NA		Total number of participations by Associated Countries	Nationality of H2020 applicants & beneficiaries (number of)	YES	Eligible proposals: - Applications: 295 - Applicants: 127 - Beneficiaries: 90 Country — Participations (Participants) Israel — 4 (3) Norway — 8 (7) Serbia — 1 (1) Switzerland — 77 (27) **Total Associated Countries — 90 (38)** (Cumulative figures as of 31/12/2018)
NA		Total amount of EU financial contribution by Associated Country (EUR millions)	Nationality of H2020 beneficiaries and corresponding EU financial contribution	YES	Country — % (EUR m) Israel — 3.1 % (0.2) Norway — 27.8 % (1.8) Serbia — 0.9 % (0.1) Switzerland — 68.2 % (4.4) **Total Associated Countries — 6.5** (Cumulative figures as of 31/12/2018)

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2018
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		Participations: 140 out of 912 (15.35 %) Participants: 99 out of 487 (20.33 %) EU funding: EUR 63.9 million (9.45 %) (Cumulative figures as of 31/12/2018, beneficiaries receiving EU funding only)
6	Gender	6.1 Percentage of women participants in H2020 projects	Gender of participants in H2020 projects	YES	53 % of the total workforce working in IMI2 projects is female.
		6.2 Percentage of women project coordinators in H2020	Gender of MSC fellows, ERC principle investigators and scientific coordinators in other H2020 activities	YES	12 women out of 56 project coordinators for IMI2 projects in 2018
		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: 99 out of 219 experts (45 %) Interim review experts: 15 out of 27 experts (56 %)
7	International cooperation	7.1 Share of third-country participants in Horizon 2020	Nationality of H2020 beneficiaries	YES	Country — Participations (Participants) Australia — 1 (1) Benin — 1 (1) Brazil — 1 (1) Burkina Faso — 1 (1)

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2018
					Canada 1 (1) Gabon 2 (1) Senegal 2 (1) Sierra Leone 3 (2) South Africa 1 (1) Tanzania 1 (1) United States 40 (23) **Total third countries 54 (34)** (cumulative figures as of 31/12/2018)

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2018
		7.2 Percentage of EU financial contribution attributed to third country participants	Nationality of H2020 beneficiaries and corresponding EU financial contribution	YES	Country % (EUR m) Australia 0.7 % (0.3) Benin 1.4 % (0.6) Brazil 0.7 % (0.3) Burkina Faso 12.1 % (5.1) Canada 0.00 % (0.0) Gabon 2.0 % (0.8) Senegal 0.9 % (0.4) Sierra Leone 70.5 % (29.5) South Africa 1.0 % (0.4) Tanzania 1.2 % (0.5) United States 9.5% (4.0) **Third Countries 41.8** (cumulative figures as of 31/12/2018)
9	Bridging from discovery to market [51]	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

[51] 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 2018
NA		Scale of impact of projects (High Technology Readiness Level)	Number of projects addressing TRL[52] between (4-6, 5-7)		-1 project TRL 6 -1 project TRL 9
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: 519 out of 1323 (39.2 %) Participants: 200 out of 601 (33.3 %) (Cumulative figures as of 31/12/2018)
		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 63.2 million out of EUR 676.2 million (9.3 %) (Cumulative figures as of 31/12/2018)
12	Funding for PPPs	12.1 EU financial contribution for PPP (Art 187)	EU contribution to PPP (Art 187)		EUR 664.9 million (total cash contribution EC in 2018)
		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)		EFPIA & Associated Partners contribution (EUR 655.6 million) divided by EU contribution (EUR 664.9 million) = leverage of 0.99.

[52] 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 2018
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	-Total number of events: 4 809 -Total funding amounts: EUR 2 197 630 -Number of people reached: 109 190 172
14	Participation patterns of independent experts	14.2 Proposal evaluators by country	Nationality of proposal evaluators		35 countries[53] (219 experts)
		14.3 Proposal evaluators by organisations' type of activity	Type of activity of evaluators' organisations	YES	86 – HES: higher or secondary education establishment 18 – REC: research organisations 28 – PUB: public bodies 36 – PRC: private for-profit entities 51 – OTH: other type of organisations

[53] Argentina (1), Australia (1), Austria (8), Belgium (13), Bulgaria (3), Canada (5), Croatia (7), Czech Republic (5), Denmark (5), Estonia (1), Finland (2), France (18), Germany (22), Greece (4), Hungary (2), Ireland (9), Israel (1), Italy (20), Latvia (1), Lithuania (2), Malta (1), Netherlands (7), Nigeria (1), Poland (4), Portugal (2), Romania (5), Serbia (1), Slovakia (2), Slovenia (4), Spain (14), Sweden (6), Switzerland (2), Turkey (2), United Kingdom (22), United States (16).

Correspondence in the general Annex 2	Cross-cutting issue	Definition / responding to question	Type of data required	Direct contribution to ERA	Results in 2018
NA	Participation of RTOs and Universities	Participation of RTO[54]s and Universities in PPPs (Art 187 initiatives)	Number of participations of RTOs to funded projects and % of the total Number of participations of Universities to funded projects and % of the total % of budget allocated to RTOs and to Universities	YES	Participations: Research Org: 226 (17.1 %) HES: 443 (33.5 %) % budget allocated: Res. Org: EUR 188.5 million (27.9 %) HES: EUR 371.4 million (54.9 %) (Cumulative figures as of 31/12/2018)
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)[55]		1
NA	Audit	Error rates	% of common representative error; % residual error		Representative error rate: 0.76 % Residual error rate: 0.67 %
NA		Implementation	Number of cases implemented; in total EUR million; ´of cases implemented/total cases		Cases implemented 4 (80 %) Amount: EUR 357 095

[54] RTO: Research and Technology Organisation

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

Annex 8 - Scoreboard of KPIs specific to IMI

Table III[56] - KPIs specific to each single JU

Reporting methodology: cumulatively reporting from the beginning of IMI2 until 31/12/2018.

These KPIs are for the IMI2 programme only. However, many of them are also relevant for IMI1. In these cases, the results for IMI1 + IMI2 are given in a separate column. The goal here is to provide readers with an overview of the results of the entire IMI programme, since its launch in 2008. In cases where the KPI is not relevant for IMI1, the IMI1 + IMI2 column is marked 'not applicable' (n/a).

As this is the first year that IMI collects data about the new KPIs, the baseline is zero, except for KPI 10, where the figure for IMI1 can be used as a comparator.

KPI	Definition	Comment	Relates to	IMI2 baseline	IMI2 target	IMI2 results	IMI1 + IMI2 results
1	Number of relevant priority areas in the WHO "Priority Medicines for Europe and the World 2013 Update" reflected in the IMI2 Strategic Research Agenda (SRA) and addressed by IMI2 projects.	Based on the SRA and including the WHO priority medicines therapeutic areas: - Expressed as a number of areas reflected in the IMI2 portfolio. - Complemented by the number and budget of grant agreements that delivered them.	IMI2 Regulation objective b1: b1: 'increase the success rate in clinical trials of priority medicines identified by the WHO'	0	12	11 Number of projects: 54 Budget committed: EUR 662 280 864	n/a
2	The number of project developed assets that completed a significant milestone during the course of an IMI2 project.	Assets are defined as new drug or diagnostic candidates, targets, biomarkers or other tools that can be shown to have reached a significant milestone or pass a significant stage gate.	IMI2 Regulation objectives b1, b2, b4, b5 and b6: b1: 'increase the success rate in clinical trials of priority medicines identified by the WHO' b2: 'reduce the time to reach clinical proof of concept in medicine development…' b4: 'develop diagnostic and treatment biomarkers for diseases clearly linked to	0	50	16	57

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

KPI	Definition	Comment	Relates to	IMI2 baseline	IMI2 target	IMI2 results	IMI1 + IMI2 results
			clinical relevance and approved by regulators' b5: 'reduce the failure rate of vaccine candidates in phase III of clinical trials through new biomarkers for initial efficacy and safety checks' b6: 'improve the current drug development process by providing the support for the development of tools, standards and approaches to assess efficacy, safety and quality of regulated health products'				
3	New or improved guidelines, methodologies, tools, technologies or solutions accepted by regulatory authorities for use in the context of R&D, specifically for: - new tools for preclinical drug development, - biomarkers and tools developed to predict clinical outcomes, - improved protocols to design and process of clinical trials, - new biomarkers developed for the efficacy and safety of vaccine candidates.	- Measured by the number of the formal qualification procedures completed (letters of support, qualification opinions received). - Complemented by number of qualification procedures launched. - Expressed as net figure. - Complemented by the number and budget of grant agreements that delivered them.	IMI2 Regulation objectives b1, b2, b4, b5 and b6: b1: 'increase the success rate in clinical trials of priority medicines identified by the WHO' b2: 'reduce the time to reach clinical proof of concept in medicine development…' b4: 'develop diagnostic and treatment biomarkers for diseases clearly linked to clinical relevance and approved by regulators' b5: 'reduce the failure rate of vaccine candidates in phase III of clinical trials through new biomarkers for initial efficacy and safety checks' b6: 'improve the current drug development process by providing the support for the development of tools, standards and approaches to assess efficacy, safety and quality of regulated health products'	0	10 (for completed procedures)	7 completed procedures: -Regulatory qualified opinion : 4 -CE mark: 3 Number of projects: 3 Budget committed: EUR 7 309 987	15 - Inclusion in regulatory guidelines: 6 - Regulatory letter of support: 1 - Regulatory qualified opinion: 5 - CE mark: 3 Number of projects: 11 Budget committed: EUR 70 649 626
4	New taxonomies of diseases and new	- Expressed as net figure.	IMI2 Regulation objectives b3 and b4:	0	30	5	20

KPI	Definition	Comment	Relates to	IMI2 baseline	IMI2 target	IMI2 results	IMI1 + IMI2 results
	stratifications (such as the definition of patient subpopulations, development, validation and use of new diagnostics) developed.	- As published and/or implemented by industrial partners and evidenced in annual reporting. - Complemented by the number and budget of grant agreements that delivered them.	b3: 'develop new therapies for diseases for which there is a high unmet need…' b4: 'develop diagnostic and treatment biomarkers for diseases clearly linked to clinical relevance and approved by regulators'			Number of projects: 2 Budget committed: EUR 23 215 937	Number of projects: 9 Budget committed: EUR 93 595 475
5	Contribution (in-kind or in-cash) from non-pharma actors (e.g. non-pharma industries, foundations, charities, professional organisations).	Expressed as total amount in EUR.	IMI2 Regulation objective a: a: 'to support… the development and implementation of pre-competitive research and of innovation activities of strategic importance to the Union's competitiveness and industrial leadership…'; and IMI2 Regulation recital 8: 'The initiative should consequently seek to involve a broader range of partners, including mid-caps, from different sectors, such as biomedical imaging, medical information technology, diagnostic and animal health industries.'	0	EUR 300 Million	EUR 90.1 million (AP: EUR 69.1 million. Partners in Research: EUR 21.0 million)	n/a
6	Share of IMI projects whose resources/outputs are made accessible beyond the consortia partners (with or without fee), such as major databases, bio-banks, in silico tools, training materials, clinical trial networks, guidance etc.	- Complemented by the number and budget of grant agreements that delivered them. - Accessibility to be evidenced by online availability (with or without fee), and documented by project reports.	IMI2 Regulation objectives a, b2 and b6: a: 'to support… the development and implementation of pre-competitive research and of innovation activities of strategic importance to the Union's competitiveness and industrial leadership…' b2: 'reduce the time to reach clinical proof of concept in medicine development' b6: 'improve the current drug development process by providing the support for the development of tools, standards and approaches to assess efficacy, safety and quality of regulated health products'	0	50 %	19.23 % Number of projects: 10 Budget committed: EUR 137 230 075	39.62 % Number of projects: 42 Budget committed: EUR 725 472 493
7	Co-authorships and cross-sector	- Expressed as net figure	IMI2 Regulation objective a:	0	1 500	*Due to the large*	

KPI	Definition	Comment	Relates to	IMI2 baseline	IMI2 target	IMI2 results	IMI1 + IMI2 results
	publications between European researchers on IMI2 projects (sectors include academia, small and mid-sized companies, pharma, regulators, patient organisations, etc.).	- Complemented by the number and budget of grant agreements that delivered them.	a: 'to support… the development and implementation of pre-competitive research and of innovation activities of strategic importance to the Union's competitiveness and industrial leadership…'			*amount of data to process and the time constraints, the contractor was unable to provide this data point in time for the AAR. It will be published in autumn 2019.*	
8	New tools and processes generated by IMI2 projects that have been implemented by the industry participants of IMI projects.	- New tools and processes: e.g. animal models, standards, biomarkers, SOPs, use of screening platforms and clinical trial networks. - Expressed as net figure. - Complemented by the number and budget of grant agreements that delivered them. - Assessment based on yearly reporting by industrial partners until the project close-out meetings.	IMI2 Regulation objectives a, b2 and b6: a: 'to support… the development and implementation of pre-competitive research and of innovation activities of strategic importance to the Union's competitiveness and industrial leadership…' b2: 'reduce the time to reach clinical proof of concept in medicine development' b6: 'improve the current drug development process by providing the support for the development of tools, standards and approaches to assess efficacy, safety and quality of regulated health products'	0	50	19 Number of projects: 9 Budget committed: EUR 50 058 369	122 Number of projects: 46 Budget committed: EUR 690 919 174
9	Share of projects involving patient organisations and healthcare professionals'	- Complemented by the number and budget of grant agreements that delivered them.	IMI2 Regulation objectives a, and b1: a: 'to support… the development and implementation of pre-competitive research and of innovation activities of strategic	0	80 %	63.46 % Number of projects: 33	57.14 % Number of projects: 60

KPI	Definition	Comment	Relates to	IMI2 baseline	IMI2 target	IMI2 results	IMI1 + IMI2 results
	associations (as consortium partners, members of advisory boards, members of stakeholder groups etc).		importance to the Union's competitiveness and industrial leadership…' b1: 'increase the success rate in clinical trials of priority medicines identified by the WHO'			Budget committed: EUR 608 788 556	Budget committed: EUR 1 492 141 318
10	Support to SMEs: share of SMEs participating as formal IMI project beneficiaries.	- To be complemented by the number of SMEs benefitting from IMI project support in other ways.	H2020 priority; IMI2 Regulation recital 9 '(…) should seek to foster the capacity of smaller actors such as research organisations, universities and SMEs for participating in open innovation models and to promote the involvement of SMEs in its activities, in line with its objectives'	16 %	20 %	SME partici-pations: 15.4% (140 out of 912) (IMI2 cumulative figures until 31/12/2018, beneficiaries receiving EU funding only)[57]	SME partici-pations: 15.7% (337 out of 2.146) (IMI1 and IMI2 cumulative figures until 31/12/2018, beneficiaries receiving EU funding only)

[57] Additional statistics on SME participation in IMI2 can be found in Annex 7 in the table 'Indicators for monitoring H2020 Cross-Cutting Issues common to all JTI JUs'.

Annex 9 – Final annual accounts

Balance sheet

EUR '000

	Note	31.12.2018	31.12.2017
NON-CURRENT ASSETS			
Intangible assets	*2.1*	*63*	*–*
Property, plant and equipment	*2.2*	*127*	*100*
Pre-financing	*2.3*	*217 790*	*173 471*
		217 980	**173 570**
CURRENT ASSETS			
Pre-financing	*2.3*	*78 451*	*59 451*
Exchange receivables and non-exchange recoverables	*2.4*	*49 739*	*76 317*
		128 190	**135 768**
TOTAL ASSETS		**346 170**	**309 339**
CURRENT LIABILITIES			
Payables and other liabilities	*2.5*	*(185 996)*	*(174 166)*
Accrued charges and deferred income	*2.6*	*(133 404)*	*(134 836)*
		(319 400)	**(309 003)**
TOTAL LIABILITIES		**(319 400)**	**(309 003)**
NET ASSETS		**26 770**	**336**
Contribution from Members	*2.7*	*1 957 247*	*1 626 324*
Accumulated deficit		*(1 625 988)*	*(1 290 548)*
Economic result of the year		*(304 489)*	*(335 440)*
NET ASSETS		**26 770**	**336**

Statement of financial performance

EUR '000

	Note	2018	2017
REVENUE			
Revenue from non-exchange transactions			
Recovery of expenses	*3.1*	*1 188*	*55*
Other		*4*	*–*
		1 192	**55**
Revenue from exchange transactions			
Financial revenue		*–*	*(6)*
Other exchange revenue		*22*	*33*
		22	**27**
Total revenue		**1 214**	**82**
EXPENSES			
Operating costs	*3.2*	*(297 476)*	*(327 103)*
Staff costs	*3.3*	*(4 573)*	*(4 480)*
Finance costs	*3.4*	*(3)*	*(8)*
Other expenses	*3.5*	*(3 651)*	*(3 931)*
Total expenses		**(305 703)**	**(335 522)**
ECONOMIC RESULT OF THE YEAR		**(304 489)**	**(335 440)**

Cash flow statement[58]

EUR '000

	2018	2017
Economic result of the year	*(304 489)*	*(335 440)*
Operating activities		
Depreciation and amortization	*35*	*40*
(Increase)/decrease in pre-financing	*(63 319)*	*11 708*
(Increase)/decrease in exchange receivables and non-exchange recoverables	*26 579*	*19 071*
Increase/(decrease) in payables	*11 829*	*(29 529)*
Increase/(decrease) in accrued charges	*(1 432)*	*30 950*
Increase/(decrease) in cash contributions	*179 400*	*126 599*
Increase/(decrease) in in-kind contributions	*151 524*	*176 618*
Investing activities		
(Increase)/decrease in intangible assets and property, plant and equipment	*(126)*	*(17)*
NET CASHFLOW	**0**	**0**
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	*–*	*–*

Statement of changes in net assets

EUR '000

	Contribution from Members	Accumulated Surplus/ (Deficit)	Economic result of the year	Net Assets
BALANCE AS AT 31.12.2016	**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**
Allocation 2017 economic result	*–*	*(335 440)*	*335 440*	*–*
Cash contribution	*179 400*	*–*	*–*	*179 400*
Contribution in-kind	*151 524*	*–*	*–*	*151 524*
Economic result of the year	*–*	*–*	*(304 489)*	*(304 489)*
BALANCE AS AT 31.12.2018	**1 957 247**	**(1 625 988)**	**(304 489)**	**26 770**

[58] 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.

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.

The representative error rate is the Most Likely Error rate (MLE%) from one or more samples.

The calculation of the residual error rate subsequently uses the representative error rate as the starting point.

The MLE% for a population from which a sample has been drawn is calculated according to the following formula:[59]

$$\text{MLE\%} = \frac{\sum_{i=1}^{n} \text{err}_i * \text{SI}_i}{\text{P}}$$

- n = total sample size
- err_i = error rate (in %) in requested IMI contribution detected on individual transaction in from the sample (in range [0, 100%]; i.e. only errors relating to overpayments are counted)
- SI_i = sampling interval used for selecting transaction in from the -sample
- P = total requested IMI contribution (EUR) in the auditable population (i.e. all paid 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.

[59] Based on the Horizon 2020 Ex-post Audit Strategy (2016 – 2025).

Annex 11 – Media highlights

- Lëtzebuerger Journal (Luxembourg), 14 December 2018
  Wenn die EU Gesundheit neu denkt (When the EU rethinks health)
- MedNous (EU), 8 December 2018
  IMI: Building a science infrastructure for Europe
- Fokus (Belgium), 1 December 2018
  Blockchain heeft grote impact op mens en bedrijf (Blockchain has a large impact on people and businesses)
- Science Business (EU), 30 November 2018
  Horizon Europe: The obstacles still facing negotiators
- Awoko Newspaper (Sierra Leone), 24 November 2018
  Vaccine to end Ebola
- Financial Times (UK), 20 November 2018
  EU's Innovative Medicines Initiative brings collaborative power to development of drugs
- Euronews - Futuris (EU), 12 November 2018
  Euronews English: Vaccine research offers fresh hope against Ebola
  Article and video also available in Arabic, French, German, Greek, Hungarian, Italian, Persian, Portuguese, Russian, Spanish, and Turkish
- MedNous (EU), 6 November 2018
  EU funding opportunities for SMEs
- Health Europa (EU), 5 November 2018
  Dementia in Europe: a public health priority?
- European Pharmaceutical Review (UK), 29 October 2018
  Widespread side effects from drugs on lungs
- Arzteblatt (Germany), 29 October 2018
  Viele Medikamente können eine interstitielle Lungenerkrankung auslösen (Many medicines can cause interstitial lung disease)
- Science Business (EU), 15 October 2018
  EU makes its pitch to member states for 12 research missions and 13 industry partnerships
- Irish Examiner (Ireland), 2 October 2018
  Infant centre will continue to lead in important research
- Science Business (EU), 28 September 2018
  Austrian science minister: governments and EU Commission 'in conflict' over research missions
- Health Europa (EU), 27 September 2018
  Rapid diagnostic technologies versus antimicrobial resistance
- Technology Networks (UK), 10 September 2018
  Binding kinetics in drug discovery
- El Global (Spain), 31 August 2018
  La innovación, reto para lograr una I+D eficiente (Innovation, a challenge to achieve efficient R&D)
- Financial Times (UK), 3 August 2018
  FT Health: Climate change is a public health problem
- Financial Times (UK), 26 July 2018
  No recommended Brexit dosage yet for medicine research
- Technology Networks (UK), 24 July 2018
  Infrared Sensor Could Speed up Drug Discovery
- European Biotechnology News (EU), 18 July 2018
  IMI to spur on antibiotics research amidst big pharma pullback
- Blik op nieuws (The Netherlands), 10 July 2018
  Onderzoekers en bedrijfsleven willen autisme ontrafelen en behandelen (Researchers and the business community want to unravel and treat autism)
- CincoDias - El Pais (Spain), 4 July 2018
  Los datos médicos, un tesoro que ya comienza a explotarse (Medical data, a treasure that is already beginning to be exploited)
- The New Yorker (US), 2 July 2018
  The Neuroscience of Pain
- Horizon Magazine (EU), 28 June 2018
  'Radical collaboration' is shaking up the pharmaceutical industry – Carlos Moedas
- Science Business (EU), 28 June 2018
  Industry in race to keep billion-euro EU partnerships alive

- Pharmaphorum (EU), 26 June 2018
  The time has come to optimise patient engagement
- Horizon Magazine (EU), 21 June 2018
  Ebola outbreak – this time it's different
- Irish Examiner (Ireland), 18 June 2018
  Largest grant ever to research autism awarded by Innovative Medicines Initiative; Trinity College to take part
- Science Business (EU), 7 June 2018
  European Commission publishes its €94.1B Horizon Europe proposal
- Arzte Zeitung (Germany), 7 June 2018
  Langfristig mehr Tote als bei Krebs (More deaths than cancer in the long term)
- ORF (Austria), 7 June 2018
  Forscher entwickeln Leitfaden für Unterzuckerung (Researchers are developing guide lines for low blood sugar)
- Pharma Market Live (UK), 6 June 2018
  Europe's public-private alliance targets pain management
- HIMSS Insights (EU), 25 May 2018
  Data projects boost precision medicine in Spain | Insights
- Horizon Magazine (EU), 23 May 2018
  Complex diseases get the big data treatment
- BioCentury (US), 22 May 2018
  European consortium launches to improve pediatric trials
- Silicon Republic (Ireland), 21 May 2018
  Europe to become focal point of paediatric medicine, led by Irish centre
- Health Europa (EU), 16 May 2018
  IMI launches milestone project focusing on hypoglycaemia
- Diabetes Daily (US), 8 May
  JDRF Participates in Study Committed to Learning about Hypoglycemia and Diabetes
- El Global (Spain), 27 April 2018
  La Comisión pide a los estados que cooperen en la puesta en común de datos sanitarios en la UE (The Commission asks states to cooperate in the sharing of health data in the EU)
- The Telegraph (UK), 23 April 2018
  10 million lives could be lost to superbugs - so how far have we got in the race to beat them?
- Science Business (EU), 22 April 2018
  EU staff propose partnership changes for next research programme
- Health Europa (EU), 20 April 2018
  Celebrating ten years of the Innovative Medicines Initiative
- Science Business (EU), 17 April 2018
  New collaboration to engage patients in drug development for better health outcomes
- Pharma Fakten (Germany), 11 April 2018
  „Die Welt ist unser Labor" ('The world is our laboratory')
- Pharma Market Live (UK), 22 March 2018
  IMI calls for advancements in machine learning and digital clinical trials
- EurActiv (EU), 7 March 2018
  Going into the real world to gather cancer data
- The BMJ (UK), 6 March 2018
  Lieven Annemans: We need to reach a common understanding about real world data
- Intellectual Property Watch (Switzerland), 27 February 2018
  Wellcome Trust Report Recommends UK-EU Agreement On Research & Innovation
- Life Science Daily (US), 27 February 2018
  Trials seek solutions to bacterial infections
- Pharmaceutical Technology (UK), 27 February 2018
  NIH joins efforts to address two common bacterial infections
- Pharma Fakten (Germany), 19 February 2018
  Vier Anreize und ein Problem (Four incentives and one problem)
- Mind Health (France), 16 February 2018
  Salah-Dine Chibout (Novartis): 'Avec le numérique nous serons plus efficaces pour identifier et investir sur de nouvelles cibles' (Salah-Dine Chibout (Novartis): With digital we will be more efficient at identifying and investing in new targets)

- Imfarmacias (Spain), 15 February 2018
  La resistencia a los antibióticos será la primera causa de muerte en 2050 (Antibiotic resistance will be the main cause of death in 2050)
- El Pais (Spain), 14 February 2018
  Grandes oportunidades para avanzar en la investigación sanitaria gracias al 'big data' (Major opportunities to advance health research thanks to 'big data')
- El Mundo (Spain), 6 February 2018
  La información como medicamento (Information as a medicine)
- Die Welt (Germany), 3 February 2018
  Damit das Leben weitergeht (So that life goes on)
- Applied Clinical Trials (US), 1 February 2018
  How social media is transforming pharma and healthcare
- Technology Networks (UK), 22 January 2018
  Cancer Stem Cell Survival is Controlled by Hedgehog Signaling Proteins
- Nutrition Insight (The Netherlands), 22 January 2018
  Antibiotic innovation: Research group calls for 50 percent investment increase as resistance threats intensify

Annex 12 - List of acronyms

Acronym	Meaning
AAR	Annual Activity Report
ABAC	Accrual Based Accounting System
AD	Alzheimer's disease
ADA	Anti-drug antibodies
ADNI	Alzheimer's Disease Neuroimaging Initiative
AER	Average error rate
AGA	Annotated Grant Agreement
AIRR	ADVANCE International Research Readiness
ALDE	Group of the Alliance of Liberals and Democrats for Europe
AMD	Age-related macular degeneration
AMR	Antimicrobial resistance
AP	Associated Partner
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
BBMRI	Biobanking and BioMolecular Resources Research Infrastructure
BD4BO	Big Data for Better Outcomes
BE	Bronchiectasis
BMGF	Bill and Melinda Gates Foundation
CA	Commitment appropriations
CA	Contract agent
CAS	Common Audit Service
CDTI	Centre for the Development of Industrial Technology
CEO	Chief Executive Officer
CF	Cystic fibrosis
CFS	Certificate on Financial Statements
cIAI	Complicated intra-abdominal infection
CNA	Copy number alterations
CNV	Copy number variation
COMPASS	H2020 workflow tool providing harmonisation between business processes & validation workflows
COPD	chronic obstructive pulmonary disease
CORDA	Common Research Data Warehouse
COST	European Cooperation in Science and Technology

Acronym	Meaning
CPC	Cost per click
CRAB	Carbapenem-resistant *Acinetobacter baumannii*
CRE	Carbapenem-resistant enterobacteriaceae
CRS	Common representative sample
CSA	Coordination and support action
CSC	Common Support Centre
CTC	Circulating tumour cell
ctDNA	Circulating tumour DNA
CTR	Click through rate
CV	Curriculum vitae
DAS	Declaration of Assurance
DG	Directorate-General
DG BUDGET	European Commission Directorate-General for Budget
DG CNECT	Directorate-General for Communications Networks, Content and Technology
DG HR	European Commission Directorate-General for Human Resources and Security
DG JRC	European Commission Joint Research Centre
DG REGIO	European Commission Directorate-General for Regional and Urban Policy
DG RTD	European Commission Directorate-General for Research and Innovation
DG SANTE	European Commission Directorate-General for Health and Food Safety
DiEPP	Dissemination and Exploitation Practitioners Platform
DIILD	Drug-induced interstitial lung disease
DKD	Diabetic kidney disease
DoA	Description of Action
DOI	Digital object identifiers
DORA	Document Registry Application
DoW	Description of Work
DW	Data warehouse
EBE	European Biopharmaceutical Enterprises
EBI	European Bioinformatics Institute
EC	European Commission
ECA	European Court of Auditors
ECDC	European Centre for Disease Prevention and Control
eCRF	Electronic case report form
ECRIN	European Clinical Research Infrastructure Network
ECSEL JU	Electronic Components and Systems for European Leadership Joint Undertaking
ED	Executive Director
EEA	European Economic Area
EFPIA	European Federation of Pharmaceutical Industries and Associations

Acronym	Meaning
EHDN	European Health Data Network
EHR	Electronic health record
E-I	Excitation–inhibition
EIT	European Institute of Innovation & Technology
ELBS	European Liquid Biopsy Society
EMA	European Medicines Agency
eMA	Electronic Missions Application
EMI	Expert Management Internal
EMPP	Expert Management Participant Portal
ENCePP	European Network of Centres for Pharmacoepidemiology and Pharmacovigilance
EORTC	European Organisation for Research and Treatment of Cancer
EP	European Parliament
EPP	European People's Party
ER	Endoplasmic reticulum
ERM	Enterprise risk management
ESOF	EuroScience Open Forum
EU	European Union
EUFEPS	European Federation for Pharmaceutical Sciences
EUFIC	European Food Information Council
EULAR	European League Against Rheumatism
FAIR	Fraud and Irregularity in Research
FAO	Food and Agriculture Organisation
FC	Financial contribution
FCH	Fuel Cells and Hydrogen JU
FDA	US Food and Drug Administration
FG	Function group
FNIH	Foundation for the National Institutes of Health
FTE	Full time equivalent
FTIH	First time in human
FO	Finance officer
FP	Full proposal
FP7	Seventh Framework Programme
FTE	Full-time equivalent
FWC	Framework contract
GA	Grant Agreement
GABA	Gamma-Aminobutyric acid
GAP	Grant Agreement preparation
GB	Governing Board

Acronym	Meaning
GCP	Good clinical practice
GDPR	General Data Protection Regulation
GPLTR	Generalised partially linear tree-based regression
GWAS	Genome-wide association study
H2020	Horizon 2020
HAP	hospital-acquired pneumonia
HCP	Healthcare practitioners
HLA	Human leukocyte antigen
HSP	Heat shock protein
HTA	Health technology assessment
HTS	High throughput screening
IaaS	Infrastructure as a Service
IAI	Intra-abdominal infections
IAS	Internal Audit Service of the European Commission
iBST	Improper bagging survival tree
ICC	Internal Control Coordinator
ICF	Internal Control Framework
ICFSR	International Conference on Frailty and Sarcopenia Research
ICI	Immune checkpoint inhibitor
ICS	Internal Control Standards
ICT	Information and communication technology
ICU	Intensive care unit
IDF	International Diabetes Federation
IKC	In-kind contribution
IMI1 JU	Innovative Medicines Initiative 1 Joint Undertaking
IMI2 JU	Innovative Medicines Initiative 2 Joint Undertaking
IP	Intellectual property
iPSC	Induced pluripotent stem cell
ISA	Information System for Absences
IT	Information technology
JAMA	Journal of the American Medical Association
JDRF	Juvenile Diabetes Research Funding and Advocacy
JIF	Journal impact factor
JPIAMR	Joint Programming Initiative on Antimicrobial Resistance
JPND	Joint Programme – Neurodegenerative Disease Research
JTI	Joint Technology Initiative
JUs	Joint Undertakings
KMP	Knowledge management platform

Acronym	Meaning
KPI	Key performance indicator
LCI	Lung clearance index
LCS	Longitudinal Cohort Study
LEAP	Longitudinal European Autism Project
LT	Long-term contract
MAPPs	Medicines adaptive pathways to patients
MBW	Multiple breath washout
MCI	Mild cognitive impairment
MDR	Multi-drug resistance
MEP	Member of the European Parliament
MMV	Medicines for Malaria Venture
MoU	Memorandum of Understanding
MRC	Medical Research Council
MRI	Magnetic resonance imaging
MRS	Magnetic resonance spectroscopy
MS	Multiple sclerosis
NAFLD	Non-alcoholic fatty liver disease
NASH	Non-alcoholic steatohepatitis
NCD	Non-communicable disease
NCI	National Cancer Institute
NCP	National Contact Point
ND4BB	New Drugs for Bad Bugs
NGO	Non-governmental organisation
NHK	Nasu-Hakola disease
NIAID	National Institute of Allergy and Infectious Diseases
NIBSC	National Institute for Biological Standards and Control
NICE	National Institute for Health and Care Excellence
NME	New molecular entity
NSCLC	Non-small cell lung cancer
NTM	Non-tubercular mycobacteria
OECD	Organisation for Economic Co-operation and Development
OLAF	European Anti-Fraud Office
PA	Payment appropriations
PA	Physical activity
PAC	Patient Advisory Committee
PBMC	Peripheral blood mononuclear cells
PCR	Polymerase chain reaction
PD	Parkinson’s disease

Acronym	Meaning
PET	Positron emission tomography
PF&S	physical frailty and sarcopaenia
PK/PD	Pharmacokinetic/pharmacodynamic
PLoS	Public Library of Science
PPI	Patient and public involvement
PPL	Priority Pathogens List
PPMI	Parkinson's Progression Markers Initiative
PPP	Public-private partnership
PRRE	Private remove research environment
PRO	Patient reported outcome
pSS	Primary Sjögren’s Syndrome
QC	Quality control
R&D	Research and development
RepER	Representative error rate
ResER	Residual error rate
RIA	Research and Innovation Action
RP	Reporting period
RSV	Respiratory syncytial virus
RVFV	Rift Valley fever
RWD	Real-world data
RWE	Real-world evidence
S&D	Group of the Progressive Alliance of Socialists and Democrats in the European Parliament
SC	Scientific Committee
SC	Short-term contract
SEP	Staff establishment plan
SEP	H2020 IT tool for submission and evaluation of proposals
SFARI	Simons Foundation Autism Research Initiative
SGG	Strategic Governing Group
SME	Small and medium-sized enterprise
SNE	Seconded national expert
SNP	Single nucleotide polymorphisms
SO	Scientific Officer
SOFIA	Submission of Information Application
SOP	Standard operating procedure
SP	Short proposal
SRA	Strategic Research Agenda
SRG	States Representatives Group

Acronym	Meaning
SRR	Strategic Risk Register
ST	Short-term contract
SyGMa	H2020 IT tool for grant management
T1D	Type 1 diabetes
T2D	Type 2 diabetes
TA	Temporary agent
TB	Tuberculosis
TTG	Time to Grant
TTI	Time to inform
TTP	Time to Pay
TTS	Time to sign
UK	United Kingdom
UNEP	United Nations Environment Programme
US	United States
UTI	Urinary tract infections
VAP	Ventilator-associated pneumonia
VTR	View through rate
WHO	World Health Organisation

Annex 13 – Table of IMI projects

(As of 31 December 2018)

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
AIMS-2-TRIALS	Autism Innovative Medicine Studies – 2 – Trials	www.aims-2-trials.eu	autism
AMYPAD	Amyloid imaging to prevent Alzheimer's disease	www.amypad.eu	Alzheimer's disease
BEAT-DKD	Biomarker enterprise to attack DKD	www.beat-dkd.eu	diabetes
BigData@Heart	Big data @ heart	www.bigdata-heart.eu	big data, cardiovascular disease
C4C	conect4children - Collaborative network for European clinical trials for children	conect4children.org	Paediatric clinical trials
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

Project acronym	Full project title	Website	Subject area
EBOMAN	Manufacturing and development for rapid access Ebola vaccine	www.ebovac.org/eboman	Ebola and related diseases
EBOVAC1	Development of a prophylactic Ebola vaccine using an heterologous prime-boost regimen	www.ebovac.org	Ebola and related diseases
EBOVAC2	Development of a prophylactic Ebola vaccine using an heterologous prime-boost regimen: Phase II	www.ebovac2.com	Ebola and related diseases
EBOVAC3	Bringing a prophylactic Ebola vaccine to licensure	no website	Ebola and related diseases
EFOEUPATI	Ensuring the future of EUPATI beyond 2020	www.eupati.eu/efoeupati	education and training
EHDEN	Electronic health data in a European network	www.ehden.eu	big data
EQIPD	European quality in preclinical data	eqipd.org	data quality, neurodegenerative diseases
ESCULAB	European screening centre; unique library for attractive biology	www.europeanleadfactory.eu	drug discovery
eTRANSAFE	Enhancing translational safety assessment through integrative knowledge management	etransafe.eu	safety
FAIRplus	FAIRplus	fairplus-project.eu	knowledge management
FILODIAG	Ultra-fast molecular filovirus diagnostics	www.filodiag.eu	Ebola and related diseases
GETREAL Initiative	The GetReal Initiative	www.imi-getreal.eu/GetReal-Initiative	relative effectiveness
HARMONY	Healthcare alliance for resourceful medicines offensive against neoplasms in hematology	www.harmony-alliance.eu	big data, cancer
HYPO-RESOLVE	Hypoglycaemia - redefining solutions for better lives	hypo-resolve.eu	diabetes
iCONSENSUS	Integrated control and sensing platform for biopharmaceutical cultivation process high-throughput development and production	www.kth.se/dib/iconsensus	Manufacturing technologies
IM2PACT	Investigating mechanisms and models predictive of accessibility of therapeutics (IM2PACT) into the brain	im2pact.org	drug delivery

Project acronym	Full project title	Website	Subject area
IMI-PainCare	Improving the care of patients suffering from acute or chronic pain	www.imi-paincare.eu	pain
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
NECESSITY	New clinical endpoints in primary Sjögren's syndrome: an interventional trial based on stratifying patients	no website	Sjögren's syndrome
NGN-PET	Modelling neuron-glia networks into a drug discovery platform for pain efficacious treatments	ngn-pet.com	pain
PARADIGM	Patients active in research and dialogues for an improved generation of medicines: advancing meaningful patient engagement in the life cycle of medicines for better health outcomes	imi-paradigm.eu	patient involvement in R&D
PERISCOPE	Pertussis correlates of protection Europe	www.periscope-project.eu	vaccines
PEVIA	Pan Ebola vaccine innovative approach	www.pevia-ebola.eu	Ebola and related diseases
PHAGO	Inflammation and AD: modulating microglia function - focussing on TREM2 and CD33	www.phago.eu	Alzheimer's disease

Project acronym	Full project title	Website	Subject area
PIONEER	Prostate cancer diagnosis and treatment enhancement through the power of big data in Europe	prostate-pioneer.eu	big data, cancer
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-AD	Remote assessment of disease and relapse – Alzheimer's disease	www.radar-ad.org	Alzheimer's disease
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
RESOLUTE	Research empowerment on solute carriers	re-solute.eu	drug development
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
VHFMoDRAD	Viral haemorrhagic fever: modern approaches for	no website	Ebola and related diseases

Project acronym	Full project title	Website	Subject area
	developing bedside rapid diagnostics		
VITAL	Vaccines and infectious diseases in the ageing population	no website	vaccines
VSV-EBOPLUS	Systems analysis of adult and pediatric responses to the VSV-ZEBOV Ebola vaccine	vsv-eboplus.eu	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
WEB-RADR 2	WEB-RADR 2	web-radr.eu/web-radr2	pharmacovigilance

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 2018 (Authorising Officer's report) was presented to the IMI2 JU Governing Board at the end of February 2019 and it is planned to have it approved by the Governing Board in June 2019.

The Governing Board is of the opinion that the IMI2 JU AAR 2018 covers well the main activities and achievements of the IMI2 JU in 2018 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 2018 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 2018 together with the draft Budget 2018 was approved by the Governing Board on 15 December 2017 (Decision IMI2-GB-DEC-2017-26), first amended by the Governing Board on 9 March 2018 (Decision IMI2-GB-DEC-2018-08), second amended on 12 June 2018 (Decision IMI2-GB-DEC-2018-15), third amended on 13 July 2018 (Decision IMI2-GB-DEC-2018-23), and last amended by the Governing Board on 5 December 2018 (Decision IMI2-GB-DEC-2018-31).
- In 2018, the JU implemented the final stages of the IMI2 Calls for proposals 12 and 13, initiated under the Horizon 2020 Framework Programme. The JU implemented also the last step for the last cut-off date of Call 8 (of 15 March 2018). The JU launched 3 new Calls under Horizon 2020, IMI2 Calls 14, 15 and 16. Those Calls represent the commitment of: €301,132,862 of EU contribution; €228,428,360 of contribution from EFPIA companies; and €71,339,000 of contribution from Associated Partners to Call 14 (topic 4) and Call 15 (topics 1, 4, 5, 6 and 8). In particular, calls 15 and 16 include several topics for a new programme on antimicrobial resistance ("AMR accelerator") representing €144,730,000 of EU contribution, €71,200,000 of contribution from EFPIA companies, and €67,000,000 of contribution from Associated Partners
- In 2018, the JU signed 20 new grant agreements from IMI2 Calls 8, 10, 11 and 12 initiated under Horizon 2020. As on 31 December 2018, the IMI portfolio of projects represented a total of 59 projects from the first phase of IMI (initiated under Framework Programme 7) of which 16 still running, plus 60 Grant Agreements signed from IMI2 Calls 1 to 12 (initiated under Horizon 2020) of which 54 projects 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 2018, IMI 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 2018. 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 2018, IMI2 projects had led to 5 patent applications and 1 patent award, and IMI1 and IMI2 projects had produced 4 500 publications in peer reviewed journals, around 20 % of which (930) were published in year 2018. The latest biblio-metric analysis demonstrated that the citation impact of papers associated with IMI projects remains stable at 1.98, twice the world average (baseline of 1), and twice the EU's average (0.97). Also, 24.64% of IMI publications are published in top 10 % of publications. This confirms, like for previous year 2017, 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 IMI website.
- In 2018, the JU continued implementing its Action Plan (agreed by Governing Board in November 2017) to address the recommendations from the interim evaluation of IMI2 JU (report published in October 2017: ISBN 978-92-79-69299-4). Notably, the Governing Board formally adopted in 2018 a new set of ten Key Performance Indicators (KPIs). These indicators are based on the RACER principles ("Relevant, Accepted, Credible, Easy, Robust"). Also, IMI2 JU started implementing actions to reinforce the participation of SMEs and of non-pharmaceutical companies.
- In 2018, the IMI2 JU States Representatives Group met 3 times. The IMI2 JU Scientific Committee held 4 meetings and 3 phone conferences. The IMI2 JU Scientific Committee is composed of 11 members, as well as additional experts. In October 2018, 6 members plus one additional expert were renewed, and 5 new members plus one new additional expert were nominated for two years, based on suggestions made by the States Representatives Group. New Chairman and vice-Chairman were subsequently elected. Notably, this Committee prepared two position papers with recommendations, on digital innovation and data integration in the discovery of novel medicines, and on the sustainability of outputs from IMI-funded projects beyond the duration of the funding. The 7 Strategic Governing Groups (in the areas of Immunology; Diabetes and metabolic disorders; Neuro-degeneration; Translational safety; Oncology; Infections control; and Digital health & patient-centric evidence generation) regularly met and held teleconferences, each 2 to 4 times.
- In 2018, communication activities continued 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 addition, IMI2 JU Programme Office ran a multi-channel communication campaign spanning several months, to promote IMI's achievements, to celebrate the 10th anniversary of the very first IMI Call for proposals. The campaign featured two high-level events, which attracted almost 700 attendees, as well as the production of several videos on IMI achievements, and a series of web, press and social media activities.
- Overall, projects were managed well, including ex-ante and ex-post financial and scientific verifications. In 2018, as was expected, IMI2 JU conducted 5 interim reviews of projects from the IMI1 Calls 6, 9 and 11 initiated under Framework Programme 7, and 5 interim reviews of projects from the IMI2 Calls 3, 5 and 6. 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 2017 and below the maxima foreseen for the Horizon 2020 Programme, with 9 days for pre-financings, 59 days for interim payments, and 54 days for final payments. The "Time To Grant" also improved from 2017, and is now below maximum foreseen for the Horizon 2020 Programme.

- For IMI projects (operating under Framework Programme 7), 67.6% of the €965.7 million EU contribution committed in total have been claimed, validated and paid, while 65.6% of the €965.1 million EFPIA contributions committed in total have been reported and validated, as on 31 December 2018. For IMI2 projects (operating under Horizon 2020), 13.5% of the €664.9 million JU contribution already committed have been claimed, validated and paid, while 20.7% of the €655.6 million EFPIA and Associated Partners contributions already committed have been reported and validated, as on 31 December 2018.
- In total 255 ex-post audits of beneficiaries under Framework Programme 7 have been launched since 2011, out of which a total of 237 have been finalised, of which 23 during the year 2018. Twenty-nine ex-post audits of beneficiaries under Horizon 2020 have been launched since 2016, out of which a total of 10 have been finalised in 2018. In 2018, the cumulative residual error rate from the finalised audits was 0.87 % for operational expenditure under Framework Programme 7, and was 0.67 % 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 2018, the declared in-kind contribution of 19 EFPIA companies participating in IMI projects (operating under Framework Programme 7) had been audited ex-post, altogether covering 97% 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 2017. The JU has in particular improved the methodology to estimate the need for fresh credits (C1) at the time of establishing the “Fiche Financière” for the following year.
- In 2018, the Commission Internal Audit Service (IAS) issued a final audit report on "*Coordination with the Common Support Centre and implementation of CSC tools and services in the IMI2 JU*", with three recommendations for improvements (classified as important). IMI2 JU Programme Office prepared an action plan that was approved by the IAS, with five actions, of which four have been implemented in 2018 as acknowledged by the IAS.
- Migration towards the Horizon 2020 IT tools progressed again very significantly, with all projects from calls 1 to 8 having been fully migrated to these IT tools.
- In relation to the use of human resources, the IMI2 JU staff assigned to the activities carried out in 2018 has been used for their intended purpose. On 31 December 2018, 48 of the 56 positions as in the Staff Establishment Plan of the IMI2 JU were occupied. Nine positions were filled during 2018, notably one Seconded National Expert position.

During 2018 the monitoring tools were fully operational and the IMI2 JU AAR 2018 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 2018 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 2018 in a realistic way.

The Governing Board considers that the following aspects require improvements:

- In 2018, the budget execution of commitment appropriations increased to 99.73%, from 97.07% in previous year. The budget execution of payment appropriations was also improved from 71.96% in 2017 to 86.25% in 2018, but doesn’t correspond yet to full execution.
- By the end of 2018, SMEs accounted for 15.6% of all EU funded beneficiaries, receiving 9.45% of the EU funding, as in the first 60 IMI2 JU signed grant agreements. SME participation should be improved, as was recommended in the interim evaluation of the IMI2 JU, to reach the target of 20% of all EU funded participations as identified for IMI2 JU Key Performance Indicator 10.

Assessment

The declaration of the Executive Director and the IMI2 JU AAR 2018 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 2018.

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 2018 of the authorizing officer. This analysis and assessment will be included into the IMI2 JU AAR 2018.

Brussels, on 21 JUIN 2019,

For the Governing Board of the Innovative Medicines Initiative 2 JU

Jean-Christophe Tellier
Chair of the IMI2 JU Governing Board

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